

カルコゲン結合を介して配座制御したロジウム二核錯体の創製と
不斉 C-H 挿入反応への展開

2021 年度

村井 琢哉

目次

略語表

理論の部

総論	1
本論	11
第1章 カルコゲン結合を有するビアリールジカルボン酸、 及びナフトチオフェン型軸性不斉 δ -アミノ酸誘導体の合成と構造解析	11
第1節 先行研究及び筆者の研究方針	11
第2節 カルコゲン元素を有する軸性不斉ビアリールジカルボン酸の合成	15
第3節 カルコゲン元素を有するビアリールジカルボン酸の絶対構造の決定	19
第4節 カルコゲン元素を有するビアリールジカルボン酸の構造解析	21
第5節 ナフトチオフェン型軸性不斉 δ -アミノ酸誘導体の合成	25
第6節 ジペプチド <i>rac</i> - 9 の構造解析	27
第2章 立体選択的な分子内 C-H 挿入反応の開発と天然 γ -ラク톤の不斉合成	31
第1節 先行研究及び筆者の研究方針	31
第2節 軸性不斉 δ -アミノ酸誘導体を配位子とするロジウム二核錯体の合成	33
第3節 立体選択的 Inside 型分子内 C-H 挿入反応の検討	34
第4節 天然 γ -ラク톤の不斉合成	39
第5節 ロジウム二核錯体の構造解析	42
結論	53

実験の部

実験項	59
第1章に関する実験	60
第2章に関する実験	116
引用文献	258
論文目録	265
謝辞	267

略語表

AcOEt	ethyl acetate
Alloc	allyloxycarbonyl
BINOL	1,1'-bi-2-naphthol
Boc	<i>tert</i> -butoxycarbonyl
Bz	benzoyl
CD	circular dichroism
CPME	cyclopentyl methyl ether
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DIPEA	<i>N,N</i> -diisopropylethylamine
DMF	<i>N,N</i> -dimethylformamide
DMSO	dimethyl sulfoxide
DPPA	diphenylphosphoryl azide
EDC	1-(3-dimethylaminopropyl)-3-ethylcarbodiimide
ee	enantiomeric excess
ESI	electrospray ionization
Et	ethyl
FAB	fast atom bombardment
Gly	glycine
HOBt	1-hydroxybenzotriazole
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectrometry
IPA	isopropyl alcohol
IR	infrared
LCMS	liquid chromatograph mass spectrometry
Me	methyl
Ms	methanesulfonyl
NBO	natural bond orbital
NMR	nuclear magnetic resonance
nOe	nuclear Overhauser effect
ORTEP	Oak Ridge Thermal Ellipsoid Plot
<i>p</i> -ABSA	<i>p</i> -acetamidobenzenesulfonyl azide
Ph	phenyl
Py	pyridine
Rh ₂ (esp) ₄	bis[rhodium(α , α , α' , α' -tetramethyl-1,3-benzenedipropionic acid)]
Rh ₂ (<i>R</i> -BPCP) ₄	dirhodium(II) tetrakis[(<i>R</i>)-1-((4-phenyl)phenyl)-2,2-diphenylcyclopropanecarboxylate]
Rh ₂ (<i>R</i> -BTCP) ₄	dirhodium(II) tetrakis[(<i>R</i>)-1-(4-bromophenyl)-2,2-diphenylcyclopropanecarboxylate]

Rh ₂ (5 <i>R</i> -MEPY) ₄	dirhodium(II) tetrakis(methyl 2-pyrrolidone-(5 <i>R</i>)-carboxylate)
Rh ₂ (<i>S</i> -NTTL) ₄	dirhodium(II) tetrakis(<i>N</i> -1,2-naphthoyl-(<i>S</i>)-tert-leucinate)
Rh ₂ (<i>S</i> -PTAD) ₄	dirhodium(II) tetrakis((<i>S</i>)-1-adamantyl- <i>N</i> -phthaloylacetate)
Rh ₂ (<i>S</i> -PTTL) ₄	dirhodium(II) tetrakis(<i>N</i> -phthaloyl-(<i>S</i>)-tert-leucinate)
Rh ₂ (<i>S</i> -TCPTTL) ₄	dirhodium(II) tetrakis(<i>N</i> -tetrachlorophthaloyl-(<i>S</i>)-tert-leucinate]
Rh ₂ (TPA) ₄	dirhodium(II) tetrakis(triphenylacetate)
r.r.	regioisomeric ratio
rt	room temperature
TBAI	tetrabutylammonium iodide
TFA	trifluoroacetic acid
TFAA	trifluoroacetic anhydride
THF	tetrahydrofuran
TLC	thin-layer chromatography
TOF	time of flight
TPCP	triphenylcyclopropane carboxylate
UV/Vis	ultraviolet/visible

理論の部

総論

立体選択的な分子変換を実現する触媒を開発するためには、触媒活性中心近傍に適切な不斉環境を構築することが重要である。しかしながら、その活性中心近傍に自由回転可能な結合が存在する場合には、結合の回転によって多様な配座を与えるため、明確かつ意図した不斉環境を構築することが困難である。

ロジウム二核錯体によって触媒される不斉 C-H 挿入反応は、通常不活性な C-H 結合を切断し、新たな炭素-炭素結合を立体選択的に構築できる強力な有機合成法である。¹ このうち、ロジウムカルボキシレート錯体 ($\text{Rh}_2(\text{OCOR})_4$) は、2つのロジウム原子が4つのカルボキシレートイオンによって架橋された構造を有し、それぞれのロジウム原子が触媒活性中心として作用する。また、かさ高い置換基を有するカルボン酸を配位子とする場合には、配位子同士の立体反発を解消するように置換基の方向性を変えるため、4種類の対称構造を形成することも知られている。² すなわち、 C_1 対称性、 C_2 対称性、 C_4 対称性、及び D_2 対称性を有する立体構造が考えられ、かさ高い置換基の方向性をロジウム中心に対する上側 (up) と下側 (down) とした場合に、Figure 1A のように表現される。このうち、 C_2 対称構造と D_2 対称構造は、双方のロジウム原子周辺に等価な不斉環境を有する対称性の高い立体構造であるため、どちらのロジウム原子上で反応が進行した場合にも等しい不斉誘起が期待できる。

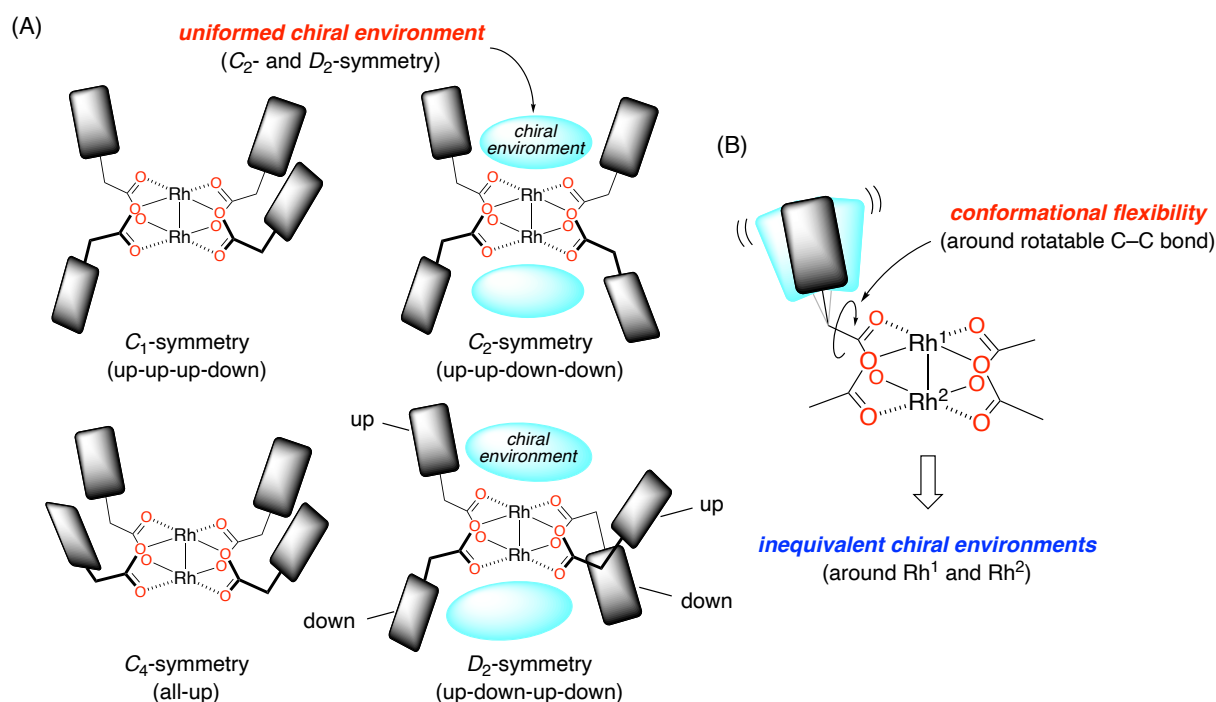


Figure 1. (A) Possible Symmetries Adopted by Dirhodium(II) Tetracarboxylate Complex. (B) Conformational Flexibility of Dirhodium(II) Tetracarboxylate Complex.

しかしながら、本錯体はカルボキシレート部位に自由回転可能な炭素-炭素結合を有するため、その構造制御がしばしば問題となる (Figure 1B)。すなわち、双方のロジウム原子周辺の立体環境が等価な C_2 対称構造や D_2 対称構造であっても、炭素-炭素結合の自由回転によって多様な配座を与える場合には、それぞれのロジウム原子上で進行した反応の生成物の光学純度が異なり、十分な立体制御には至らない。したがって、本触媒系の立体制御には「いかにロジウム中心の上下に等価な不斉環境を構築するか」が重要になるが、カルボキシレート部位のような単結合を介した構造に対する配座制御を全ての配位子に対して行う必要があるため、意図した立体構造の構築は困難であることが予想される。

以上のような背景のもと、様々な不斉触媒の開発が進められ、位置・立体選択的な分子変換が数多く報告されてきた。³ まず、それら既存の不斉触媒のうち、分子全体の立体配座が制御された錯体について紹介する。

(I) $Rh_2(S\text{-TCPTTL})_4$ とその誘導体

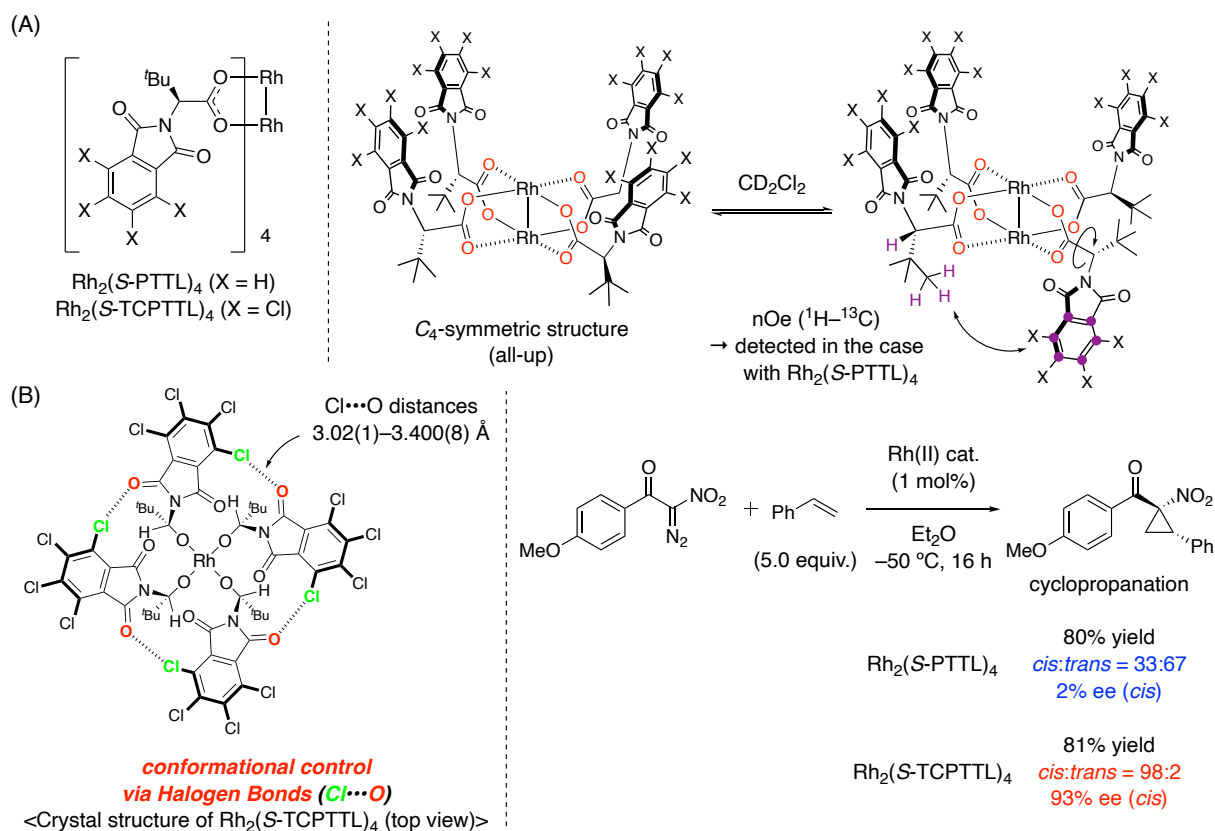
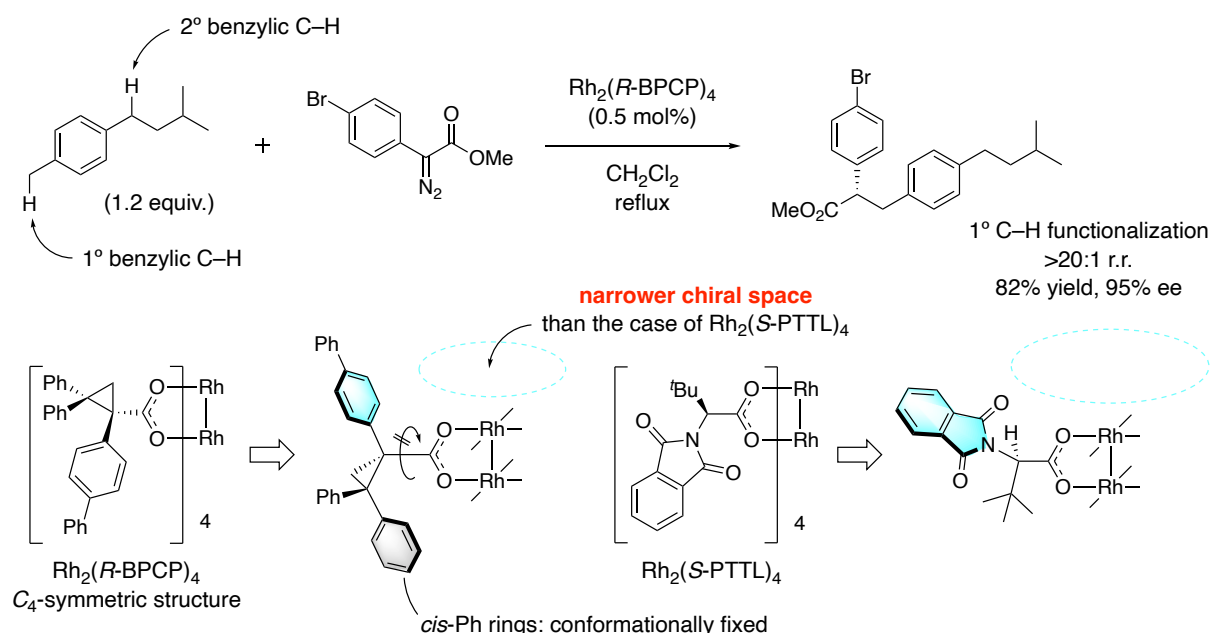


Figure 2. (A) Conformational Flexibility of $Rh_2(S\text{-PTTL})_4$. (B) Conformational Control via Halogen-Bonding Interactions (Cl...O) of $Rh_2(S\text{-TCPTTL})_4$.

橋本らによって報告された $Rh_2(S\text{-PTTL})_4$ ⁴ は、それぞれの配位子のフタルイミド基がロジウム中心に対して全て上側を向いた C_4 対称 (all-up) 構造を形成することが知られている (Figure 2A)。⁵ 本錯体は、双方のロジウム原子周辺の立体環境が非等価な C_4 対称構造であるにも関わらず、かさ高い *tert*-

ブチル基が密集した下側のロジウム原子への基質の接近が妨げられるため、反応場を上側のロジウム原子のみに制限することが可能になる。しかしながら、溶液中では少なくとも1つのフタルイミド基が下側に反転した立体構造もとり得ることが NMR 実験から明らかになったため、⁶ 比較的柔軟な立体構造を有することが示唆されている。一方で、 $\text{Rh}_2(\text{S-PTTL})_4$ のフタルイミド基上の水素原子を全て塩素原子に置換した $\text{Rh}_2(\text{S-TCPTTL})_4$ ⁷ では、溶液中のフタルイミド基の反転が抑制され、より強固な C_4 対称構造を形成することが明らかになった。⁶ この配座制御の主要因は、隣接する配位子間に形成されたハロゲン結合 ($\text{Cl}\cdots\text{O}$)⁸ であることが結晶構造から示唆され、実際に Figure 2B に示すシクロプロパン化反応の立体選択性は大きく改善された。このように、配位子間の非共有結合性相互作用を介して配位子の配座が制御される $\text{Rh}_2(\text{S-TCPTTL})_4$ とその誘導体は、不斉誘起能に優れたロジウム二核錯体として様々な不斉反応に用いられている。⁹

(2) トリフェニルシクロプロパンカルボキシラート (TPCP) 型のロジウム二核錯体

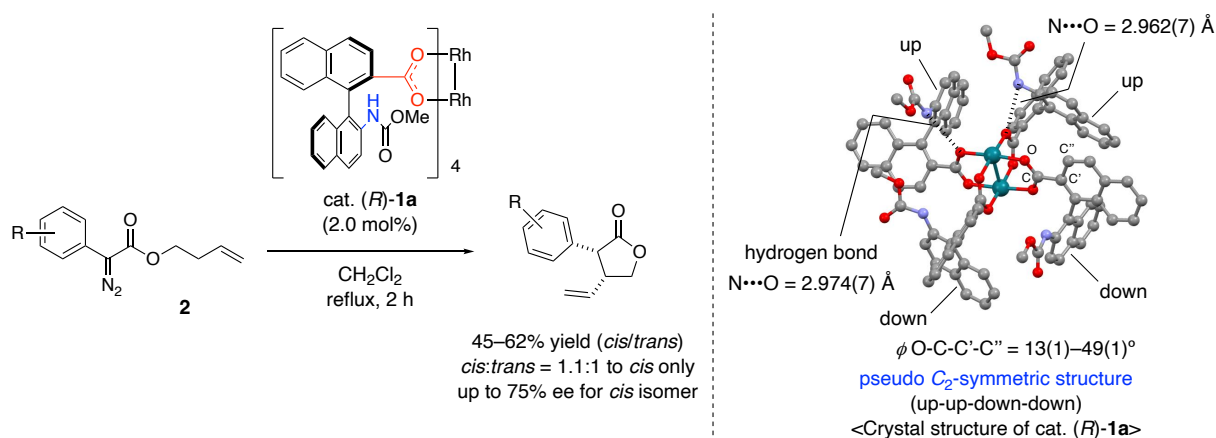


Scheme 1. Catalyst-Controlled Site-Selective C-H Functionalization by TCP-TPC-Type Dirhodium(II) Complex.

近年、Davies らはトリフェニルシクロプロパンカルボキシラート (TPCP) 骨格を有するロジウム二核錯体を用いた脂肪族炭化水素類の位置・立体選択的な分子間 C-H 挿入反応を多く報告している。^{9i,j,10c-f} この触媒制御による分子変換の先駆けとなった $\text{Rh}_2(\text{R-BPCP})_4$ ^{10c} は、ともに電子的に活性化されたベンジル位第1級、第2級 C-H 結合を持つ基質に対して、より立体的に空いている第1級 C-H 結合が位置・立体選択的に官能基化された生成物を与えることが知られている (Scheme 1)。この錯体は、全ての $p\text{-PhC}_6\text{H}_4$ 基がロジウム中心に対して上側を向く C_4 対称構造を有するが、¹¹ 同様に C_4 対称構造を有する $\text{Rh}_2(\text{S-PTTL})_4$ よりもロジウム原子周辺が混み合った立体構造を形成していることが明らかになった。これは、カルボキシ基に対して cis に置換した Ph 基が、互いに立体反発を生じないように配座制御されることに起因しており、その結果としてかさ高い $p\text{-PhC}_6\text{H}_4$ が触媒活性中心を囲ん

だ混み合った立体環境の構築が可能になる。また、カルボキシ基に対して *cis* に置換した 4 つの Ph 基が、下側のロジウム原子を覆うように配置されることで基質の接近を妨げるため、上側のロジウム原子上でのみ反応が進行すると考えられている。このような混み合った立体環境により、電子的に反応性の類似したベンジル位 C-H 結合の中で最も立体的に空いている第 1 級 C-H 結合のみが活性中心に接近でき、選択的な官能基化が可能になった。以上のように、TPCP 骨格を有するロジウム二核錯体は配位子の立体的要因によって配座が制御され、ベンゼン環上の置換基を変えることで様々な対称性に変化することも知られている。¹¹

ここまで説明してきたように、非共有結合性相互作用や立体的要因によって配座制御されたロジウム二核錯体が多く知られているが、筆者は新たなコンセプトによって配座制御されるロジウム二核錯体の創製に取り組んだ。筆者の所属研究室ではこれまでに、カルボキシ基とアニリン性アミノ基を持ち、ビナフチル骨格からなる軸性不斉 δ -アミノ酸の合成を報告している。¹² さらに、この軸性不斉 δ -アミノ酸を配位子とするビアリール型のロジウム二核錯体 **1a** を合成し、この錯体が基質 **2** の分子内 C-H 挿入反応を中程度の立体選択性で触媒することを見出した (Scheme 2)。¹³ X 線結晶構造解析の結果、錯体 **1a** はメチルカルバメート基が置換したナフチル環が、ロジウム中心に対してそれぞれ up-up-down-down に並んだ C_2 対称構造を形成していることが明らかになった。また、カルボキシレート部位の酸素原子とカルバメート基の間に、2 つの分子内水素結合 (O...H-N) を形成していることがわかった (水素結合を形成している酸素-窒素原子間距離: 2.974(7) Å, 2.962(7) Å)。錯体 **1a** は、この分子内水素結合を介して配座制御されていると考えられるが、いずれのカルボキシレート部位の配座制御も不十分であり (カルボキシレート部位の二面角: 13(1)–49(1)°)、それぞれのロジウム原子周辺の立体環境が互いに大きく異なることがわかった。このような非等価な立体環境が中程度の立体選択性にとどまった要因であると考えられ、この配座制御に関する課題を解決する方法について考察した。



Scheme 2. Asymmetric Intramolecular C-H Insertion of **2** Catalyzed by Complex (*R*)-**1a**.

錯体 **1a** の配位子として用いられた芳香族カルボン酸は、芳香環とカルボキシ基が同一平面上に位置することで共役できるため (Figure 3A, $\pi_{C-C} \rightarrow \pi^*_{C-O}$ 相互作用)、本来その錯体では、共役を介したカルボキシラート部位の配座制御が期待できる。実際に、安息香酸を配位子とする $Rh_2(OBz)_4$ では、それぞれのカルボキシ基が共役を介してベンゼン環とほぼ同一平面上に配座制御されることが明らかになっている (二面角: $1.4-6.0^\circ$)。¹⁴ 一方で、ビアリール型の錯体 **1a** では、軸性不斉を付すためにカルボキシ基のオルト位にアリール基を導入する必要があるが、そのアリール基とカルボキシ基の立体反発を避けるように炭素-炭素結合が回転するため、カルボキシラート部位を配座制御できないことが結晶構造から読み取れた (Figure 3B)。¹⁵ このように、芳香族カルボン酸を配位子とするロジウム二核錯体は、構造的特徴である共役系を活かすことでカルボキシラート部位の配座制御を実現する潜在能力を秘めているが、立体障害による影響を受けやすいことが課題であった。

この課題を解決する方法の1つとして、芳香環とカルボキシ基の間に非共有結合性相互作用を導入し、炭素-炭素結合の回転を抑制する方法を考えた (Figure 3C)。この付加的な相互作用を介して芳香環とカルボキシ基を同一平面上に配座制御できれば、立体障害による影響を凌駕したカルボキシラート部位の配座制御が期待できる。筆者は、この非共有結合性相互作用として、カルコゲン元素 (第16族元素) と Lewis 塩基 (酸素や窒素原子など) の間に働く“カルコゲン結合”に着目した。

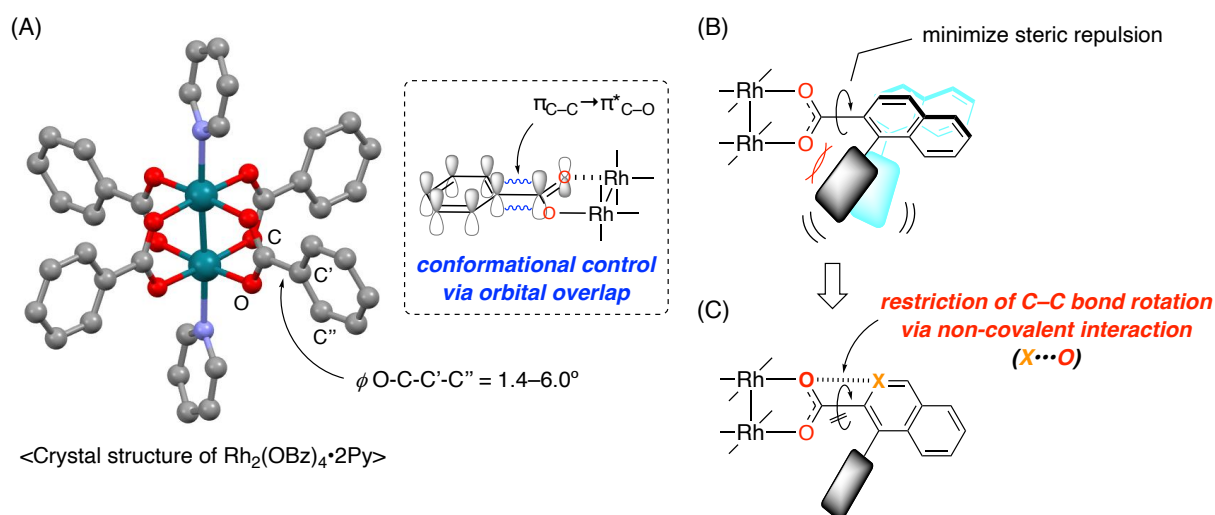


Figure 3. (A) Crystal Structure of $Rh_2(OBz)_4 \cdot 2Py$. (B) Limitation of Conformational Control via Orbital Overlaps for Biaryl-Type Complex. (C) Conformational Control via Additional Non-Covalent Interaction.

医薬品や有機材料の配座固定に寄与する相互作用として認知されてきたカルコゲン結合¹⁶は、近年、分子認識を担う相互作用としても注目が集まっている。¹⁷ カルコゲン結合は、ヘテロ原子 X（酸素や窒素原子など）の非結合性軌道と、Ch-C 結合（Ch：酸素原子を除くカルコゲン原子 S, Se, Te）の反結合性軌道の間に働く $n_X \rightarrow \sigma^*_{Ch-C}$ 軌道相互作用に起因することが知られている。^{16a} また、溶媒に依存せずに水素結合と同等の強さを示し、水素結合よりも方向性に優れた相互作用であることが特徴である。さらには、分散力による寄与も大きく、カルコゲン結合ドナー Ch が高周期元素になるほど相互作用エネルギーが増すことが理論計算により明らかにされている。^{16b} カルコゲン結合は、カルコゲン原子とヘテロ原子とが適切な関係に位置することで分子内にも働き、Ch...X 部分も含めた複素環の大きさによって 1,4 型や 1,5 型のカルコゲン結合に分類される。^{16c} このとき、単結合の自由回転が抑制されることで、その擬似的な複素環に含まれる全ての原子がほぼ同一平面上に位置するように配座制御することも可能である。Figure 4A には、これまでに結晶構造から明らかになった分子内、分子間のカルコゲン結合を示すが、いずれの場合にも相互作用する原子同士の距離がファンデルワールス半径の和よりも短くなっていることが見て取れる。そこで筆者は、カルボキシレート部位の硫黄-酸素原子間に 1,4 型のカルコゲン結合を形成可能な、チオフェン-2-カルボン酸骨格を有する配位子を用いたビアリール型のロジウム二核錯体を設計した (Figure 4B)。本錯体は、1,4 型のカルコゲン結合を介したカルボキシ基の配座制御によって炭素-炭素結合の自由回転が抑制されるため、双方のロジウム原子周辺に等価な立体環境の構築が期待できる。また、触媒活性中心を囲う壁として働くチオフェン環の 3 位のアリール基が錯体の内側に傾いた状態で保持されることで、ロジウム原子周辺が立体的に混み合った明確な不斉空間を構築できると考えられる。

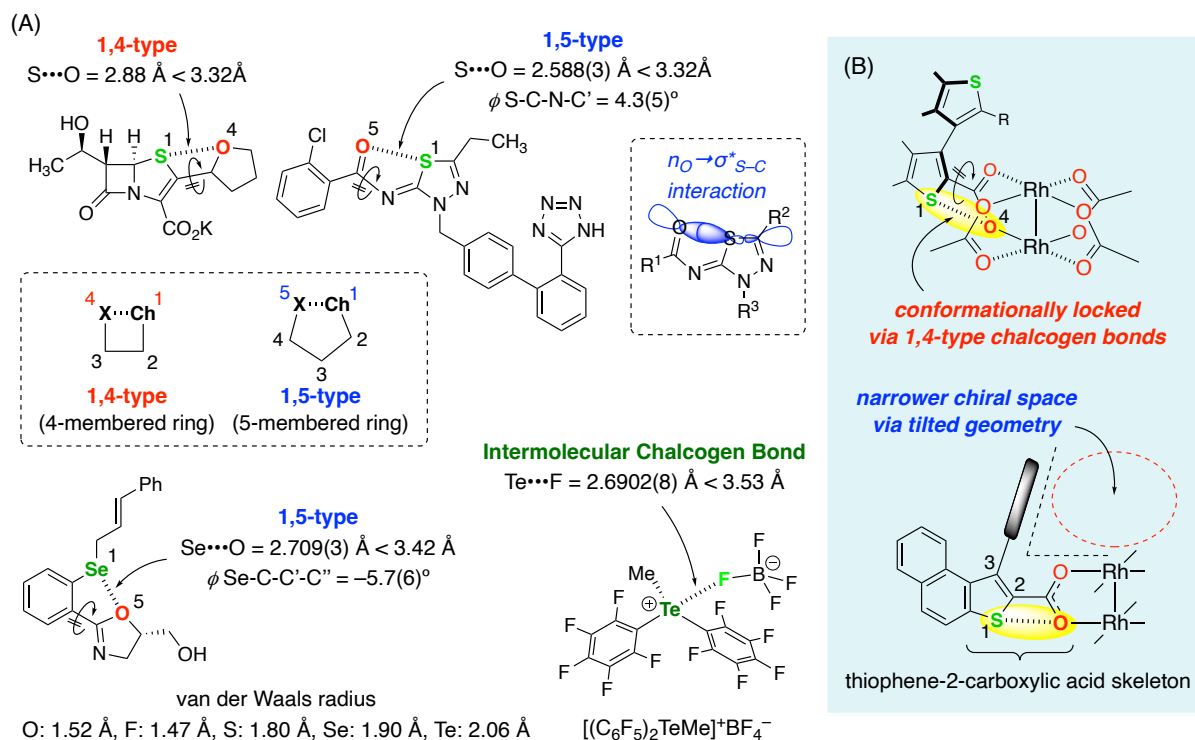


Figure 4. (A) Chalcogen Bonds in Various Compounds. (B) Catalyst Design.

設計したロジウム二核錯体の配位子として想定する軸性不斉 δ -アミノ酸は、光学活性なピアリールジカルボン酸のモノエステル化反応、クルチウス転位等の分子変換によって合成可能である (Figure 5)。^{12b} 一方で、錯体合成の最終段階では、クロロベンゼン (沸点: 132 °C) を溶媒として加熱還流条件下で錯体化を行うため、一連の化合物は容易にラセミ化しない軸性不斉を有する必要がある。したがって、チオフェン-2-カルボン酸骨格を有するピアリールジカルボン酸のうち、ナフトチオフェン型の **3** やベンゾチオフェン型の **4** がその候補として挙げられる。実際に、ベンゾチオフェン型のジカルボン酸 **4** は、ジグリム溶液中、128 °C で観測された光学純度の経時変化に基づいて算出されたラセミ化障壁が 31.1 kcal/mol であり、¹⁸ 室温では容易にラセミ化しないことが明らかになっている。しかしながら、芳香環のサイズが類似した BINOL のラセミ化障壁: 37.8 kcal/mol (ジフェニルエーテル中、220 °C) と比較して不十分な値であるため、¹⁹ ベンゼン環を一枚増やして縮環構造を拡張したナフトチオフェン型のジカルボン酸 **3** を標的化合物とした。

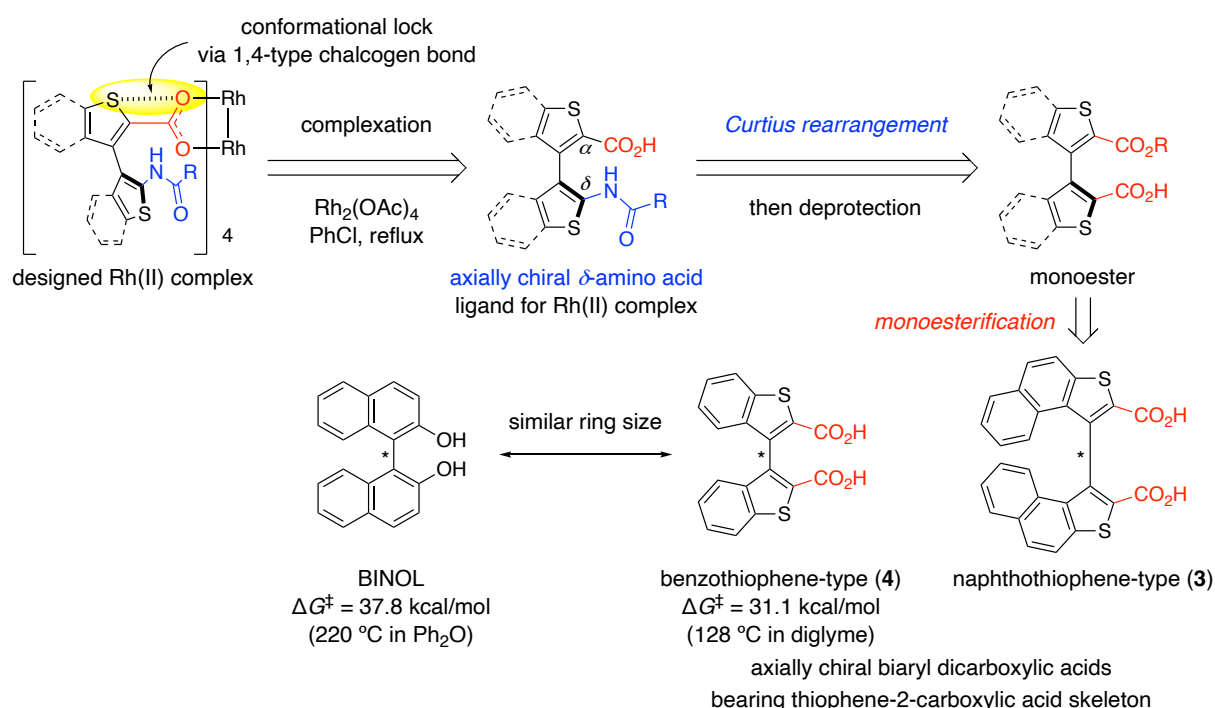
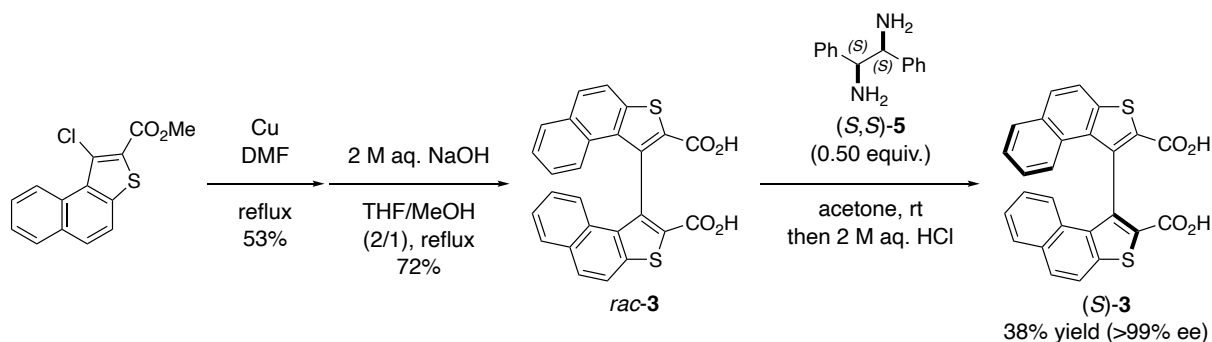


Figure 5. Synthetic Strategy for Conformationally Locked Dirhodium(II) Complex via Chalcogen Bond.



Scheme 3. Synthesis of Axially Chiral Naphthothiophene-Type Biaryl Dicarboxylic Acid (*S*)-**3**.

このような背景のもと、筆者の所属研究室ではナフトチオフエン型のビアリアルジカルボン酸 **3** の合成を、本研究に先駆けて報告した (Scheme 3)。²⁰ また、合成したラセミ体のジカルボン酸 **3** に対して、0.5 当量の (1*S*,2*S*)-ジフェニルエチレンジアミン ((*S,S*)-**5**) を用いたジアステレオマー塩法を行ったところ、99% ee 以上の光学純度で *S* 体のジカルボン酸 **3** を与えることも明らかになった。ラセミ体のジカルボン酸 **3** の X 線結晶構造解析の結果、硫黄-酸素原子間の距離はいずれもファンデルワールス半径の和である 3.32 Å よりも短く (ファンデルワールス半径: S = 1.80 Å, O = 1.52 Å)、硫黄、酸素原子が分子内で 1,4 型のカルコゲン結合を形成可能な距離に位置していることがわかった (Figure 6)。さらに、それぞれのカルボキシ基がナフトチオフエン環とほぼ同一平面上に位置しており、硫黄-酸素原子間に働く 1,4 型のカルコゲン結合がカルボキシ基の配座制御に寄与していることが示唆された。以上の結果から、ナフトチオフエン型の軸性不斉 δ -アミノ酸を配位子とするロジウム二核錯体についても、1,4 型のカルコゲン結合を介したカルボキシラート部位の配座制御が期待されたため、その合成を検討した。

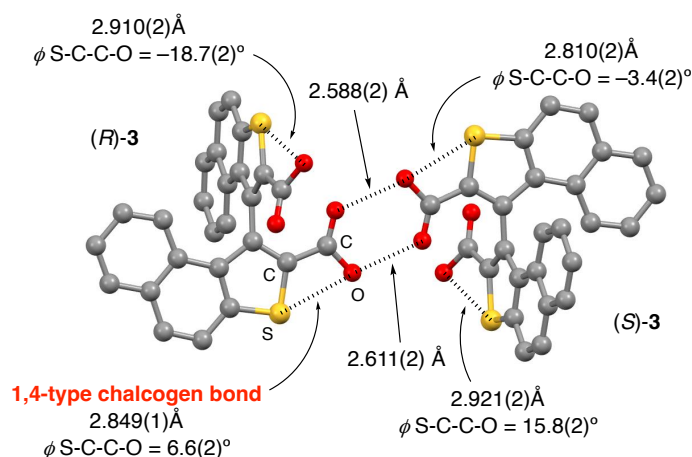


Figure 6. Crystal Structure of Racemic **3**. Hydrogen atoms are omitted for clarity. (*R*)-**3** and (*S*)-**3** were assembled in a 1:1 ratio through the hydrogen bonds between the carboxy groups (O...O distances in the hydrogen bonds: 2.588(2) Å and 2.611(2) Å).

筆者は、本研究においてナフトチオフエン骨格を有するロジウム二核錯体を合成し、その不斉誘起能を分子内 C-H 挿入反応にて評価した。また、合成した錯体、及びその合成中間体に対して X 線結晶構造解析と NBO 解析を行い、硫黄-酸素原子間に働くカルコゲン結合を介した配座制御を評価した。次ページに示す内容について、本論でその詳細を述べる。

(1) カルコゲン元素を有するビアリールジカルボン酸、及びナフトチオフェン型軸性不斉 δ -アミノ酸誘導体の合成と構造解析 (第1章)

まず第1章では、先のナフトチオフェン型のジカルボン酸 **3** の硫黄原子をその他のカルコゲン原子 (酸素、セレン原子) に変えたジカルボン酸 **6** と **7** を合成し、X線結晶構造解析およびNBO解析を行うことで“カルコゲン結合を介したカルボキシ基の配座制御”を評価した (Figure 7)。その結果、ナフトチオフェン型のジカルボン酸 **3**、及びセレン原子を有するナフトセレンフェン型のジカルボン酸 **7** では、1,4型のカルコゲン結合を介してカルボキシ基が芳香環とほぼ同一平面上に配座制御されていることがわかった。一方で、酸素原子を有するナフトフラン型のジカルボン酸 **6** では、予想通り酸素原子同士の間には働くカルコゲン結合は確認されなかったが、炭素-酸素原子間のテトレル結合²¹を介してカルボキシ基が配座制御されていることがNBO解析から確認された。このテトレル結合は硫黄やセレン原子を有するジカルボン酸でも確認され、カルコゲン結合と同じくカルボキシ基の配座制御に寄与する相互作用であることが明らかになった。また、ナフトチオフェン型のジカルボン酸 *rac*-**3** を軸性不斉 δ -アミノ酸 *rac*-**8** に誘導し、*N*-tert-ブトキシカルボニルグリシンと縮合することでジペプチド *rac*-**9** を得た (Scheme 4)。²² このジペプチドの結晶構造からは、エステル部位の1,4型のカルコゲン結合に加えて、アミド部位の1,5型のカルコゲン結合を介して配座制御されていることがわかり、それぞれが明確な立体構造の形成に寄与していることを見出した。

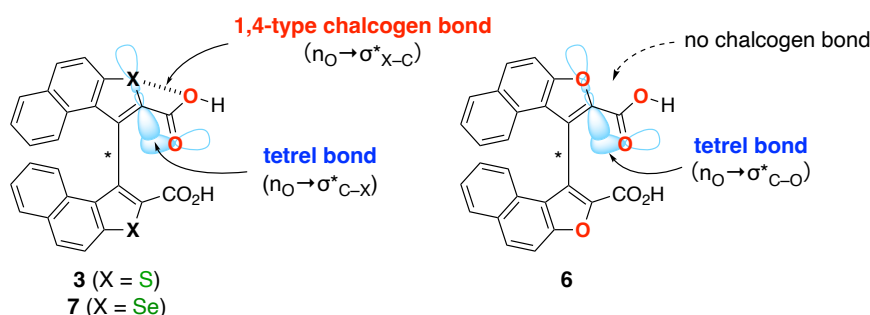
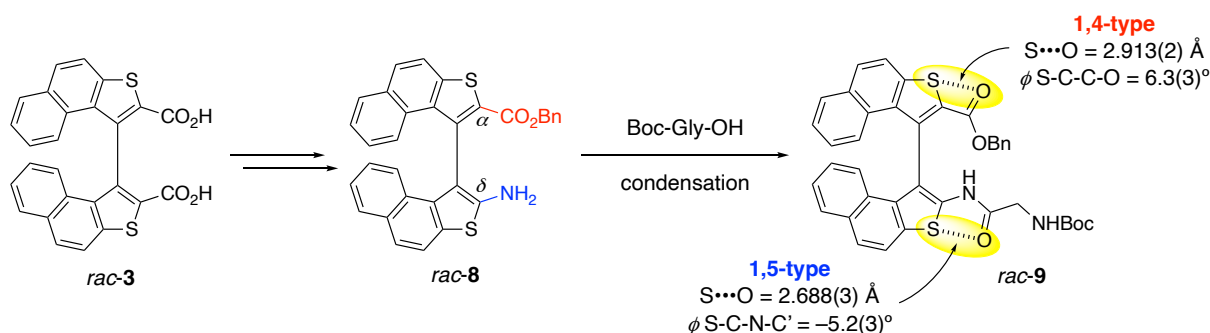


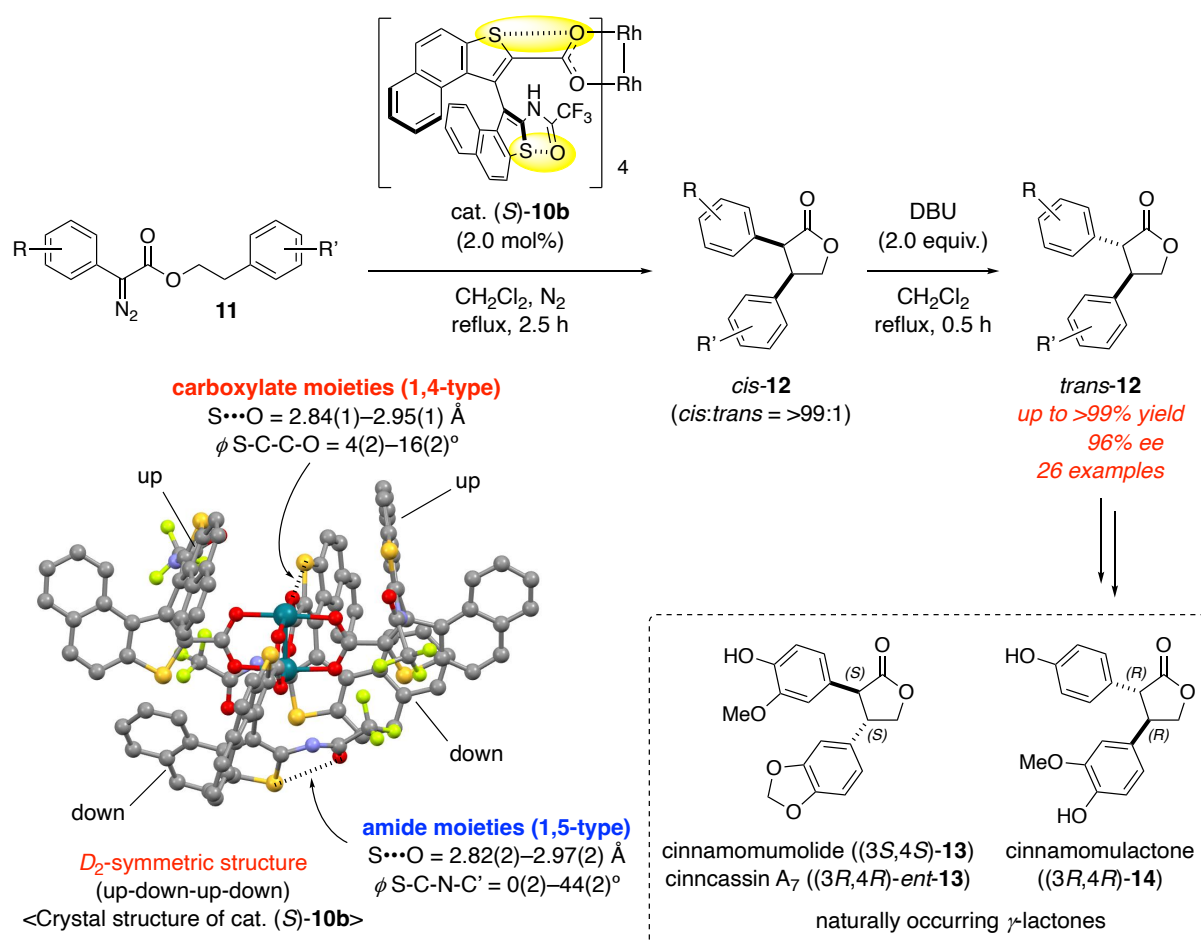
Figure 7. Structural Properties for Axially Chiral Biaryl Dicarboxylic Acids Containing Chalcogen Atoms.



Scheme 4. Transformation to Axially Chiral δ -Amino Acid Derivatives Such as Artificial Peptide *Rac*-**9**.

(2) 立体選択的な分子内 C-H 挿入反応の開発と天然 γ -ラク톤の不斉合成 (第2章)

第2章では、ナフトチオフェン型のロジウム二核錯体 (**(S)-10b**) を合成し、基質 **11** の分子内不斉 C-H 挿入反応を検討した (Scheme 5)。²³ その結果、分子内 C-H 挿入反応ではジアステレオ選択的に *cis*-**12** が得られ、DBU を用いた異性化によって得られる *trans*-**12** の光学純度は最高で 96% ee であった。本触媒系は、様々な置換基を有する α,β -ジアリール γ -ラク톤の立体選択的な合成に用いることができ、cinnanomumolide (**13**)²⁴、cinncassin A₇ (*ent*-**13**)²⁵、及び cinnanomulactone (**14**)²⁶ の不斉合成も達成した。X 線結晶構造解析の結果、錯体 (**(S)-10b**) はトリフルオロアセトアミド基が置換したナフトチオフェン環が、ロジウム中心に対してそれぞれ up-down-up-down に並んだ D_2 対称構造を有することが明らかになった。また、カルボキシレート部位とアミド部位の硫黄-酸素原子間に複数のカルコゲン結合が確認され、縮環構造内に導入した硫黄原子が、実際にカルボキシレート部位の配座制御に寄与していることがわかった。さらに、この構造制御によってロジウム中心の上下に等価な不斉環境が形成されており、カルコゲン結合を介した配座制御が分子内 C-H 挿入反応の立体選択性向上の主要因であることが示唆された。



Scheme 5. Stereoselective Intramolecular C-H Insertion of **11** Catalyzed by Complex **10b** and Asymmetric Syntheses of Naturally Occurring α,β -Diaryl γ -Lactones.

本論

第1章 カルコゲン元素を有するビアリールジカルボン酸、 及びナフトチオフェン型軸性不斉 δ -アミノ酸誘導体の合成と構造解析

第1節 先行研究及び筆者の研究方針

総論で述べたように、筆者は硫黄-酸素原子間の 1,4 型のカルコゲン結合を介してカルボキシレート部位が配座制御されるナフトチオフェン型のロジウム二核錯体を設計した (Figure 4, 5)。また、筆者の所属研究室では、その錯体の合成に必要なビアリールジカルボン酸 *rac*-3 を合成し (Scheme 3)、それぞれのカルボキシ基が芳香環とほぼ同一平面上に配座制御されていることを結晶構造から明らかにした (Figure 6)。²⁰ 結晶構造を精査したところ、硫黄-酸素原子間に働く 1,4 型のカルコゲン結合がカルボキシ基の配座制御に寄与していることが示唆されたため、まずはこの“1,4 型のカルコゲン結合を介した配座制御”を実験的、計算化学的に評価することにした。その際、Smith らが、イソカルコゲノウレア **15-Ch** を用いた触媒系における“1,5 型のカルコゲン結合”を評価した際の方法を参考にした (Figure 8)。^{17f}

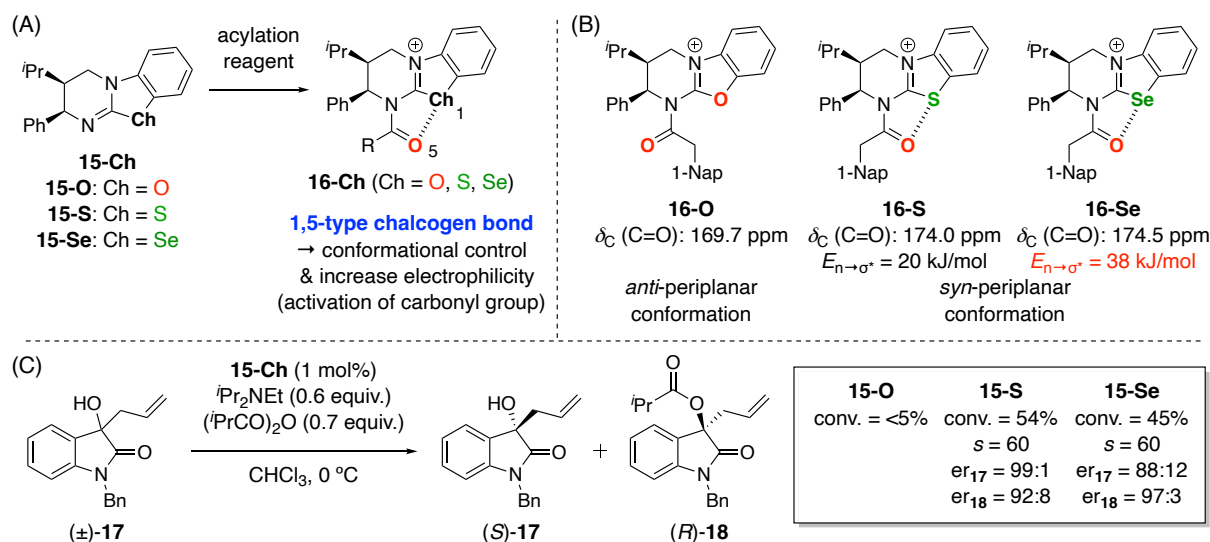


Figure 8. The Importance of 1,5-Type Chalcogen Bonds in Enantioselective Isochalcogenourea Catalysis.

アルコールのエナント選択的なアシル化反応²⁷に頻用されるイソチオウレア **15-S** (Ch = S) は、*N*-アシル化された中間体 **16-S** の構造制御、及び活性化に、硫黄-酸素原子間の 1,5 型のカルコゲン結合が関与していると考えられてきた (Figure 8A)。Smith らは、この 1,5 型のカルコゲン結合の重要性を評価すべく、硫黄原子を酸素やセレン原子に置換したイソカルコゲノウレア **15-Ch** を合成し、*N*-アシル化された中間体 **16-Ch** の X 線結晶構造解析を行った (Figure 8B)。その結果、硫黄やセレン原子を有する中間体 **16-S** と **16-Se** は、カルコゲン原子と酸素原子を近づけるシンペリプラナー

配座を与えたため、1,5 型のカルコゲン結合を形成していることが示唆された。一方で、一般的にカルコゲン結合を形成しない酸素原子を有する中間体 **16-O** は、酸素原子同士を遠ざけるアンチペリプラナー配座を与えることが明らかになった。このように、酸素原子を有する中間体 **16-O** では、酸素原子間に電子反発を生じるために 1,5 型のカルコゲン結合を形成できないことが示唆された。中間体 **16-S** と **16-Se** の結晶構造に基づいた NBO 解析からは $n_O \rightarrow \sigma^*_{Ch-C}$ 軌道相互作用が確認され (Ch = S, Se)、より高周期のセレン原子を有する中間体 **16-Se** では硫黄誘導体 **16-S** よりも強力な相互作用を形成していることが明らかにされている (対応する二次摂動エネルギー $E_{n \rightarrow \sigma^*}$; **16-Se**: 38 kJ/mol > **16-S**: 20 kJ/mol)。また、1,5 型のカルコゲン結合の形成により、形式的に Lewis 酸として働くカルコゲン原子がカルボニル基の電子密度を低下させるため、硫黄、及びセレン誘導体ではカルボニル炭素の ^{13}C NMR シグナルの低磁場シフトも確認された (**16-O**: 169.7 ppm v.s. **16-S**: 174.0 ppm, **16-Se**: 174.5 ppm)。さらに、触媒 **15-Ch** を用いて第 3 級アルコール **17** のアシル化による速度論的光学分割を試みたところ、酸素原子を有する **15-O** では全く反応が進行せず、セレン原子を有する **15-Se** は硫黄誘導体 **15-S** と比べて遜色ない結果を示すことがわかった (Figure 8C)。このとき、*N*-アシル化された中間体においてより強い 1,5 型のカルコゲン結合の形成が示唆されたセレン誘導体 **15-Se** を用いた場合には、硫黄誘導体 **15-S** を用いた場合よりもアシル化の反応速度が大きくなることもわかった。以上のように、Smith らは種々のカルコゲン元素を有する触媒 **15-Ch** を合成し、その *N*-アシル化された中間体 **16-Ch** を実験的、理論的に解析することで、活性中間体の構造制御、及び活性化には 1,5 型のカルコゲン結合が重要であると結論づけた。

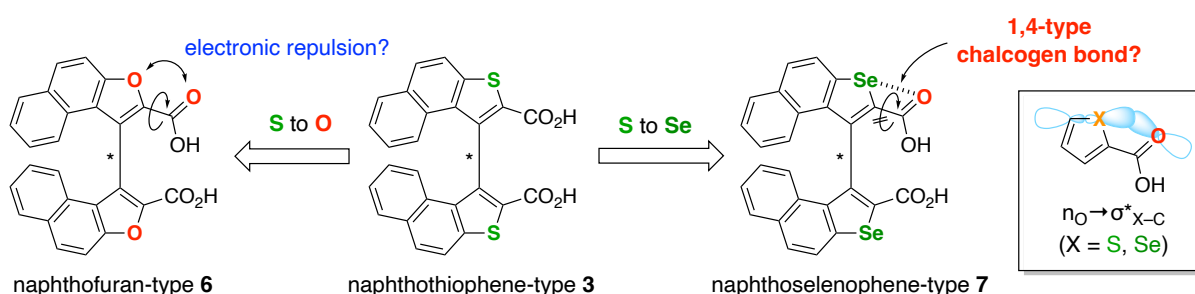


Figure 9. Evaluation of 1,4-Type Chalcogen Bonds in Axially Chiral Biaryl Dicarboxylic Acids Containing Chalcogen Atoms.

そこで筆者は、1,4 型のカルコゲン結合がナフトチオフェン型のジカルボン酸 **3** のカルボキシ基の配座制御に寄与することを実証すべく、硫黄原子を酸素やセレン原子に変えたビアリールジカルボン酸の合成を検討した (Figure 9)。次いで、合成したジカルボン酸について X 線結晶構造解析を行い、ナフトチオフェン型のジカルボン酸 **3** の結晶構造と比較することで“1,4 型のカルコゲン結合を介したカルボキシ基の配座制御”を評価した。このとき、セレン原子を有するナフトセレンフェン型のジカルボン酸 **7** では、ナフトチオフェン型のジカルボン酸 **3** と同様に 1,4 型のカルコゲン結合を介したカルボキシ基の配座制御が期待できる。一方で、酸素原子を有するナフトフラン型のジカルボン酸 **6** では、酸素原子同士の電子反発を避けるようにカルボキシ基がナフトフラン環との同一平面から逸れることが予想される。また、これら一連のジカルボン酸の結晶構造に基づいた NBO 解析を行い、

カルコゲン原子と酸素原子の間に働く $n_O \rightarrow \sigma^*_{Ch-C}$ 軌道相互作用を評価することにした。この解析では、硫黄やセレン原子を有するジカルボン酸の場合に軌道相互作用の形成を確認できると予想されるが、特に、ナフトセレンフェン型のジカルボン酸 **7** では、より高周期のセレン原子を介した強力な軌道相互作用が期待できる。以上のような種々のカルコゲン元素を有するビアリールジカルボン酸を用いた実験的・計算化学的な解析により、ナフトチオフエン型のジカルボン酸 **3** において示唆された“1,4型のカルコゲン結合を介した配座制御”を評価した。これらの詳細について、第2節から第4節で説明する。

さらには、ロジウム二核錯体の合成に向けて、ナフトチオフエン型のジカルボン酸 **3** の軸性不斉 δ -アミノ酸への誘導化を検討した。ところで、ビアリール骨格の 2,2'位にカルボキシ基とアニリン性アミノ基を有する軸性不斉 δ -アミノ酸 (Figure 10A) は、アリール環同士のねじれに基づいた独特な構造を有するため、人工ペプチドなどのキラルビルディングブロックとしての応用が期待されるが、合成については未だ開拓途上の化合物である。²⁸ その数少ない合成例として、筆者の所属研究室ではビナフチル型の軸性不斉 δ -アミノ酸誘導体の合成を報告しているが、^{12,13} N末端に保護基を持たない誘導体は安定性に乏しいことが明らかになっていた。特に、無保護アミノ酸 (S)-**19** は、自発的な環化反応により [5]ヘリセン様化合物 **20** を与えるほど不安定であることも判明している。^{12a} この安定性について下記のように考察した。

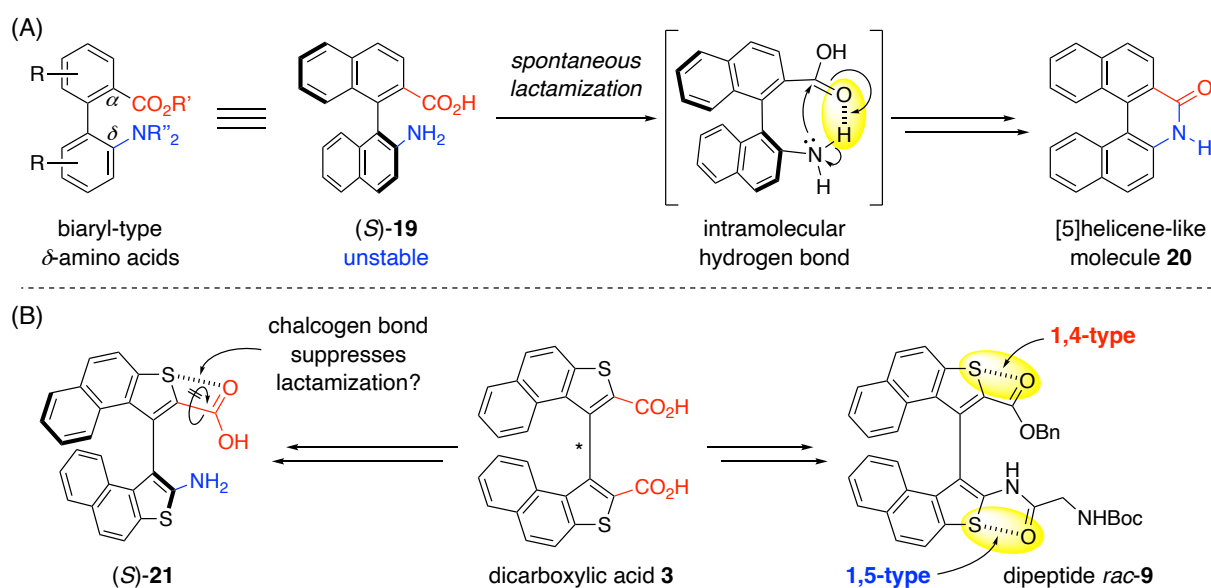
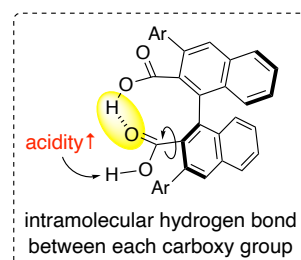


Figure 10. (A) Spontaneous Lactamization of (S)-**19**. (B) Transformation of Dicarboxylic Acid **3** to Axially Chiral δ -Amino Acid Derivatives.

先に丸岡らは、ビナフチル型の軸性不斉ビアリールジカルボン酸について、カルボキシ基同士が分子内水素結合を形成していることを結晶構造から明らかにし、それがカルボキシ基の酸性度の上昇に寄与していることを見出した。²⁹ このような分子内での相互作用は、ナフチル環とカルボキシ基間の炭素-炭素結合が、カルボキシ基間に水素結合を形成す

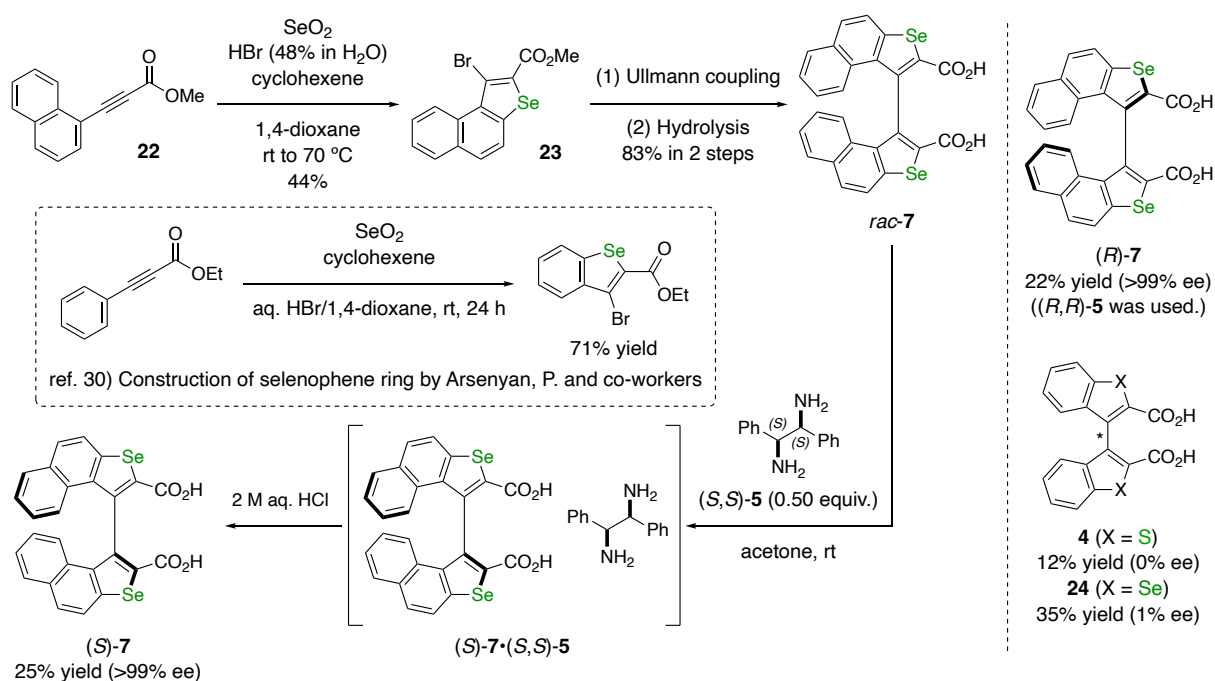


るように回転したことに起因すると考えられる。この知見を考慮して無保護アミノ酸 (**S**)-**19** が環化しやすい要因を考えると、丸岡らの例と同様に、アミノ酸 (**S**)-**19** のカルボキシ基は、炭素-炭素結合が回転するとアミノ基と分子内水素結合を形成可能な距離に位置していることが示唆された。この分子内水素結合を介してカルボキシ基の求電子性、及びアミノ基の求核性が向上した結果、自発的な環化反応が促進されたと考えられる。一方で、ナフトチオフエン型のジカルボン酸 (**S**)-**3** から合成される無保護アミノ酸 (**S**)-**21** では、カルコゲン結合を介してカルボキシ基が芳香環との同一平面上、すなわち水素結合を形成しにくい位置に配座制御されることになるが、この構造をとる場合にはアミノ基との水素結合は形成されず、活性化されないと考えられる。そのため、安定性の向上が期待でき、より安定なキラルビルディングブロックとして利用可能であると考えた (Figure 10B)。

そこで本研究では、ナフトチオフエン型のジカルボン酸 (**S**)-**3** から軸性不斉 δ -アミノ酸誘導体を合成し、ロジウム二核錯体の配位子としてのみならず、キラルビルディングブロックとしての可能性についても評価することにした。まず始めに、筆者はナフトチオフエン型の無保護アミノ酸 (**S**)-**21** やその誘導体の合成を検討し、化合物としての安定性を評価した。その後、キラルビルディングブロックとしての構造展開を目的にジペプチド *rac*-**9** を合成し、その構造的特徴を X 線結晶構造解析および NBO 解析によって明らかにした。これらの詳細について、第 5 節と第 6 節で説明する。

第2節 カルコゲン元素を有する軸性不斉ビアリールジカルボン酸の合成

始めに、種々のカルコゲン元素を有する軸性不斉ビアリールジカルボン酸の合成を検討した。その際、合成したジカルボン酸のロジウム二核錯体への誘導化を見越し、光学活性体として合成することにした。光学活性なビアリールジカルボン酸を合成するためには光学分割法の検討が課題となるが、まずはナフトチオフェン型のジカルボン酸 **3** の光学分割条件を参考にした (Scheme 3)。²⁰ すなわち、先の報告では、ラセミ体のジカルボン酸 **3** に対して 0.5 当量のジアミン (*S,S*)-**5** を用いたジアステレオマー塩法を行ったところ、99% ee 以上の光学純度で *S* 体のジカルボン酸 **3** を与えることが明らかになっていた。そこで、ラセミ体のジカルボン酸の合成が容易なセレン原子を有するナフトセレンフェン型のジカルボン酸 **7** に対し、この光学分割法を試みた (Scheme 6)。



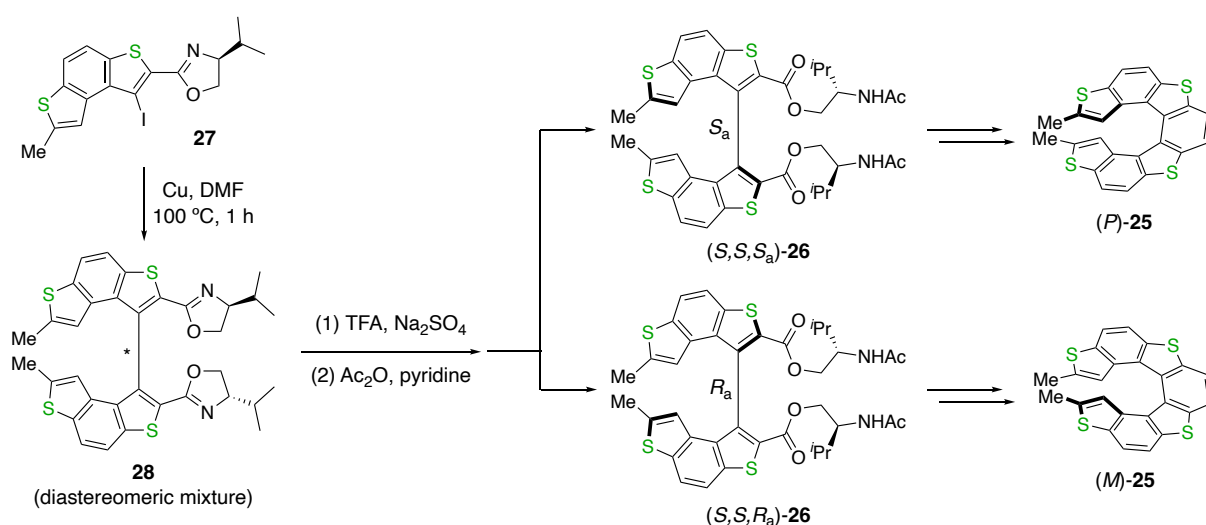
Scheme 6. Syntheses of Axially Chiral Naphthoselenophene-Type Biaryl Dicarboxylic Acids (*S*)-**7** and (*R*)-**7** via Diastereomeric Salt Formation Methods.

まず、Arsenyan らが報告したセレンフェン環の構築法³⁰を参考に、methyl 3-(naphthalen-1-yl)propionate (**22**)³¹ に対して二酸化セレン、臭化水素酸およびシクロヘキセンを作用させたところ、縮環構造内にセレン原子が導入され、ナフトセレンフェン環の2位にエステル基、3位に臭素原子が置換した化合物 **23** を44%の収率で与えた。次いで、化合物 **23** に対してウルマンカップリング及び加水分解を行うことで、所望のジカルボン酸 **7** をラセミ体として合成した (2段階、収率 83%)。このラセミ体のジカルボン酸 **7** に対して、アセトン溶媒中、0.5 当量のジアミン (*S,S*)-**5** を作用させたところ、(*S*)-**7** と (*S,S*)-**5** の塩が析出した。続いて、回収した塩に含まれるジアミンを酸性条件下で除去し、25%の収率でジカルボン酸 (*S*)-**7** を得た。このとき、キラルカラムを用いた HPLC 分析により、その光学純度が 99% ee 以上であることを明らかにした。ここで得られたジカルボン酸の絶対配置は、第3節にて述

べるように、CD スペクトルのコットン効果によって *S* 体であると決定した。また、この光学分割法は、ジアミン (*S,S*)-**5** のエナンチオマーである (*R,R*)-**5** を用いた場合にも同様に進行し、ジカルボン酸 (*R*)-**7** を高い光学純度で与えた (22% 収率、>99% ee)。

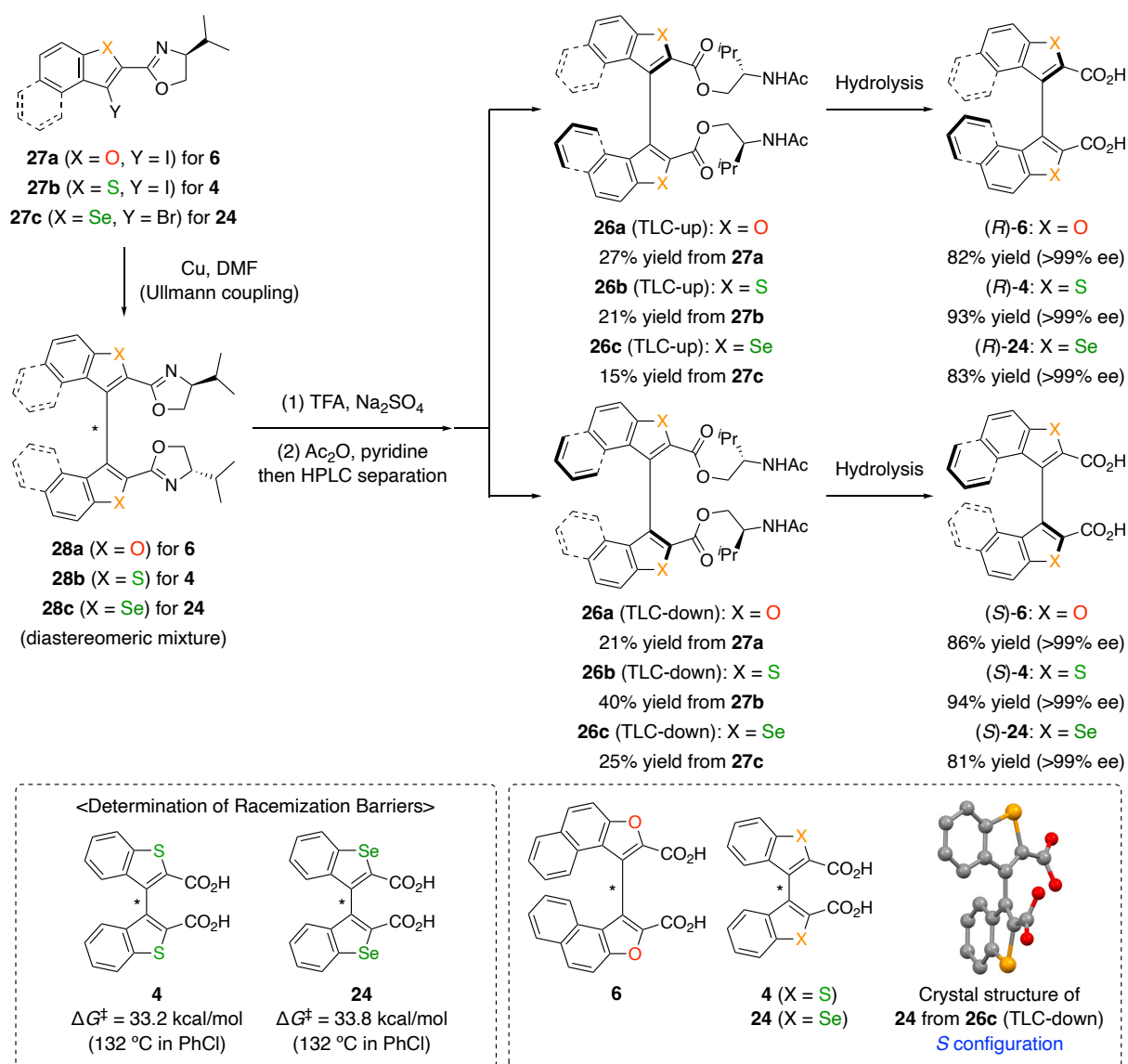
次いで、ラセミ体のジカルボン酸の合成が容易なベンゾチオフェン型のジカルボン酸 *rac*-**4**¹⁸ とベンゾセレンフェン型のジカルボン酸 *rac*-**24**³² に対しても、本法を用いた光学分割を検討した。総論で述べたように、縮環構造のベンゼン環が一枚少ないベンゾチオフェン型のジカルボン酸 **4** は、芳香環のサイズが類似した BINOL と比較してラセミ化障壁が不十分であることが明らかになっている (Figure 5)。^{18,19} ジカルボン酸 **4** の硫黄原子をセレン原子に変換したベンゾセレンフェン型のジカルボン酸 **24** のラセミ化障壁も同様に不十分な値であることが予測されるが、実際にジカルボン酸 **4** 及び **24** のラセミ化障壁を比較することで、カルコゲン元素の変化がラセミ化障壁に与える影響について評価することにした。しかしながら、ラセミ体のジカルボン酸 **4** 及び **24** に対してジアミン (*S,S*)-**5** を用いたジアステレオマー塩法を行った場合には、いずれも光学活性体を得ることができなかった (それぞれ 0% ee、1% ee)。そこで、これらのジカルボン酸 **4** と **24**、及びラセミ体のジカルボン酸の合成に多段階を要するナフトフラン型のジカルボン酸 **6** については、ジアステレオマーとして分離した後にそれぞれのエナンチオマーへと誘導することにした。

先に田中らは、光学活性なヘリセン様化合物 (*P*)-**25** 及び (*M*)-**25** の合成において、縮環構造内に複数の硫黄原子が導入されたビアリール型の化合物 **26** のジアステレオマー混合物を、シリカゲルカラムクロマトグラフィーによってそれぞれのジアステレオマーに分離可能であることを報告している (Scheme 7-1)。³³ この化合物 **26** のジアステレオマー混合物は、L-バリノール由来のオキサゾリン環を不斉補助基として有する化合物 **27** のウルマンカップリングで得られたジアステレオマー混合物 **28** に対し、オキサゾリン環の加水分解および末端のアミノ基のアセチル化を行うことで合成されている。今回は、このジアステレオマーとしての分離法を参考にして、光学活性なナフトフラン型、ベンゾチオフェン型及びベンゾセレンフェン型のビアリールジカルボン酸 **6**、**4** 及び **24** の合成を検討した (Scheme 7-2)。



Scheme 7-1. Previous Work: Syntheses of Optically Active [7]Helicene-Like Molecules (*P*)-**25** and (*M*)-**25**.

まず、L-バリノール由来のオキサゾリン環を不斉補助基として持ち、所望のジカルボン酸に対応する縮環構造を有するカップリング前駆体 **27a-c** を合成し、それぞれに対してウルマンカップリングを行うことで化合物 **28a-c** をジアステレオマーの混合物として得た。このジアステレオマー混合物を化合物 **26a-c** に誘導し、分取 HPLC による分離を試みたところ、いずれも **26a-c** (TLC-up) と **26a-c** (TLC-down) のジアステレオマーに分離することが可能であった。最後に、**26a-c** の各ジアステレオマーをそれぞれ加水分解することでジカルボン酸 **6**、**4** 及び **24** に誘導し、いずれの光学純度も 99% ee 以上であることを HPLC 分析によって確認した。このとき、**26c** (TLC-down) から誘導されるベンゾセレンフェン型のジカルボン酸 **24** は、*S* の絶対配置を有することを X 線結晶構造解析によって明らかにした。また、ジカルボン酸 **6** と **4** については、第 3 節で述べるように、TLC-up のジアステレオマーから得られるエナンチオマーは *R* の絶対配置を、TLC-down のジアステレオマーから得られるエナンチオマーは *S* の絶対配置を有することを CD スペクトルのコットン効果により決定した。



Scheme 7-2. This Work: Syntheses of Optically Active Biaryl Dicarboxylic Acids **6**, **4**, and **24** through the Separation of Diastereomeric Mixtures, and Determination of Racemization Barriers for **4** and **24**.

さらに、合成したベンゾチオフェン型のジカルボン酸 (*S*)-**4**、及びベンゾセレンフェン型のジカルボン酸 (*R*)-**24** を用いてラセミ化障壁の測定を行った。ジカルボン酸 (*S*)-**4** 及び (*R*)-**24** をクロロベンゼン（沸点：132 °C）に溶解させて加熱還流し、観測された光学純度の経時変化に基づいてラセミ化障壁を算出したところ、それぞれ 33.2 kcal/mol、及び 33.8 kcal/mol であることがわかった (Figure S7, S8)。このように、ジカルボン酸 **4** と **24** は室温で容易にラセミ化しないことがわかったが、その値は芳香環のサイズが類似した BINOL（37.8 kcal/mol、ジフェニルエーテル中、220 °C）と比較して不十分であった。また、より高周期のセレン原子を有するベンゾセレンフェン型のジカルボン酸 **24** の方が、硫黄原子を有するベンゾチオフェン型のジカルボン酸 **4** よりラセミ化しにくいことも明らかになった。この要因を探るべく、DFT 計算によってそれぞれのジカルボン酸のラセミ化障壁を算出したところ、ベンゾチオフェン型のジカルボン酸 **4** では実測値に近い値を与えたが (Figure S9、34.2 kcal/mol)、ベンゾセレンフェン型のジカルボン酸 **24** では実測値よりも大きな値となった (Figure S10、37.3 kcal/mol)。そこで、それぞれの遷移状態の構造に対して NBO 解析を行ったところ、ベンゾセレンフェン型のジカルボン酸 **24** ではセレン原子と酸素原子の間に 0.7 kcal/mol 程度のカルコゲン結合 ($n_O \rightarrow \sigma^*_{Se-C}$ 相互作用) を形成していることがわかった (Figure 11、汎関数及び基底関数： ω B97XD/6-311G(d,p))。ベンゾセレンフェン型のジカルボン酸 **24** のラセミ化の遷移状態では、このカルコゲン結合を介してカルボキシ基が芳香環とほぼ同一平面上に配座制御されていると考えられ、ラセミ化の際に芳香環と立体障害を生じるためにラセミ化障壁が高くなったと考えられる。

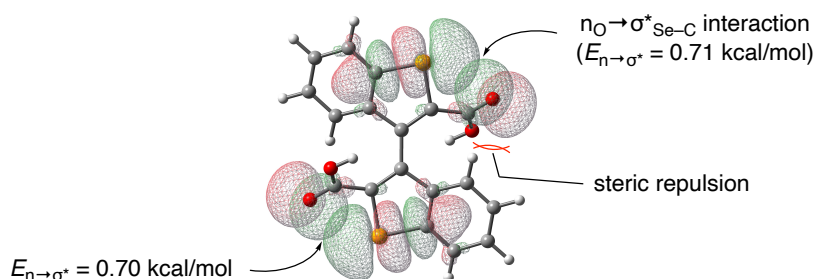


Figure 11. NBO Analysis for the Optimized Structure of the Transition State in Racemization Pathway for Benzoselenophene-Type Biaryl Dicarboxylic Acid **24**. NBO overlaps between the oxygen lone pairs (n_O) and the antibonding orbitals of the C–Se bonds (σ^*_{C-Se}), together with the corresponding second order perturbation energies ($E_{n \rightarrow \sigma^*}$).

第3節 カルコゲン元素を有するビアリールジカルボン酸の絶対構造の決定

先に述べたように、筆者の所属研究室では、ナフトチオフェン型のビアリールジカルボン酸 **3** の絶対構造と CD スペクトルを明らかにしている。²⁰ そのナフトチオフェン型のジカルボン酸 (*R*)-**3** と (*S*)-**3** のアセトニトリル中における CD スペクトル及び UV スペクトルを Figure 12A に示すが、*R* 体は 220 nm から 270 nm の極大吸収波長付近において長波長側から負-正のコットン効果を示し、*S* 体は長波長側から正-負のコットン効果を示すことがわかっている。このジカルボン酸 **3** が示した分裂型のコットン効果は、2つのナフトチオフェン発色団 ($\pi \rightarrow \pi^*$ 遷移) 間の相互作用によって生じていると考えられ、(*R*)-**3** と (*S*)-**3** を構成するナフトチオフェン環が、それぞれ不斉軸に対して負、正にねじれていることを示すものである。このような分裂型のコットン効果は、1,1'-ビナフチル-2,2'-ジカルボン酸 (**29**) をはじめとするビナフチル型の軸性不斉化合物でも観測され、そのコットン効果から絶対配置を決定できることが示されている。³⁴ 同様に、ナフトチオフェン型のジカルボン酸 **3** は CD スペクトルによってその絶対構造を予測できることが明らかになっているため、第2節にて合成した種々のカルコゲン元素を有するビアリールジカルボン酸についても、CD スペクトルを測定することでその絶対構造を推定することにした。

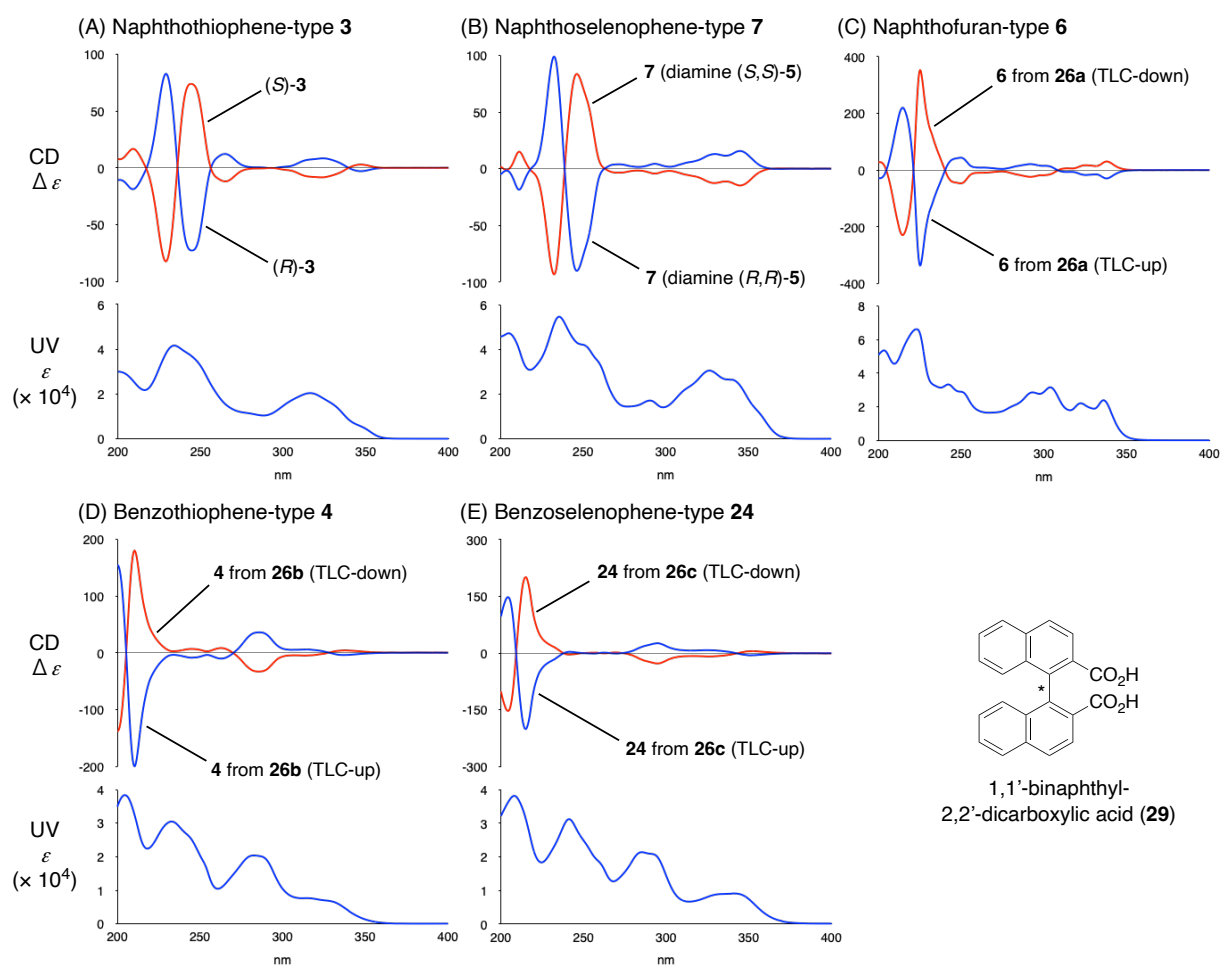


Figure 12. CD and UV Spectra in MeCN for Biaryl Dicarboxylic Acids Containing Chalcogen Atoms.

第2節にて合成したジカルボン酸のアセトニトリル中におけるCDスペクトル及びUVスペクトルをFigure 12B-Eに示す。まず、ジアミン **5** を用いたジアステレオマー塩法によって光学分割したナフトセレンフェン型のジカルボン酸 **7** のCDスペクトルでは、ジアミン (*S,S*)-**5** を用いた際に得られたエナンチオマーは長波長側から正-負のコットン効果を示し、ジアミン (*R,R*)-**5** を用いた際に得られたエナンチオマーは長波長側から負-正のコットン効果を示すことがわかった (Figure 12B)。この結果から、ジアミン (*S,S*)-**5** を用いた際に得られたエナンチオマーは *S* の絶対配置を、ジアミン (*R,R*)-**5** を用いた際に得られたエナンチオマーは *R* の絶対配置を有すると考えられる。また、ジアミン **5** を用いたジアステレオマー塩法で優先的に得られるナフトセレンフェン型のジカルボン酸 **7** の絶対配置は、ナフトチオフェン型のジカルボン酸 **3** の場合と一致していることも明らかになった (Scheme 3)。

一方で、化合物 **26a-c** の各ジアステレオマーから誘導されるジカルボン酸 **6**、**4** 及び **24** のCDスペクトルでは、TLC-up のジアステレオマーから得られるエナンチオマーは長波長側から負-正のコットン効果を示し、TLC-down のジアステレオマーから得られるエナンチオマーは長波長側から正-負のコットン効果を示すことがわかった (Figure 12C-E)。この結果から、TLC-up のジアステレオマーから得られるエナンチオマーは *R* の絶対配置を、TLC-down のジアステレオマーから得られるエナンチオマーは *S* の絶対配置を有すると考えられる。これは、**26c** (TLC-down) から誘導されるベンゾセレンフェン型のジカルボン酸 **24** の結晶構造から明らかにした絶対配置と一致している。以上のように、CDスペクトルからカルコゲン結合を有するビアリアルジカルボン酸の絶対構造を決定した。

第4節 カルコゲン元素を有するビアリールジカルボン酸の構造解析

ここまで種々のカルコゲン元素を有するビアリールジカルボン酸を合成できたので、それぞれの構造を比較すべく、縮環様式が同じナフトチオフェン型、ナフトフラン型、及びナフトセレンフェン型のジカルボン酸 **3**、**6**、**7** に対してX線結晶構造解析を行った (Figure 13)。その結果、いずれのジカルボン酸についても、2つの芳香環が不斉軸に対してほぼ垂直にねじれており (Top view: $\phi a, b, c, d = 81.4(3) - 98.5(8)^\circ$)、ビアリール型アトロプ異性体特有の二面角を有していることがわかった。続いて、それぞれの結晶構造についてカルコゲン-酸素原子間の距離 ($X \cdots O$) およびカルボキシ基の二面角 ($\phi X-C-C-O$, それぞれ $X = O, S, Se$) に着目し、カルコゲン原子と酸素原子の間に1,4型のカルコゲン結合が形成されているかを評価した。

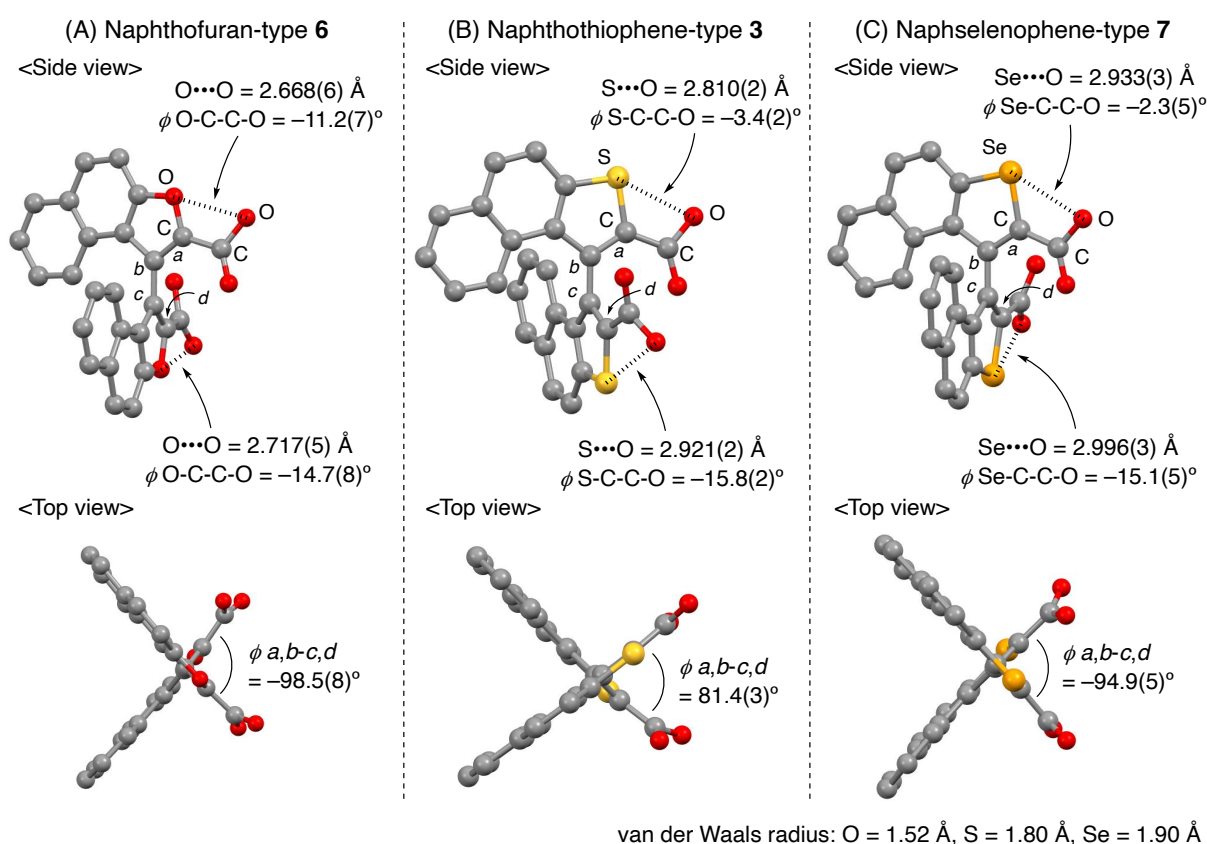


Figure 13. Crystal Structures of Biaryl Dicarboxylic Acids Containing Chalcogen Atoms. (A) (*R*)-**6**. (B) *Rac*-**3** ((*S*)-**3** is shown in the figure). (C) *Rac*-**7** ((*R*)-**7** is shown in the figure). Hydrogen atoms are omitted for clarity.

Figure 13B には、以前報告したナフトチオフェン型のジカルボン酸 **3** の結晶構造を示すが、²⁰ 硫黄-酸素原子間の距離がいずれもファンデルワールス半径の和である 3.32 \AA よりも短く ($S \cdots O = 2.810(2) \text{ \AA}$, $2.921(2) \text{ \AA}$ 、ファンデルワールス半径: $S = 1.80 \text{ \AA}$, $O = 1.52 \text{ \AA}$)、1,4型のカルコゲン結合を形成可能な距離に位置していることがわかる。さらには、それぞれのカルボキシ基が芳香環とほぼ同一平面上に位置しているため ($\phi S-C-C-O = -3.4(2)^\circ$, $15.8(2)^\circ$)、硫黄-酸素原子間に1,4型のカルコゲン結合を形成していることが示唆されていた。また、新たに合成したナフトセレンフェン型のジカル

ボン酸 **7** についても、それぞれのカルボキシ基が芳香環とほぼ同一平面上に位置していることが明らかになった (Figure 13C, $\text{Se}\cdots\text{O} = 2.933(3) \text{ \AA}, 2.996(3) \text{ \AA} < 3.42 \text{ \AA}$, $\phi \text{ Se-C-C-O} = -2.3(5)^\circ, -15.1(5)^\circ$)。このように、より高周期のセレン原子を導入してもカルボキシ基が芳香環とほぼ同一平面上に配座制御されているため、1,4 型のカルコゲン結合の形成を強く示唆する結果となった。一方で、酸素原子を導入したナフトフラン型のジカルボン酸 **6** については、当初、酸素原子間の電子反発を避けるようにカルボキシ基が芳香環との同一平面上から大きく逸れることが予想されたが、意外にも酸素原子間の距離がファンデルワールス半径の和よりも短く、同様に配座制御されていることがわかった (Figure 13A, $\text{O}\cdots\text{O} = 2.668(6) \text{ \AA}, 2.717(5) \text{ \AA} < 3.04 \text{ \AA}$, $\phi \text{ O-C-C-O} = -11.2(7)^\circ, -14.7(8)^\circ$)。そこで、その要因を明らかにするために、これらの結晶構造に基づいた NBO 解析を行った (Figure 14)。

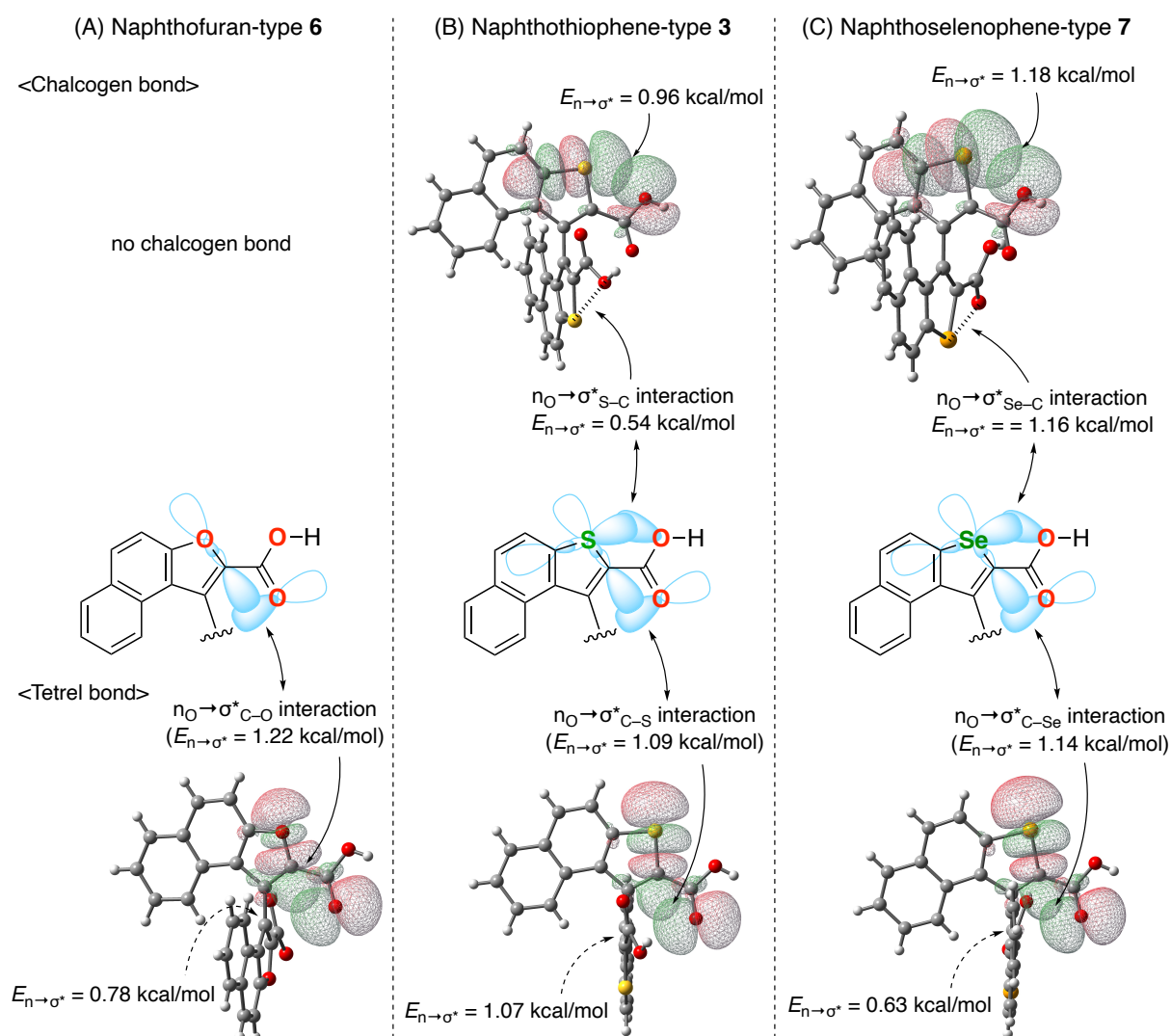


Figure 14. NBO Analyses Based on the Crystal Structures of Biaryl Dicarboxylic Acids Containing Chalcogen Atoms. (A) (*R*)-**6**. (B) *Rac*-**3** ((*S*)-**3** is shown in the figure). (C) *Rac*-**7** ((*R*)-**7** is shown in the figure). NBO overlaps between the oxygen lone pairs (n_{O}) and the antibonding orbitals of the C-X bonds ($\sigma^*_{\text{X-C}}$ and $\sigma^*_{\text{C-X}}$, X = O, S, Se), together with the corresponding second order perturbation energies.

NBO 解析の結果（汎関数及び基底関数： ω B97XD/6-311G(d,p)）、ナフトチオフェン型およびナフトセレンフェン型のジカルボン酸 **3** と **7** では、期待通り硫黄またはセレン原子と酸素原子の間にカルコゲン結合（ $n_O \rightarrow \sigma^*_{X-C}$ 相互作用、 $X = S, Se$ ）を形成していることが確認された（Figure 14B, C）。また、その二次摂動エネルギー $E_{n \rightarrow \sigma^*}$ はそれぞれ 1 kcal/mol 程度であるが、より高周期のセレン原子を介したカルコゲン結合の方が強力な相互作用であることがわかった（S: 0.96, 0.54 kcal/mol < Se: 1.18, 1.16 kcal/mol）。一方で、一般的にはカルコゲン結合を形成しない酸素原子を有するナフトフラン型のジカルボン酸 **6** では、予想通り酸素原子間に軌道相互作用は認められず、カルコゲン結合は確認されなかった（Figure 14A）。しかしながら、興味深いことに、全てのジカルボン酸の炭素－酸素原子間に 1 kcal/mol 程度のテトレル結合（ $n_O \rightarrow \sigma^*_{C-X}$ 相互作用）³⁵ が確認されたため、この相互作用がナフトフラン型のジカルボン酸 **6** のカルボキシ基の配座制御に寄与していると考えられる。このテトレル元素（第 14 族元素：炭素、ケイ素、ゲルマニウムなど）と Lewis 塩基（酸素や窒素原子など）との間に働くテトレル結合は、カルコゲン結合に類似した非共有結合性の相互作用であり、 S_N2 反応の初期段階に形成される相互作用としても知られている相互作用である。^{35c} 以上のように、硫黄やセレン原子を有するジカルボン酸 **3** と **7** では、芳香環とカルボキシ基の間にカルコゲン結合だけでなく、テトレル結合も形成されていることが明らかになった。NBO 解析から示されたように、これらの相互作用はいずれも強力な軌道相互作用ではないものの（1 kcal/mol 程度）、カルボキシ基と芳香環の共役に対して付加的に働くことでカルボキシ基の配座制御に寄与していることがわかった。

さらに、合成したジカルボン酸の重メタノール中における ^{13}C NMR を測定したところ（Figure 15）、縮環構造内に導入されたカルコゲン原子が高周期になるにつれて、カルボニル炭素に対応するシグナルのケミカルシフト値が低磁場シフトすることが明らかになった。このような低磁場シフトは、カルコゲン原子が形式的な Lewis 酸としてカルボニル基の電子密度を低下させることで生じると考えられるため、硫黄やセレン原子を有するジカルボン酸 **3** と **7** において 1,4 型のカルコゲン結合が形成されていることを示す結果であると考察した。

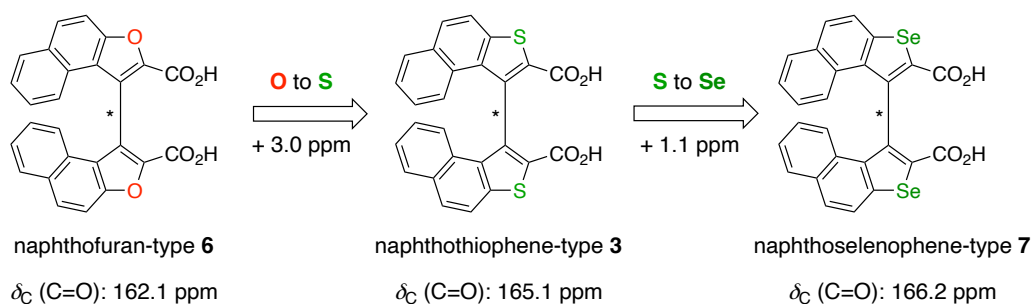
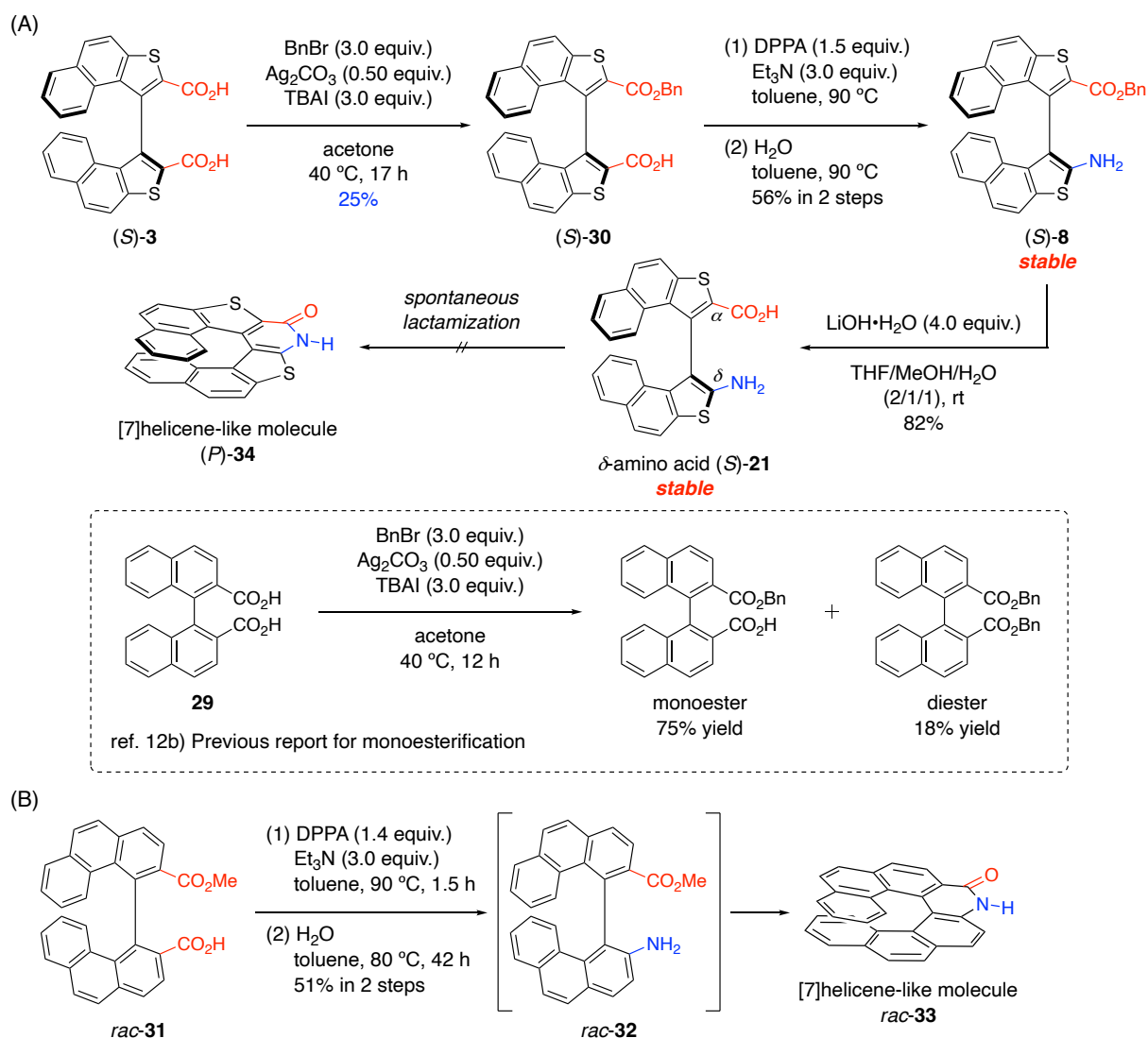


Figure 15. Chemical Shift Values for Carbonyl Carbons of Biaryl Dicarboxylic Acids Containing Chalcogen Atoms in ^{13}C NMR Signals (CD_3OD).

以上のように、筆者は種々のカルコゲン元素を有するビアリールジカルボン酸を合成し、X線結晶構造解析およびNBO解析を行うことで、ナフトチオフェン型のジカルボン酸 **3** のカルボキシ基の配座制御に1,4型のカルコゲン結合が寄与することを明らかにした。また、炭素原子を介したテトレル結合の形成も確認し、カルコゲン結合と共に共役系に対して付加的に作用することでカルボキシ基の配座制御に関与していることを見出した。このテトレル結合を介した配座制御は、通常はカルコゲン結合を形成しない酸素原子を導入したナフトフラン型のジカルボン酸 **6** のカルボキシ基の配座制御に重要な役割を果たしていることもわかった。第5節では、この1,4型のカルコゲン結合を介してカルボキシラート部位が配座制御されるロジウム二核錯体の創製に向けて、ナフトチオフェン型のジカルボン酸 **3** の軸性不斉 δ -アミノ酸への誘導化を検討した。

第5節 ナフトチオフェン型軸性不斉 δ -アミノ酸誘導体の合成

ナフトチオフェン型のジカルボン酸 (**S**)-**3** を原料として、軸性不斉 δ -アミノ酸 (**S**)-**21** の合成を検討した (Scheme 8A)。まず、筆者の所属研究室で開発したビアリールジカルボン酸の選択的モノエステル化条件に従い、^{12b} 炭酸銀、及び臭化ベンジルを用いてジカルボン酸 (**S**)-**3** のモノベンジルエステル化反応を行った。以前の報告では、ビナフチル型のジカルボン酸 **29** に対して本反応を行った場合には、75%の収率でモノベンジルエステル体を与え、過剰なエステル化が進行したジエステル生成は少量にとどまることが明らかになっていた。しかしながら、本反応をナフトチオフェン型のジカルボン酸 (**S**)-**3** に適用したところ、モノベンジルエステル (**S**)-**30** は 25%と低収率にとどまり、効率的にモノエステル化することはできなかった。このとき、同程度のジエステルの生成が確認され、さらには原料 (**S**)-**3** も多く残存しており、従来の反応系に比べて精製が困難であることも課題であった。このように、縮環構造内に硫黄原子を導入したために、ジカルボン酸 (**S**)-**3** は従来のビアリールジカルボン酸とは異なる反応性を示すことがわかった。

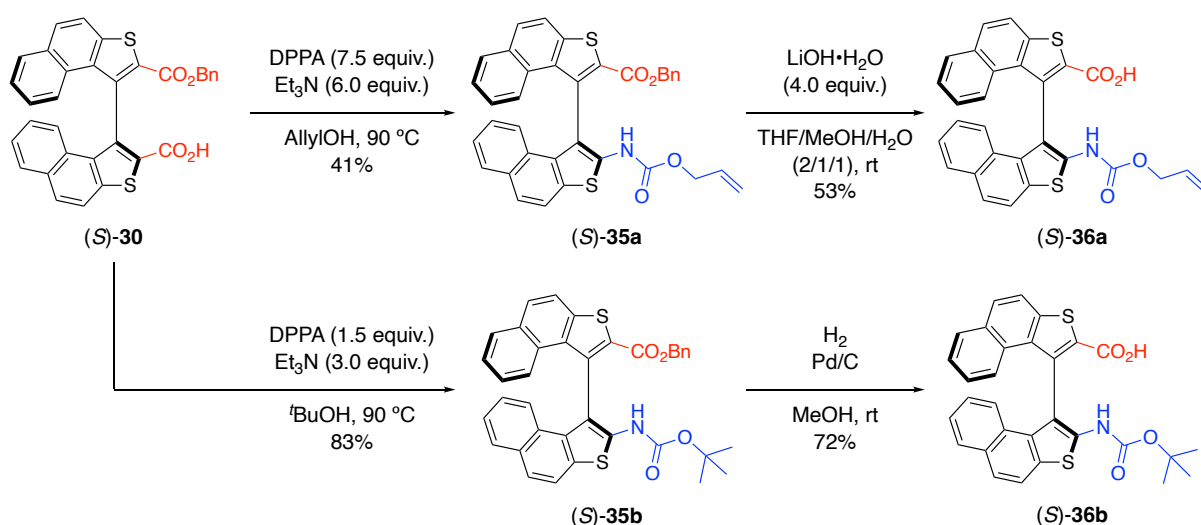


Scheme 8. (A) Synthesis of Axially Chiral δ -Amino Acid (**S**)-**21**. (B) Intramolecular Amidation of Racemic **31**.

次いで、モノベンジルエステル (**S**)-**30** に対してジフェニルホスホリルアジド (DPPA) を用いたクルチウス転位を行い、系中で生じたイソシアナートを加水分解することで、軸性不斉 δ -アミノ酸 (**S**)-**21** の C 末端がベンジル保護された化合物 (**S**)-**8** を得た。このとき、クルチウス転位段階ではラセミ化しないことを HPLC 分析によって確認し、化合物 (**S**)-**8** は、トルエン溶媒中、100 °C で 12 時間加熱した際にもラセミ化せずに安定に存在することを確認した。ところで、類似化合物の安定性に関して、筆者の所属研究室では、フェナントレン型のモノメチルエステル体 *rac*-**31** を同様のクルチウス転位・加水分解条件下、長時間加熱すると、系中で生じた化合物 *rac*-**32** が分子内で環化して [7]ヘリセン様化合物 *rac*-**33** を与えることを明らかにしている (Scheme 8B)。³⁶ 一方で、化合物 (**S**)-**8** は、縮環構造のサイズが類似しているにも関わらず、長時間加熱しても分子内環化反応は進行せず、[7]ヘリセン様化合物 (**P**)-**34**³² をほとんど与えなかった。

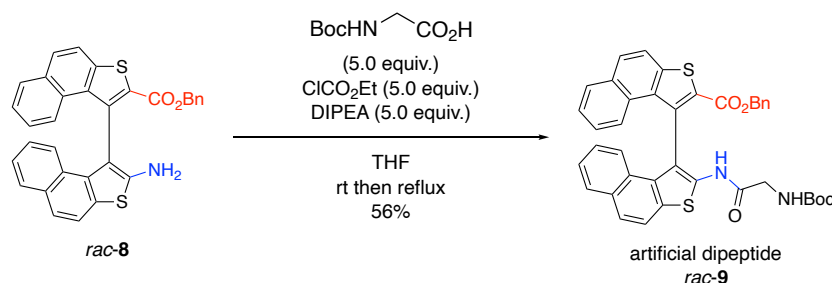
最後に、化合物 (**S**)-**8** に対して加水分解を行うことでベンジル基を脱保護し、ナフトチオフェン型の軸性不斉 δ -アミノ酸 (**S**)-**21** を得た。ビナフチル型の無保護アミノ酸 (**S**)-**19** は自発的な環化反応によって [5]ヘリセン様化合物 **20** を与える性質があるが (Figure 10)、対照的に、この無保護アミノ酸 (**S**)-**21** は [7]ヘリセン様化合物 (**P**)-**34** を与えず、少なくとも 1 ヶ月は冷蔵庫 (4 °C) で保管可能であることがわかった。この安定性の要因の 1 つとして、ナフトチオフェン型のジカルボン酸 **3** の結晶構造から判明したように、硫黄-酸素原子間の 1,4 型のカルコゲン結合を介してカルボキシ基がナフトチオフェン環とほぼ同一平面上に配座制御されていることが挙げられる。すなわち、このカルコゲン結合を介した配座制御のために、カルボキシ基はアニリン性アミノ基との間に分子内水素結合を形成しにくく、自発的な分子内環化反応が進行しなかったと考えられる。

さらには、アミノ基を保護したナフトチオフェン型の軸性不斉 δ -アミノ酸誘導体の合成も試みた (Scheme 9)。モノベンジルエステル (**S**)-**30** に対し、アリルアルコールまたは *tert*-ブチルアルコールを溶媒としてクルチウス転位を行ったところ、それぞれ *N*-Alloc 体 (**S**)-**35a** 及び *N*-Boc 体 (**S**)-**35b** をラセミ化することなく与えた。次いで、加水分解条件もしくは接触還元条件に付すことでベンジル基の脱保護を行い、*N* 保護軸性不斉 δ -アミノ酸 (**S**)-**36a** と (**S**)-**36b** を得た。以上のように合成したナフトチオフェン型の軸性不斉 δ -アミノ酸誘導体は、いずれも安定なアミノ酸として存在できることが判明したため、キラルビルディングブロックとした構造展開を目的にジペプチド *rac*-**9** の合成を行った。



Scheme 9. Transformation to *N*-Protected Axially Chiral δ -Amino Acids **36**.

Scheme 10 に示すように、ラセミ体の δ -アミノ酸 *rac-8* に対し、クロロギ酸エチルを用いて *N*-tert-ブトキシカルボニルグリシンとの縮合反応を試みたところ、中程度の収率でジペプチド *rac-9* を与えた。第6節では、このジペプチド *rac-9* の構造的特徴を、X 線結晶構造解析およびNBO 解析によって明らかにした。



Scheme 10. Synthesis of Artificial Peptide *Rac-9*.

第6節 ジペプチド *rac-9* の構造解析

ジペプチド *rac-9* の X 線結晶構造解析の結果、グリシン残基の N-H 基およびカルボニル酸素間の水素結合を介して、*R* 体と *S* 体のジペプチド **9** が1対1で会合していることがわかった (Figure 16A、水素結合を形成している窒素-酸素原子間距離 : 2.934(3) Å)。このうち、*S* 体のジペプチドの構造を精査したところ、硫黄-酸素原子間の距離が、エステル部位では 2.913(2) Å、アミド部位では 2.688(3) Å であることがわかった (Figure 16B)。ナフトチオフェン型のジカルボン酸 **3** の場合と同様に、これらの距離はいずれも硫黄原子と酸素原子のファンデルワールス半径の和である 3.32 Å よりも短く、エステル部位では 1,4 型の、アミド部位では 1,5 型のカルコゲン結合を形成可能な距離に位置していた。また、ナフトチオフェン環とエステル基、及びアミド基の二面角は、それぞれ 6.3(3)° (エステル部位) と -5.2(3)° (アミド部位) であるため、これらの官能基がカルコゲン結合を介して芳香環とほぼ同一平面上に配座制御されていることがわかった。この配座制御の結果、エステル部位では2結合 (C-C' 結合、C'-O' 結合) を、アミド部位では3結合 (C''-N 結合、N-C''' 結合、C'''-C'''' 結合) を介しても、それぞれの原子がナフトチオフェン環とほぼ同一平面上に位置していることも明らかになった (Figure 16C)。特にアミド部位では、1,5 型のカルコゲン結合を介して擬似的な複素5員環が形成されることで、ナフトチオフェン環の共役系が拡張したような大きな平面構造を形成していた。さらに、2つのナフトチオフェン環が不斉軸まわりにほぼ直交しており (二面角 : 88.3(3)°)、エステル基とアミド基が互いに直行した位置関係にあることが明らかになった。以上のように、1,4 型のカルコゲン結合を介して芳香環とほぼ同一平面上に配座制御されたエステル基は、アミド基から十分に遠ざかることで官能基間に相互作用を形成しないことがわかった。この立体構造は、ナフトチオフェン型の軸性不斉 δ -アミノ酸 (*S*)-**21** において、分子内の官能基間で水素結合を形成しないことがその安定性の要因と考える推測を裏付けるものである。

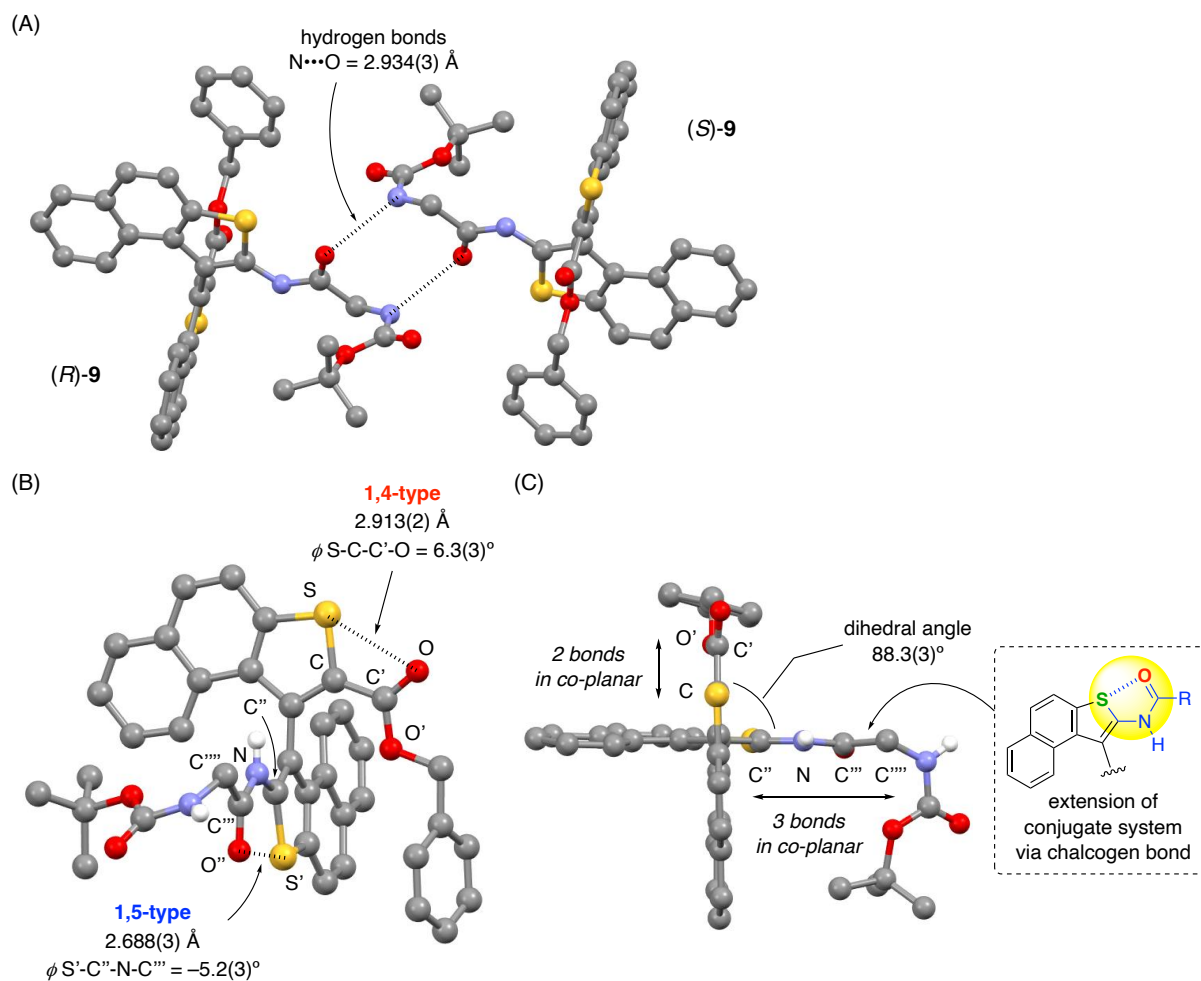
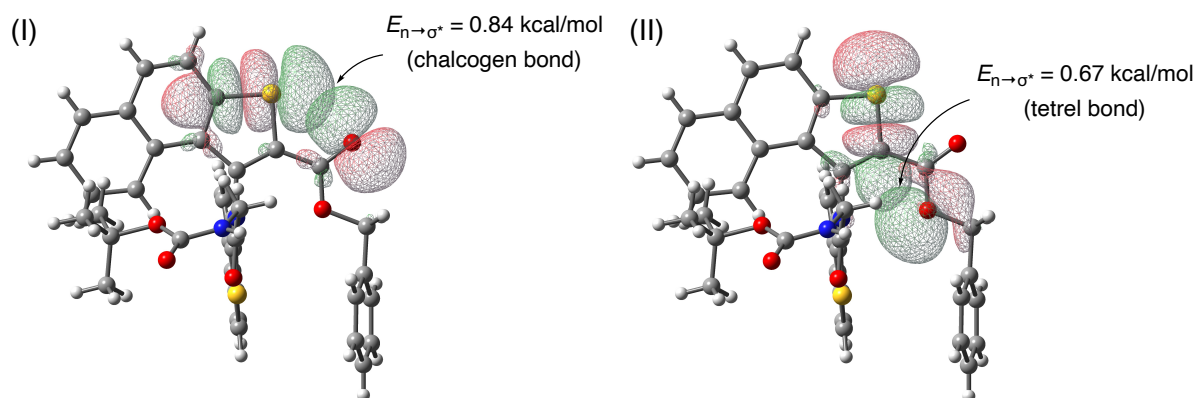


Figure 16. Crystal Structure of Dipeptide *Rac-9*. (A) Packing structure of *Rac-9*. Side view (B) and top view (C) of (*S*)-**9** in the crystal structure of *rac-9* are shown. Hydrogen atoms are omitted for clarity except for the ones of N-H groups for (B) and (C).

最後に、ジペプチド *rac-9* の結晶構造に基づいて NBO 解析を行った (Figure 17、汎関数及び基底関数: $\omega\text{B97XD}/6\text{-}311\text{G(d,p)}$)。その結果、1,4 型のカルコゲン結合が示唆されたエステル部位では、ナフトチオフェン環とエステル基の間に、カルコゲン結合 (Figure 17A-I) と同時にテトレル結合 (Figure 17A-II) も確認され (それぞれの二次摂動エネルギー: $E_{n \rightarrow \sigma^*} = 0.84 \text{ kcal/mol}$, 0.67 kcal/mol)、ジカルボン酸 **3** で確認された相互作用と同程度の強さを示すことがわかった。また、アミド部位では、酸素原子の非結合性軌道 n_O の広がりの違いに起因する 2 種類の軌道相互作用が確認された (Figure 17B)。すなわち、カルボニル基の左右に広がる n_O 軌道と $\sigma^*_{\text{S-C}}$ 軌道の間に 3.06 kcal/mol の (Figure 17B-I)、カルボニル酸素上に球状に広がる n_O 軌道と $\sigma^*_{\text{S-C}}$ 軌道の間に 1.05 kcal/mol の 1,5 型のカルコゲン結合が見られた (Figure 17B-II)。これらを足し合わせると、 4.11 kcal/mol と顕著な軌道相互作用となり、エステル部位に形成された 1,4 型のカルコゲン結合よりも強力な相互作用であることがわかった。結晶構造からは、アミド部位の硫黄-酸素原子間の距離はエステル部位よりも短いことが明らかになっているため (Figure 16B, $\text{S} \cdots \text{O} = 2.688(3) \text{ \AA} < 2.913(2) \text{ \AA}$)、より軌道の重なりが大きく、このような強力な相互作用を形成できたと考えられる。さらに、アミド部位では、N-H 結合の結合性軌道 $\sigma_{\text{N-H}}$ と

C-S 結合の反結合性軌道 σ^*_{C-S} の間に強力な軌道相互作用が形成されていることもわかった (Figure 17B-III、 $E_{\sigma \rightarrow \sigma^*} = 4.77$ kcal/mol)。これらの相互作用が協同的に働くことで、ジペプチド *rac-9* のアミド部位では、自由回転可能な単結合を2つ挟んでいるにもかかわらず、アミド基を芳香環とほぼ同一平面上に配座制御できたと考えられる。

(A) Ester moiety (1,4-type)



(B) Amide moiety (1,5-type)

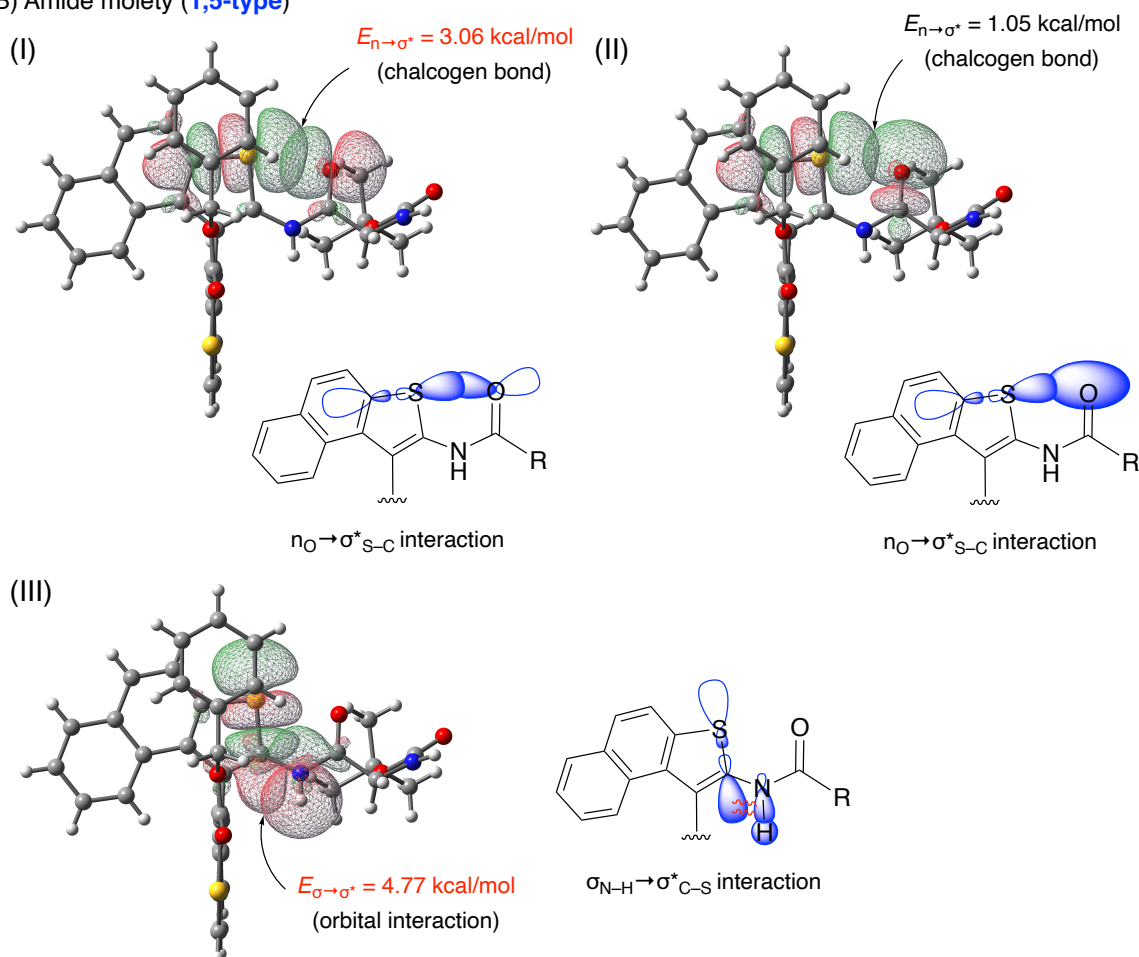


Figure 17. NBO Analysis for Dipeptide *Rac-9*. NBO overlaps between the oxygen lone pairs (n_O) or the bonding orbital of the N-H bond (σ_{N-H}) and the antibonding orbitals of the S-C bonds (σ^*_{S-C} and σ^*_{C-S}), together with the corresponding second order perturbation energies for (*S*)-**9** in the crystal structure of *rac-9*.

以上のように、ナフトチオフエン型の軸性不斉 δ -アミノ酸誘導体は、複数の軌道相互作用が共役系に付加的に作用することで立体構造を強く制御できることが明らかになった。そのため、これらの分子をロジウム二核錯体の配位子に用いれば、明確な立体構造に基づいた不斉誘起能の改善が期待できる。すなわち、カルボキシ基が配座制御されることで、ロジウム中心の上下に等価な不斉環境が形成され、共役系の拡張によってアミド部位に形成される大きな平面構造は、ロジウム中心を囲う大きな不斉空間の構築に寄与すると考えられる。この考察に基づき、ナフトチオフエン型の軸性不斉 δ -アミノ酸を配位子とするロジウム二核錯体の合成、及び不斉誘起能の評価を行った。その詳細を、第2章にて述べる。

第2章 立体選択的な分子内 C-H 挿入反応の開発と天然 γ -ラク톤の不斉合成

第1節 先行研究及び筆者の研究方針

α -ジアゾ酢酸エステルを基質とする分子内不斉 C-H 挿入反応は、様々な環状化合物を立体選択的に構築できる強力な有機合成法である。本反応は、環化生成物において、環外にエステル基を持つ生成物を与える *outside* 型³⁷の反応と、環内にエステル基を含むラク톤を与える *inside* 型³⁸の反応に分けて考えることができる (Figure 18)。

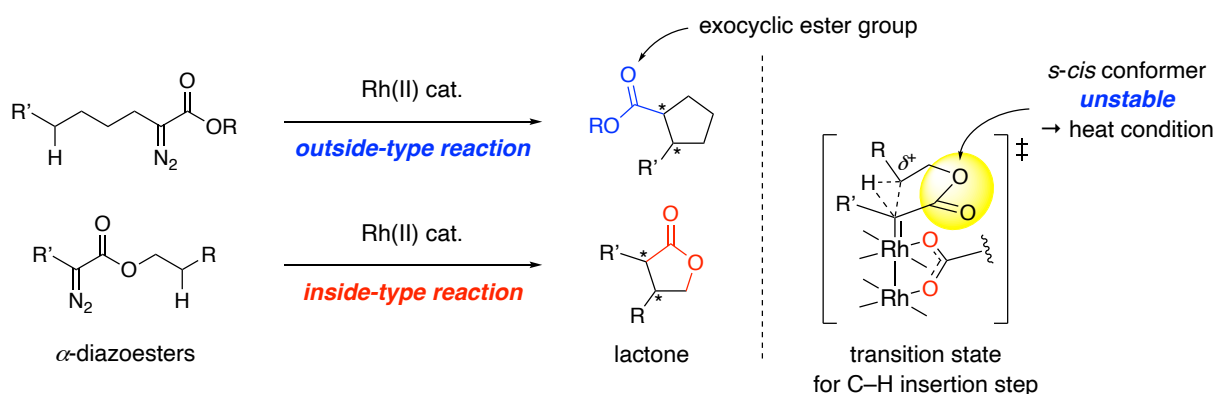
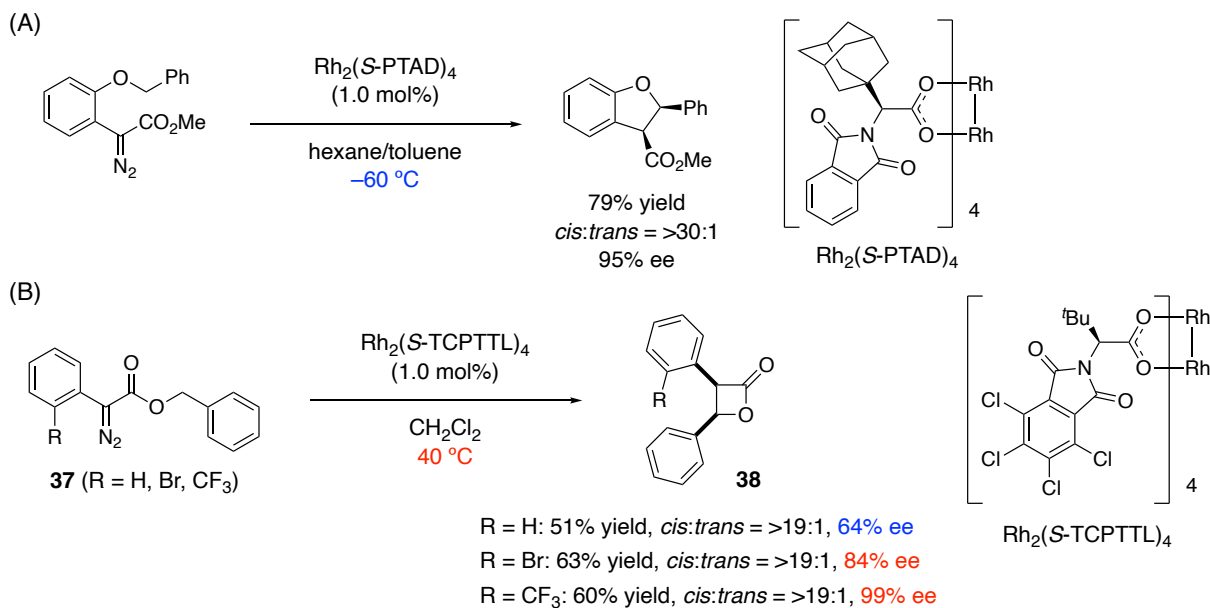


Figure 18. Rh(II)-Catalyzed Intramolecular C-H Insertions of α -Diazoesters (Outside-Type and Inside-Type).

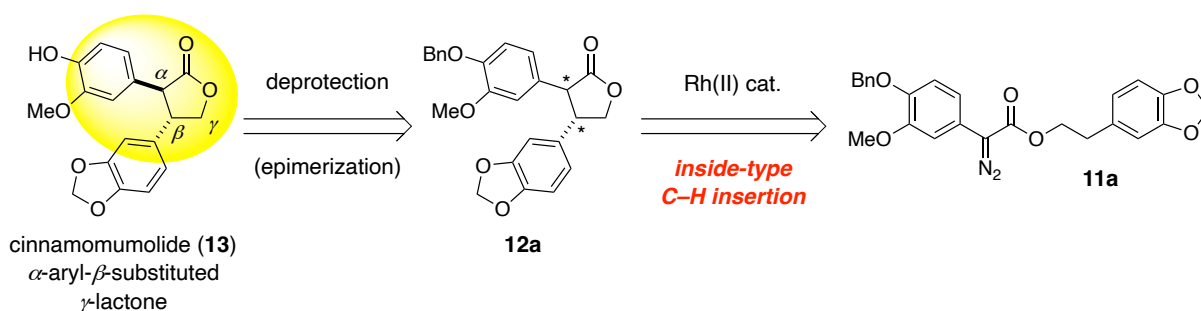
このうち、*outside* 型の反応は低温でも速やかに進行し、これまでに数多くの立体選択的な反応が報告されてきた (Scheme 11A)。一方で、*inside* 型の分子内 C-H 挿入反応は、C-H 挿入段階の遷移状態においてエステル基が不安定な *s-cis* 配座をとる必要があるために反応が進行しにくく、多くの場合に加熱条件が必要になる。その結果、前述のようにロジウム二核錯体が多様な配座を与えるため、本反応の立体制御は困難になる。特に、 α -アリール- α -ジアゾ酢酸エステルを基質とし、 α,β -二置換ラク톤を与える *inside* 型の反応については、エナンチオ選択性およびジアステレオ選択性を同時に制御した例はほとんど報告されていない。唯一の成功例として、Davies らによる基質 **37** の *inside* 型分子内 C-H 挿入反応が挙げられ、 $\text{Rh}_2(\text{S-TCPTTL})_4$ を触媒とすることで α,β -ジアリール β -ラクトン **38** をエナンチオ、及びジアステレオ選択的に与えることが明らかにされている (Scheme 11B)。^{9f} しかしながら、本反応の立体制御には α -アリール基のオルト位のトリフルオロメチル基、もしくはハロゲン原子が重要であり、オルト位の置換基を水素原子に置換した基質では立体選択性が大きく低下することが報告されている。

筆者の所属研究室でも、ロジウム二核錯体 (**R**)-**1a** を触媒とする基質 **2** の *inside* 型分子内 C-H 挿入反応を報告したが、その立体選択性は中程度にとどまり、検討の余地を残していた (Scheme 2)。¹³ そこで筆者は、カルコゲン結合を介して配座制御したロジウム二核錯体を用いてこの *inside* 型分子内 C-H 挿入反応を行い、不斉誘起能を評価することにした。第1章で述べたように、ナフトチオフェン型の軸性不斉 δ -アミノ酸誘導体を配位子とする錯体は、カルコゲン結合を介した配座制御により明確かつ堅固な不斉環境を有することが予想され、本反応の十分な立体制御が期待できる。



Scheme 11. Rh(II)-Catalyzed Asymmetric Intramolecular C–H Insertions of α -Diazoacetates. (A) Stereoselective Outside-Type Reaction. (B) Enantio- and Diastereoselective Inside-Type Reaction.

ところで、基質 **2** の inside 型分子内 C–H 挿入反応で得られる α -アリール- β -置換 γ -ラク톤は、シナニッケイから単離される天然物 cinnamomumolide (**13**)²⁴ の基本骨格であるため、 α -アリール- α -ジアゾ酢酸エステル **11a** を基質とし、その不斉合成を検討することにした (Scheme 12)。この基質 **11a** の分子内 C–H 挿入反応によって得られる α,β -ジアリール γ -ラクトン **12a** は、ベンジル基の脱保護により cinnamomumolide (**13**) に誘導でき、短工程での不斉合成が可能になる。



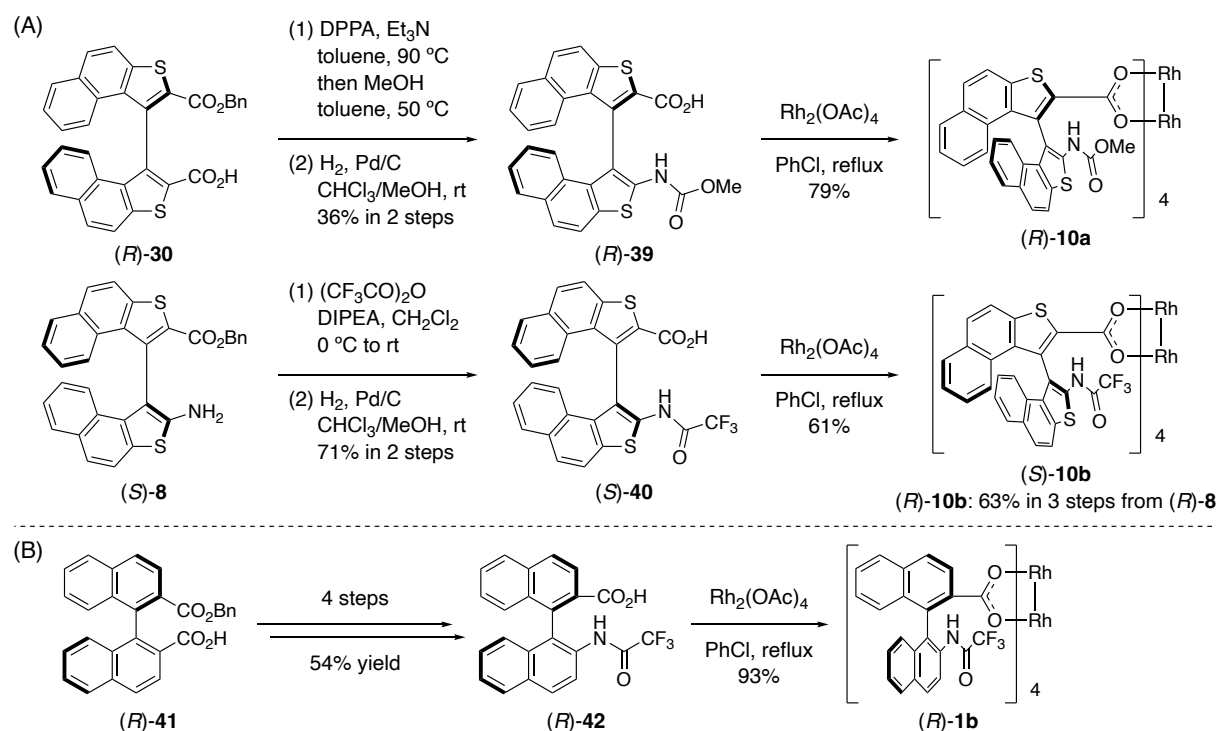
Scheme 12. Synthetic Strategy for Cinnamomumolide (**13**) via Asymmetric Intramolecular C–H Insertion.

以上の背景のもと、まずナフトチオフェン型の軸性不斉 δ -アミノ酸誘導体を配位子とするロジウム二核錯体 **10a** 及び **10b** を合成した。さらに、その不斉誘起能を比較するために、ビナフチル型の錯体 **1b** も合成した。このうち、トリフルオロアセトアミド基を有する錯体 **10b** は、基質 **11a** の分子内 C–H 挿入反応を高収率・高立体選択的に触媒し、幅広い基質一般性を示すことも明らかにした。また、cinnamomumolide (**13**) に加えて、類似天然物 cinncassin A₇ (*ent*-**13**)²⁵ および cinnamomulactone (**14**)²⁶ の不斉合成を達成し、cinnamomulactone (**14**) については CD スペクトルにより絶対構造を決定

した。錯体 **10b** の結晶構造からは、期待通り硫黄—酸素原子間のカルコゲン結合を介してカルボキシレート部位、及びアミド部位の配座が制御されていることが確認され、これが錯体 **10b** の優れた不斉誘起能の主要因であることを明らかにした。以下、その詳細について説明する。

第2節 軸性不斉 δ -アミノ酸誘導体を配位子とするロジウム二核錯体の合成

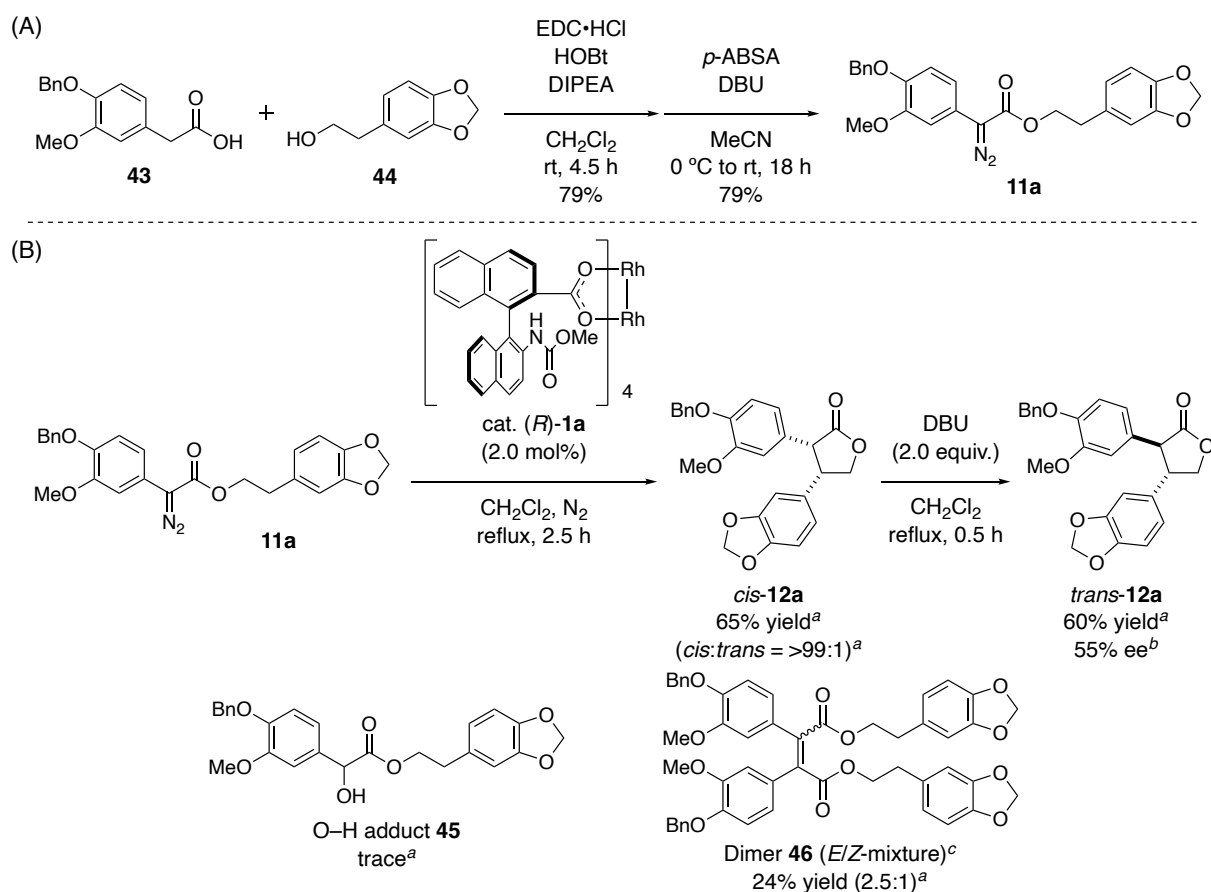
まず、ナフトチオフェン型の軸性不斉 δ -アミノ酸誘導体を配位子とするロジウム二核錯体を合成した (Scheme 13A)。ビナフチル型の錯体 (*R*)-**1a** と同じくメチルカルバメート基を有する錯体 (*R*)-**10a** の合成では、モノベンジルエステル (*R*)-**30** に対してクルチウス転位を行い、系中で生成したイソシアナートにメタノールを作用させることでメチルカルバメート基を導入した。その後、ベンジル基の脱保護により得られた配位子 (*R*)-**39** に対し、クロロベンゼン溶媒中、加熱還流下で $\text{Rh}_2(\text{OAc})_4$ を作用させることで配位子交換を行い、錯体 (*R*)-**10a** を得た。また、総論で述べたように、ビナフチル型の錯体 (*R*)-**1a** はカルバメート基の N-H 結合を介した分子内水素結合によって配座制御されることが示唆されたため (Scheme 2)、より N-H 基の酸性度が高く、強力な水素結合の形成が期待されるトリフルオロアセトアミド基を導入した錯体 (*S*)-**10b** の合成も検討した。Scheme 13A に示すように、錯体 (*S*)-**10b** は軸性不斉 δ -アミノ酸 (*S*)-**8** のトリフルオロアセチル化、及びベンジル基の脱保護によって得られる化合物 (*S*)-**40** を用いた配位子交換によって合成した。このとき、そのエナンチオマーである錯体 (*R*)-**10b** も、化合物 (*R*)-**8** から3段階、63% 収率で合成した。さらに、その比較対象として、トリフルオロアセトアミド基を有するビナフチル型の錯体 (*R*)-**1b** も、モノベンジルエステル (*R*)-**41** から4段階、54% 収率で得られる配位子 (*R*)-**42** を用いて合成した (Scheme 13B)。このように合成したロジウム二核錯体の不斉誘起能を、基質 **11a** の分子内 C-H 挿入反応にて評価した。



Scheme 13. Preparation of (A) Naphthothiophene-Type Complex and (B) Binaphthyl-Type Complex.

第3節 立体選択的 Inside 型分子内 C-H 挿入反応の検討

Inside 型分子内 C-H 挿入反応に用いる基質 **11a** を、市販の **43** と **44** の縮合反応、及びレグッツジアゾ転移により、2 段階、62% 収率で合成した (Scheme 14A)。この基質 **11a** を用いた inside 型分子内 C-H 挿入反応について、ビナフチル型の錯体 (*R*)-**1a** を用いて溶媒や温度等の反応条件の検討を行った (Table S1)。その結果、2.0 mol% の錯体 (*R*)-**1a** 存在下、塩化メチレン中、基質 **11a** の溶液を 1.5 時間かけてシリンジポンプで滴下し、1 時間加熱還流したところ、分子内 C-H 挿入反応が進行し、ジアステレオ選択的に *cis*-**12a** を与えることがわかった (Scheme 14B、*cis:trans* =>99:1)。本反応では、O-H 挿入反応生成物 **45**、及び基質の二量体 **46** が副生するが、窒素雰囲気下で反応を行うことで O-H 挿入体 **45** の生成は抑制され、基質のスローアディクションにより二量体 **46** の生成量は減少した (Table S2)。得られた *cis*-**12a** は単離可能な生成物ではあるものの、時折、単離中に *trans*-**12a** への異性化が確認されたため、DBU を用いて *trans*-**12a** に異性化させた後に光学純度を測定した。まず、錯体 (*R*)-**1a** の反応では 60% 収率、55% ee で *trans*-**12a** が得られるのみであり、十分な立体制御には至らなかったため、触媒の検討を行った (Table 1)。



Scheme 14. (A) Preparation of Substrate **11a**. (B) (*R*)-**1a**-Catalyzed Intramolecular C-H Insertion of **11a**.

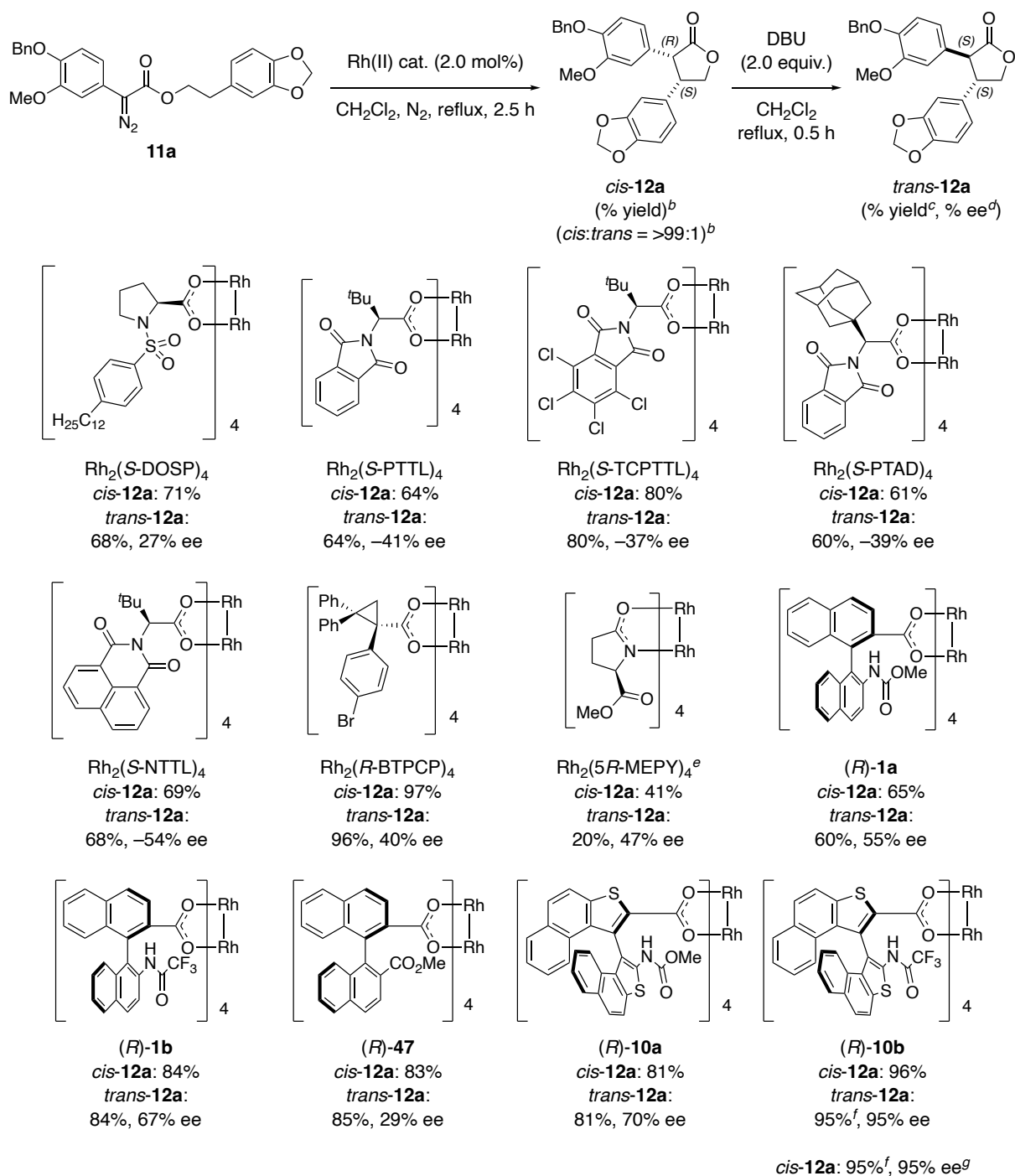
^aDetermined by integrating the ¹H NMR signals in the presence of 1,3,5-trimethoxybenzene as an internal standard. ^bDetermined by chiral HPLC analysis. ^cThe stereochemistries of these *E/Z*-isomers have yet to be determined.

まず、既存の不斉触媒として、 $\text{Rh}_2(\text{S-DOSP})_4^2$ 、 $\text{Rh}_2(\text{S-PTTL})_4$ 、 $\text{Rh}_2(\text{S-TCPTTL})_4$ 、 $\text{Rh}_2(\text{S-PTAD})_4^{9a}$ 、 $\text{Rh}_2(\text{S-NTTL})_4^{39}$ 、 $\text{Rh}_2(\text{R-BTPCP})_4^{10a}$ 、及び $\text{Rh}_2(\text{5R-MEPY})_4^{40}$ を用いて基質 **11a** の分子内 C-H 挿入反応を行ったが、いずれも低いエナンチオ選択性にとどまった。このとき、いずれの不斉触媒を用いた場合にも、1 段階目の分子内 C-H 挿入反応では *cis*-**12a** のみを与えることがわかった (*cis:trans* = >99:1)。また、 $\text{Rh}_2(\text{R-BTPCP})_4$ を用いた場合には、副生成物である二量体 **46** の生成が全く確認されなかった (Table S2)。この二量体は、ジアゾ化合物の分解に伴って形成されるロジウムカルベノイド中間体同士の反応によって生成するため、⁴¹ TPCP 型の錯体である $\text{Rh}_2(\text{R-BTPCP})_4$ のロジウム原子周辺の立体環境が混み合っていることが実験的にも裏付けられた (Scheme 1)。

続いて、ビナフチル型の錯体としてトリフルオロアセトアミド基を有する錯体 (*R*)-**1b** を触媒として用いたところ、67% ee で *trans*-**12a** を与え、55% ee の *trans*-**12a** を与えるメチルカルバメート型の錯体 (*R*)-**1a** よりも選択性が改善されることがわかった。一方で、窒素官能基を持たないエステル型の錯体 (*R*)-**47**^{15b} を用いた場合には 29% ee にとどまった。このように、錯体 (*R*)-**1a** と (*R*)-**1b** はエナンチオ選択性こそ不十分であるが、エステル型の錯体 (*R*)-**47** や既存の不斉触媒よりも高い選択性を示したため、軸性不斉 δ -アミノ酸誘導体を配位子とする錯体が本反応の立体制御に効果的であることが示唆された。

最後に、カルコゲン結合を介した配座制御が期待されるナフトチオフェン型の錯体 (*R*)-**10a** と (*R*)-**10b** の不斉誘起能を評価した。その結果、メチルカルバメート基を有する錯体 (*R*)-**10a** を用いた場合には 70% ee にとどまったが、同じ置換基を有するビナフチル型の錯体 (*R*)-**1a** を用いた場合 (55% ee) よりも高いエナンチオ選択性を示すことがわかった。一方で、トリフルオロアセトアミド基を有する錯体 (*R*)-**10b** を用いた場合には収率およびエナンチオ選択性が大きく改善し、95% 収率、95% ee で *trans*-**12a** を与えることが明らかになった。このとき、いずれのナフトチオフェン型の錯体を用いた場合にも二量体 **46** の生成は確認されず (Table S2)、ナフトチオフェン型の錯体のロジウム原子周辺が $\text{Rh}_2(\text{R-BTPCP})_4$ と同様に立体的に混み合っていることが示唆された。錯体 (*R*)-**10a** を用いた場合には O-H 挿入体 **45** が 16%ほど生成したために収率は 81%にとどまったが、二量体 **46** が全く生成しなかったことで、C-H 挿入体 **12a** の収率が向上したと考えられる。さらに、錯体 (*R*)-**10b** を触媒とする分子内 C-H 挿入反応でジアステレオ選択的に生成する *cis*-**12a** は、95% ee と高い光学純度で得られていることも判明した。なお、錯体 (*R*)-**10b** を用いたときに得られる *trans*-**12a** の主エナンチオマーの絶対配置は、第4節で述べるように 3*S*,4*S* 体であると決定した。以上のように、トリフルオロアセトアミド基を有するナフトチオフェン型の錯体 (*R*)-**10b** は、基質 **11a** の inside 型分子内 C-H 挿入反応をエナンチオ・ジアステレオ選択的に触媒し、*cis*-**12a** 及び *trans*-**12a** を高い光学純度で与える有用な錯体であることが明らかになった。

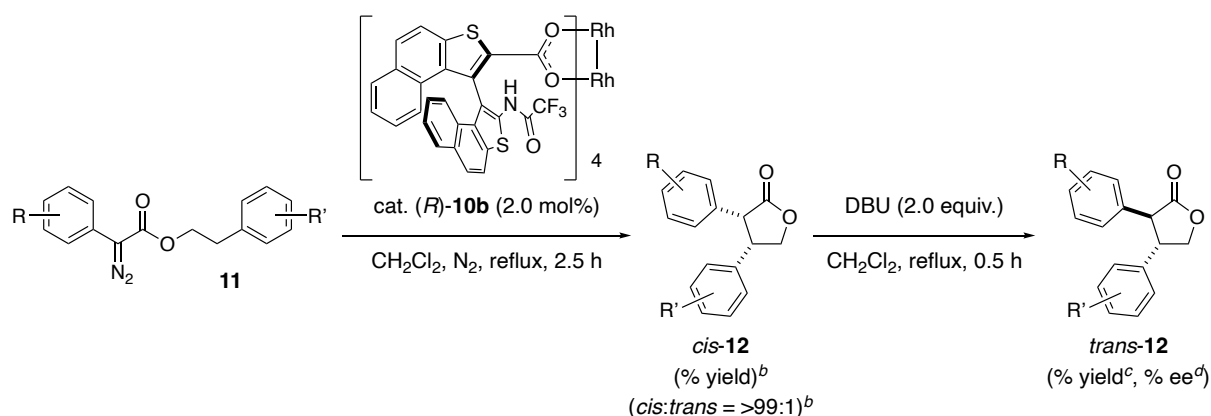
Table 1. Survey of Rh(II) Catalysts for Asymmetric Intramolecular C–H Insertion of **11a.^a**



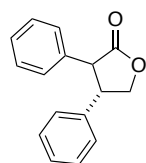
^aStandard reaction conditions: **11a** (33.5 mg, 0.0750 mmol, 1.00 equiv.) in degassed CH₂Cl₂ (0.75 mL) was added over 1.5 h to 4.5 mL of a refluxing CH₂Cl₂ solution of the dirhodium(II) catalyst (1.50 μmol, 2.00 mol%); then, refluxing was continued for 1 h. ^bDetermined by integrating the ¹H NMR signals in the presence of 1,3,5-trimethoxybenzene as an internal standard. ^cNMR yield over two steps. ^dDetermined by chiral HPLC analysis. ^e5.0 mol% of Rh₂(5*R*-MEPY)₄ was used. ^fIsolated yield. ^gEe (%) of isolated *cis-12a*.

続いて、錯体 (*R*)-**10b** を用いた *inside* 型分子内不斉 C-H 挿入反応の基質一般性を評価した。まず、基質 **11** の α 位の芳香環上の置換基 (R) を検討したところ (Table 2-1)、無置換の基質 **11b**、及びパラ位もしくはメタ位にハロゲン原子を有する基質 **11c-11e** では、対応する生成物 *trans*-**12b-12e** を良好な収率・高いエナンチオ選択性 (90-95% ee) で与えることがわかった。また、パラ位に *tert*-ブチル基を有する基質 **11f** では、多少エナンチオ選択性は低下するものの (81% ee)、良好な収率で *trans*-**12f** を与えた。一方で、3,4-ジメトキシフェニル基を有する基質 **11g** では、高エナンチオ選択的に *trans*-**12g** を与えたが (93% ee)、その収率は 34%にとどまった。これは、電子供与性の共鳴効果を示すパラ位のメトキシ基が、ロジウムカルベノイド中間体の求電子性を低下させることが原因であると考察した。対照的に、3,4,5-トリメトキシフェニル基を有する基質 **11h** では、3,5 位に置換した 2 つのメトキシ基が電子求引性の誘起効果を示すためにロジウムカルベノイド中間体の求電子性が増し、高収率・高エナンチオ選択的に *trans*-**12h** を与えることがわかった (96% 収率、94% ee)。さらに、ナフチル基を持つ基質に対しても適用可能であり、特に、2-ナフチル型の基質 **11j** では最も高いエナンチオ選択性で *trans*-**12j** を与えることが明らかになった (96% ee)。

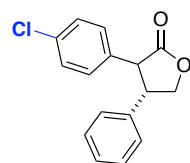
Table 2-1. Substrate Scope for Asymmetric Intramolecular C-H Insertion Catalyzed by Complex **10b** (1).^a



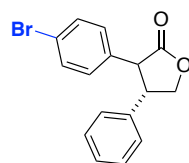
Substituent R on α -aryl ring



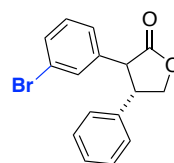
cis-**12b**: 66%
trans-**12b**: 65%, 90% ee



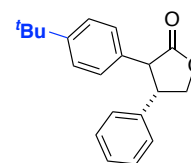
cis-**12c**: 81%
trans-**12c**: 73%, 94% ee



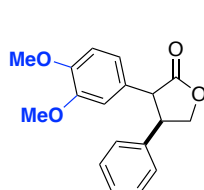
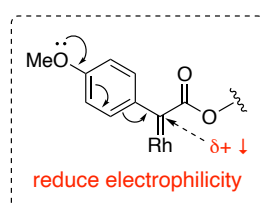
cis-**12d**: 87%
trans-**12d**: 86%, 95% ee



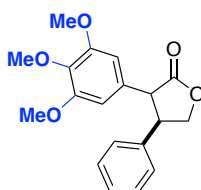
cis-**12e**: 73%
trans-**12e**: 70%, 91% ee



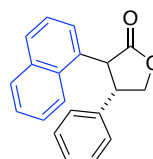
cis-**12f**: 80%
trans-**12f**: 78%, 81% ee



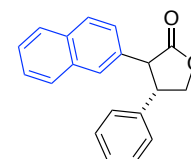
cis-**12g**^e: 36%
trans-**12g**^e: 34%, 93% ee



cis-**12h**^e: 100%
trans-**12h**^e: 96%, 94% ee



cis-**12i**: 87%
trans-**12i**: 85%, 85% ee



cis-**12j**: 90%
trans-**12j**: 85%, 96% ee

次に、基質 **11** のエステル部位の芳香環上の置換基 (R') を検討したところ (Table 2-2A)、基質 **11k–11r** では概ね高いエナンチオ選択性で *trans*-**12k–12r** を与えたが (87–93% ee)、収率は芳香環の電子状態に依存することがわかった。すなわち、電子求引性の塩素、臭素原子を有する基質 **11k–11n** では収率が大きく低下し (31–55% 収率)、電子供与性のメトキシ基を有する基質 **11o** と **11p** では高い収率で γ -ラクトンを与えた。これは、電子豊富な芳香環の方が、C–H 挿入段階の遷移状態でベンジル位に生じる部分正電荷をより安定化できるためであると考察した。⁴² 一方で、チオフェン環を有する基質 **11s**、及び以前の報告で用いた基質 **2** を用いた場合には、生成物 **12s** と **48** がそれぞれ低収率・中程度のエナンチオ選択性で得られるにとどまった。

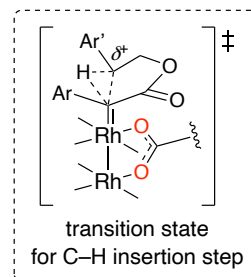
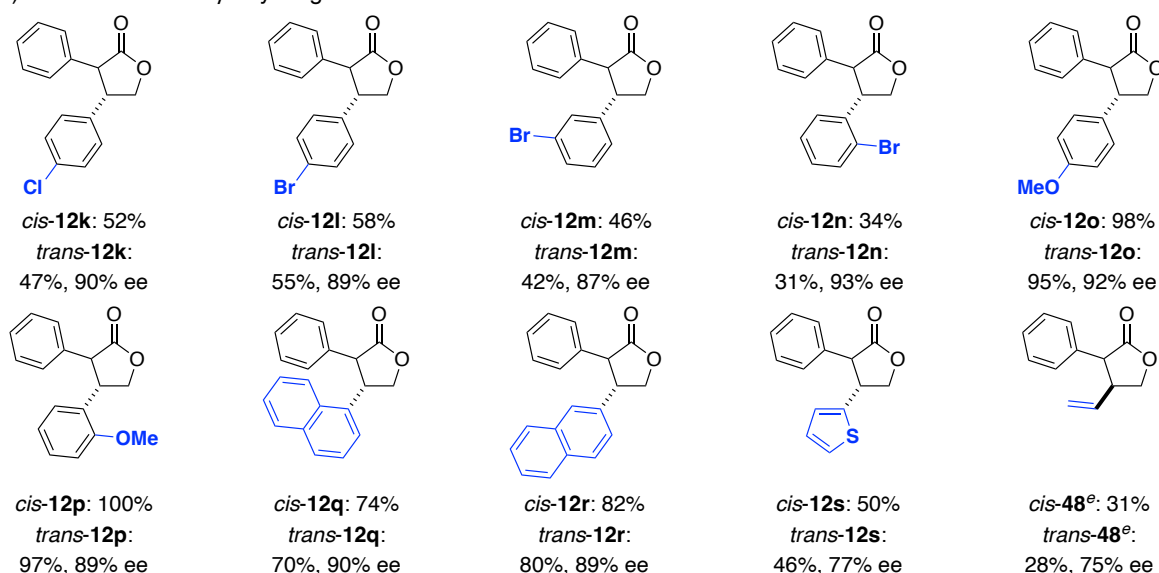
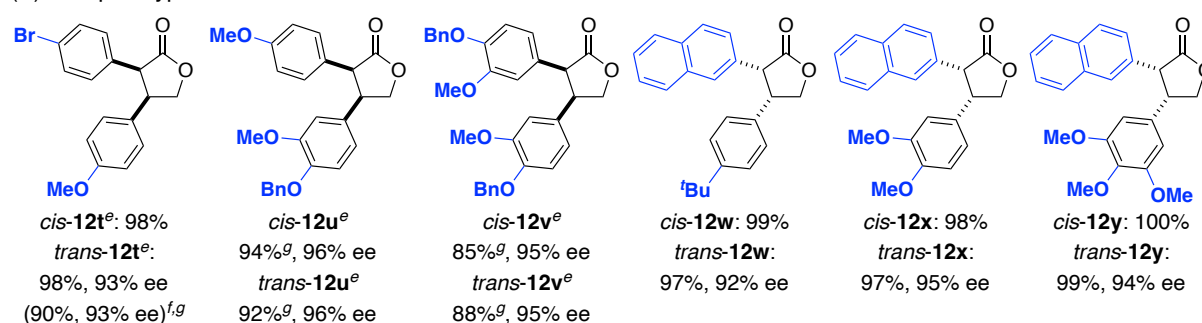


Table 2-2. Substrate Scope for Asymmetric Intramolecular C–H Insertion Catalyzed by Complex **10b** (**2**).^a

(A) Substituent R' on β -aryl ring



(B) Complex type



^aStandard reaction conditions: **11** (0.0750 mmol, 1.00 equiv.) in degassed CH_2Cl_2 (0.75 mL) was added over 1.5 h to 4.5 mL of a refluxing CH_2Cl_2 solution of (*R*)-**10b** (3.43 mg, 1.50 μmol , 2.00 mol%); then, refluxing was continued for 1 h. ^bDetermined by integrating the ^1H NMR signals in the presence of 1,3,5-trimethoxybenzene as an internal standard. ^cNMR yield over two steps. ^dDetermined by chiral HPLC analysis. ^e(*S*)-**10b** was used. ^f**11t** (1.13 g, 3.00 mmol, 1.00 equiv.) and (*S*)-**10b** (34.3 mg, 15.0 μmol , 0.500 mol%) were used. ^gIsolated yield.

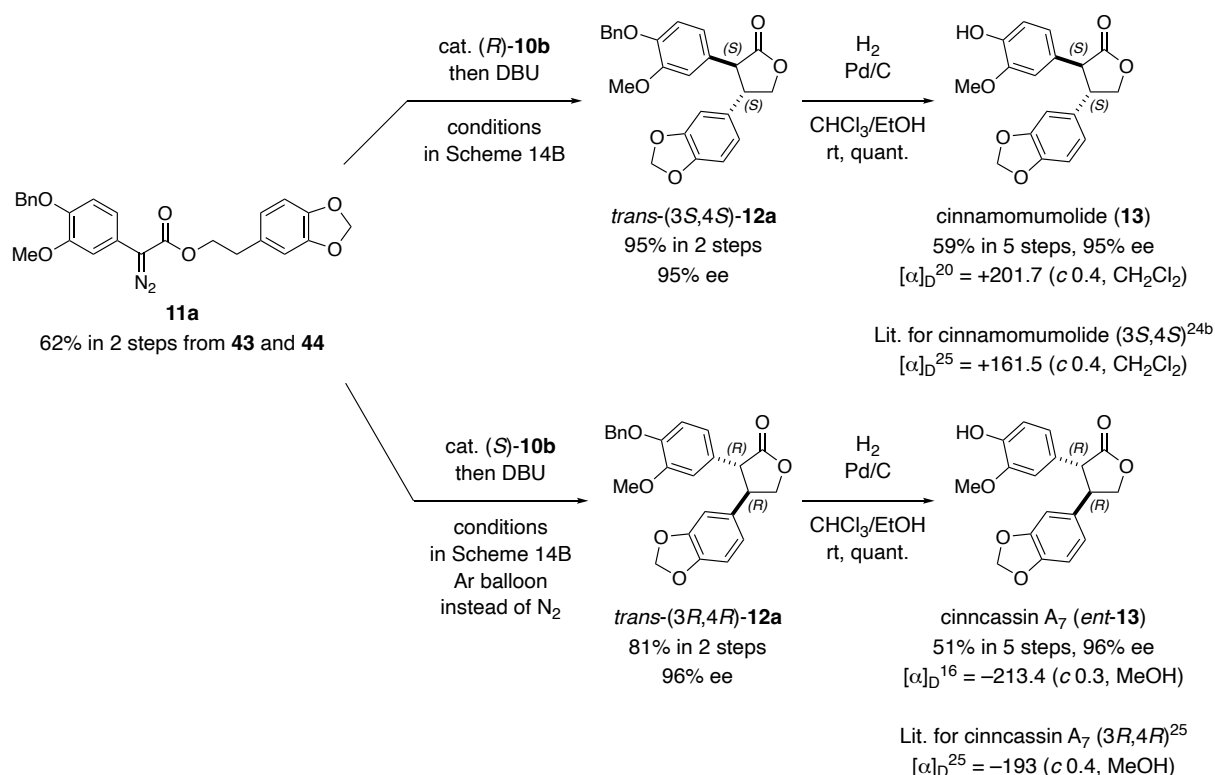
以上の結果を踏まえると、 α 位の芳香環として2-ナフチル基を有する基質やエステル部位の芳香環上に電子供与を有する基質を用いる反応では、高収率・高立体選択的に生成物が得られると考えられるため、いずれの芳香環上にも置換基を有する基質 **11t–11y** を用いた検討も行った (Table 2-2B)。その結果、期待通り高収率・高立体選択的に *trans*-**12t–12y** を与えることが判明し (88–99% 収率、92–96% ee)、基質 **11u** と **11v** を用いる反応では *cis* 体の γ -ラク톤を単離することも可能であった。また、臭素原子、及びメトキシ基を有する基質 **11t** を用いる反応は、3.00 mmol スケールでの触媒反応も可能であり、エナンチオ選択性を損なうことなく触媒量を 0.500 mol%まで低減することも可能であった。このように筆者は、トリフルオロアセトアミド基を有するナフトチオフェン型の錯体 **10b** が、様々な置換基を有する α,β -ジアリール γ -ラクトン **12** を立体選択的に与える有用な触媒として働くことを見出した。

第4節 天然 γ -ラクTONの不斉合成

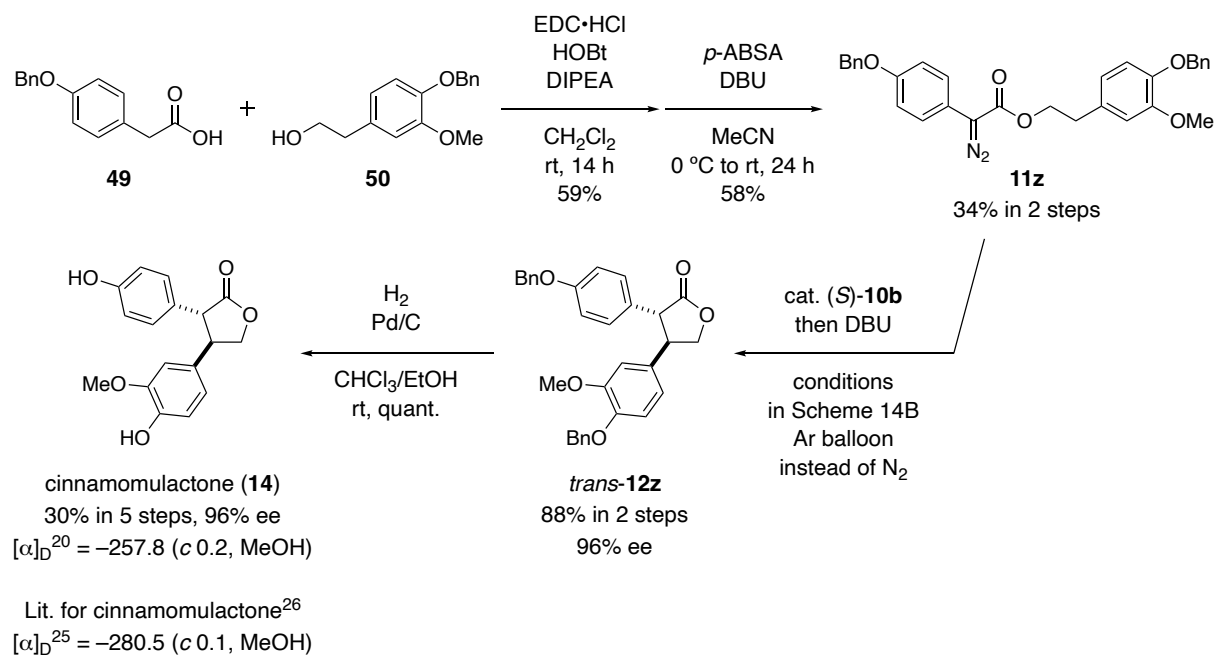
第3節にて開発した立体選択的な分子内 C–H 挿入反応を、天然 γ -ラクTON cinnamomumolide (**13**) とそのエナンチオマーである cinncassin A₇ (*ent*-**13**) の不斉合成に展開した (Scheme 15)。まず、基質 **11a** に対して触媒 (*R*)-**10b** を用いた際に 95% 収率、95% ee で得られた *trans*-**12a** のベンジル基を脱保護し、市販品から5段階、総収率 59%で cinnamomumolide (*trans*-(3*S*,4*S*)-**13**) の不斉合成を達成した。この **13** の比旋光度の符号が天然物の文献値^{24b}と一致したため、原料として用いた *trans*-**12a** の主エナンチオマーは3*S*,4*S*の絶対配置を有することが明らかになった。この結果から、錯体 (*R*)-**10b** を触媒とする基質 **11a** の分子内 C–H 挿入反応では、3*R*,4*S*の絶対配置を有する *cis*-**12a** が主エナンチオマーとして得られることが判明した。先の基質一般性の検討 (Table 2) では、全ての絶対配置を検討していないが、錯体 (*R*)-**10b** からは *trans*-(3*S*,4*S*)-**12** が、錯体 (*S*)-**10b** からは *trans*-(3*R*,4*R*)-**12** が主エナンチオマーとして得られたと考えられる。さらに、cinnamomumolide (**13**) のエナンチオマーである cinncassin A₇ (*ent*-**13**) の不斉合成も行った。すなわち、錯体 (*S*)-**10b** を用いて基質 **11a** の分子内 C–H 挿入反応を行い、立体選択的に得られた *trans*-**12a** のベンジル基を脱保護することで cinncassin A₇ (*trans*-(3*R*,4*R*)-**13**) に誘導した (5段階、総収率 51%、96% ee)。この **13** についても、比旋光度の符号が天然物の文献値²⁵と致していることを確認した。

続いて、同様に天然 γ -ラクTONとして知られる cinnamomulactone (**14**) の不斉合成も行った (Scheme 16)。Choi らは、cinnamomulactone (**14**) の比旋光度 ($[\alpha]_D^{25} = -280.5$ in MeOH) の符号が、cinnamomumolide (*trans*-(3*S*,4*S*)-**13**) の比旋光度 ($[\alpha]_D^{25} = +161.5$ in CH₂Cl₂) の符号と異なるために、3*R*,4*R*の絶対配置を有すると推定している。²⁶ しかしながら、その絶対配置は未だ決定されていないため、合成した天然 γ -ラクTONの CD スペクトルを比較することでその絶対配置を決定することにした。まず、市販の **49** と **50** の縮合反応、及びレギッツジアゾ転移により基質 **11z** を合成し (2段階、34% 収率)、主エナンチオマーとして *trans*-(3*R*,4*R*)-**12z** を与えると予想される錯体 (*S*)-**10b** を用いて分子内 C–H 挿入反応を行った。その結果、88% 収率、96% ee で *trans*-**12z** が得られ、2つのベンジル基を脱保護することで cinnamomulactone (**14**) に誘導した (市販品から5段階、総収率 30%、96% ee)。得られたサ

ンプルの比旋光度を測定したところ、その符号が天然物の文献値²⁶と一致したため、反応で得られた主エナンチオマーは天然型であることがわかった。



Scheme 15. Asymmetric Syntheses of Cinnamomumolide (**13**) and Its Enantiomer Cinnassin A₇ (*ent*-**13**).



Scheme 16. Asymmetric Synthesis of Cinnamomulactone (**14**).

以上のように合成した 3 種類の天然 γ -ラクトンについて、メタノール中における CD スペクトル及び UV スペクトルを測定した (Figure 19)。3*S*,4*S* の絶対配置を有する cinnamomumolide (**13**) の CD スペクトルは、長波長側から正 (270–300 nm)、正 (230–250 nm)、正 (200–220 nm) のコットン効果を示し、そのエナンチオマーである cinncassin A₇ ((3*R*,4*R*)-**13**) の CD スペクトルとは鏡像関係にあることを確認した。ここで、cinnamomulactone (**14**) は長波長側から負 (270–290 nm)、負 (220–240 nm)、負 (200–220 nm) のコットン効果を示し、cinncassin A₇ ((3*R*,4*R*)-**13**) と類似した CD スペクトルを示したことから、その絶対配置は cinncassin A₇ ((3*R*,4*R*)-**13**) と同じ 3*R*,4*R* であると決定した。

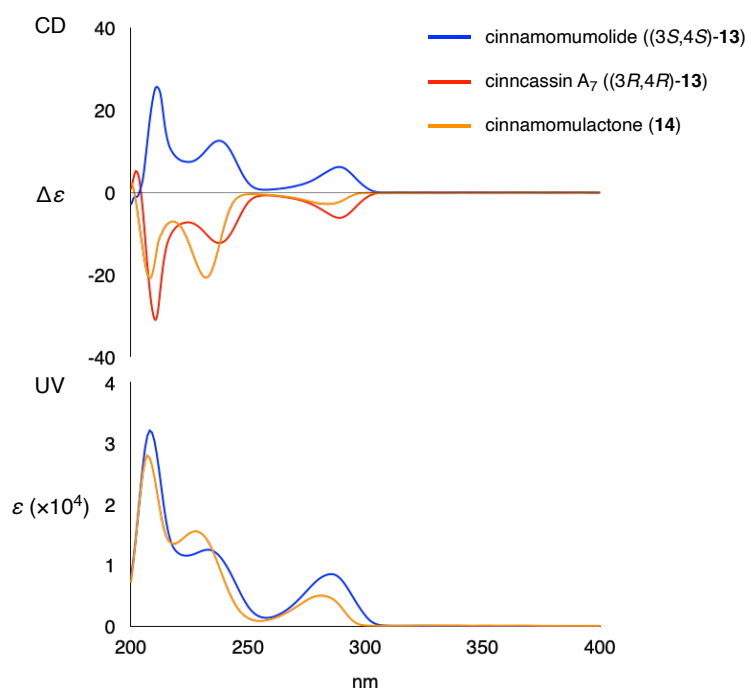


Figure 19. CD and UV Spectra of Cinnamomumolide ((3*S*,4*S*)-**13**), Cinncassin A₇ ((3*R*,4*R*)-**13**), and Cinnamomulactone (**14**) in MeOH. The UV spectrum of cinncassin A₇ ((3*R*,4*R*)-**13**) is not depicted as it is identical with that of cinnamomumolide ((3*S*,4*S*)-**13**).

第5節 ロジウム二核錯体の構造解析

筆者は、基質 **11a** の分子内 C-H 挿入反応の触媒検討において (Table 1)、ビアリール型のロジウム二核錯体の不斉誘起能が、置換基や骨格の変化によって大きく変化することを明らかにした。すなわち、Figure 20 に示すように、ビナフチル骨格を有する錯体ではエステル型、カルバメート型、アミド型の順に選択性が向上し、アミド型の錯体 (**R**)-**1b** をナフトチオフェン骨格に変えた錯体 (**R**)-**10b** は、分子内 C-H 挿入反応を高い立体選択性で触媒することがわかった。そこで、このエナンチオ選択性の変化を、それぞれの錯体の X 線結晶構造解析により考察した。

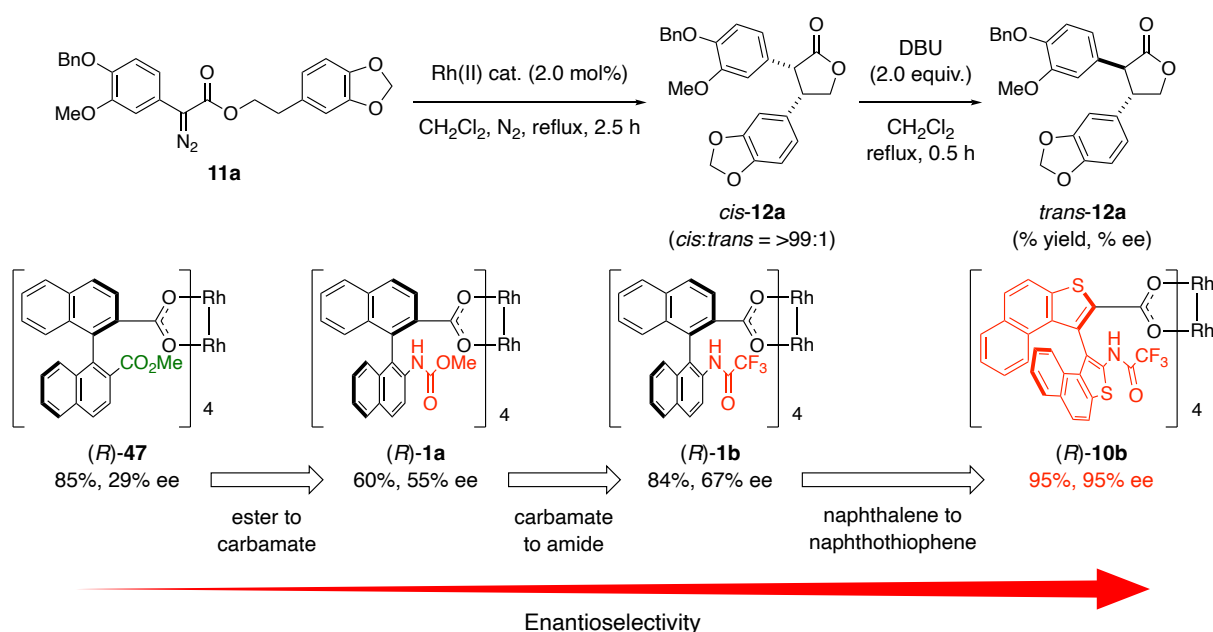


Figure 20. Comparison of the Stereo-Induction Abilities of Biaryl-Type Dirhodium(II) Complexes.

まず、基質 **11a** の反応におけるエナンチオ選択性が 29% ee にとどまっていたエステル型の錯体 (*R*)-**47** について、同様にメトキシカルボニル基を持つビフェニル型の錯体 (*S*)-**51**^{15b} の結晶構造を基に考察した。橋本らによって報告された錯体 (*S*)-**51** は、エステル基が置換したベンゼン環がロジウム中心に対してそれぞれ up-up-down-down に並んだ C_2 対称構造を有することが明らかにされている (Figure 21A)。この結晶構造では、それぞれの配位子のカルボキシレート部位の二面角 ($\phi_{C-C'-C''-O}$) が不均一であり (13(1)–35(1)°)、その配座制御が不十分であることが明らかになった。実際、この錯体のロジウム原子 Rh(1) と Rh(2) 周辺の立体構造を比べたところ、ロジウム中心の上側に位置する青色のベンゼン環によって形成される不斉環境は互いに大きく異なっていることがわかる (Figure 21B)。同様に、触媒検討で用いた錯体 (*R*)-**47** も擬 C_2 対称型の立体構造を形成していると考え、このような上下で非対称な立体環境を形成しているために、不斉誘起が 29% ee にとどまったと考えられる。

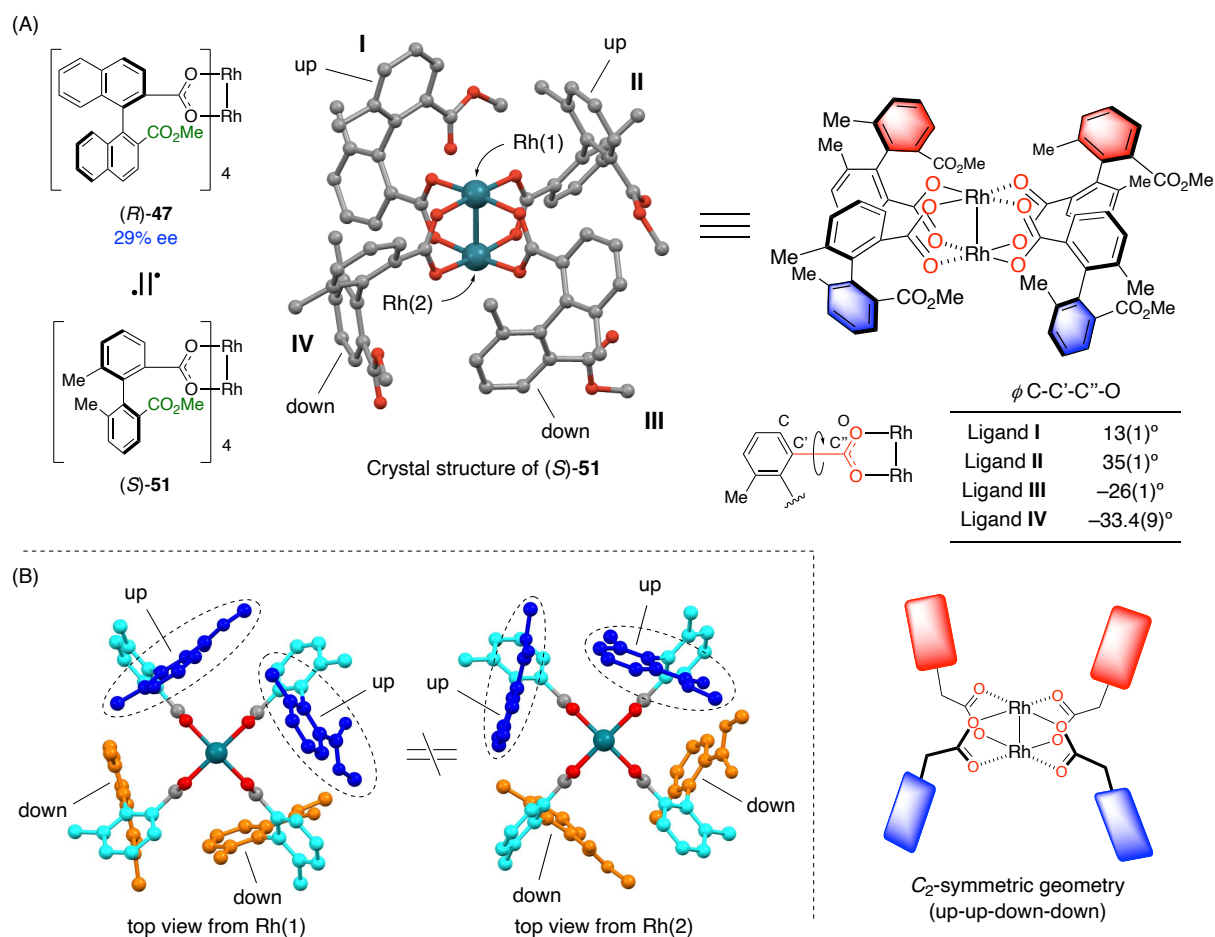


Figure 21. Crystal Structure of Complex (*S*)-**51**. Hydrogen atoms and solvent molecules coordinated at the axial positions are omitted for clarity. In the top views of the complex (B), the pairs of ester-substituted benzene rings located at the upper or lower side relative to the indicated Rh center are shown in blue and orange, respectively.

Scheme 2 で述べたように、55% ee を示したメチルカルバメート基を有する錯体 (*R*)-**1a** も、カルバメート基が置換したナフチル環がロジウム中心に対してそれぞれ up-up-down-down に並んだ C_2 対称構造を有することがわかった (Figure 22A)。この錯体のそれぞれの配位子のカルボキシラート部位の二面角も一様でなく (ϕ C-C'-C''-O = 13(1)–49(1)°)、錯体 (*S*)-**51** と同様にカルボキシラート部位の配座を制御できていないことが判明した。そのため、ロジウム原子 Rh(1) と Rh(2) 周辺の立体構造に関して、ロジウム中心の上側に位置する青色のナフチル環によって形成されるそれぞれの不斉空間が非等価になることが示唆された (Figure 22B)。このように、錯体 (*R*)-**1a** と (*R*)-**47** はいずれも擬 C_2 対称構造を有することが明らかになったが、基質 **11a** の分子内 C-H 挿入反応に用いたときのエナンチオ選択性は大きく異なっている ((*R*)-**1a**: 55% ee v.s. (*R*)-**47**: 29% ee)。総論で述べたように、錯体 (*R*)-**1a** の配位子 **I** と **II** では、カルボキシラート部位の酸素原子とカルバメート基の間に分子内水素結合 (O...H-N) を形成しており (水素結合を形成している酸素–窒素原子間距離: 2.974(7) Å, 2.962(7) Å)、この分子内水素結合を介した配座制御によって錯体 (*R*)-**47** よりも高い不斉誘起を示したと考えられる。

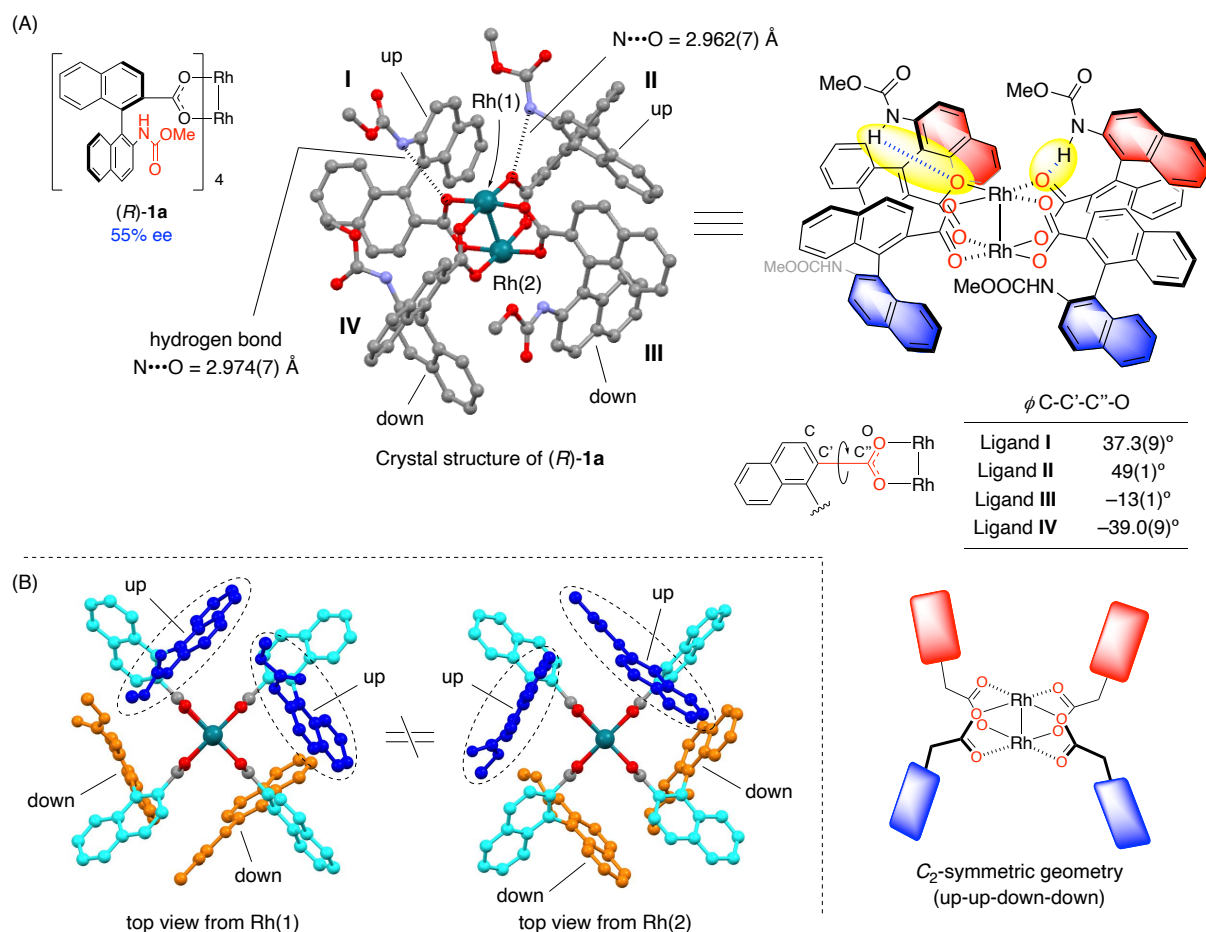


Figure 22. Crystal Structure of Complex (*R*)-**1a**. Hydrogen atoms and solvent molecules coordinated at the axial positions are omitted for clarity. In the top views of the complex (B), the pairs of carbamate-substituted naphthyl rings located at the upper or lower side relative to the indicated Rh center are shown in blue and orange, respectively.

一方で、67% ee を示したトリフルオロアセトアミド基を有する錯体 (*R*)-**1b** は、アミド基が置換したナフチル環がロジウム中心に対してそれぞれ up-down-up-down に並んだ D_2 対称構造を有し、先の 2 つの錯体とは異なる対称構造を有することが明らかになった (Figure 23A)。結晶構造を精査したところ、配位子 **I** と **IV** のトリフルオロメチル基のフッ素原子同士がファンデルワールス半径の和である 2.94 Å よりも短い距離に位置しており (フッ素原子同士の距離 : 2.89(1) Å)、フッ素原子間に相互作用が働いていることが示唆された。⁴³ この相互作用は、隣接する配位子のトリフルオロメチル基同士が向かい合うように配置する D_2 対称構造を安定化している可能性があり、対称性が変化した要因の 1 つとして考えられる。また、錯体 (*R*)-**1a** と同様に、カルボキシレート部位の酸素原子とアミド基の間に分子内水素結合 (O \cdots H-N) を形成していることもわかった (水素結合を形成している酸素-窒素原子間距離 : 2.71(1) Å)。

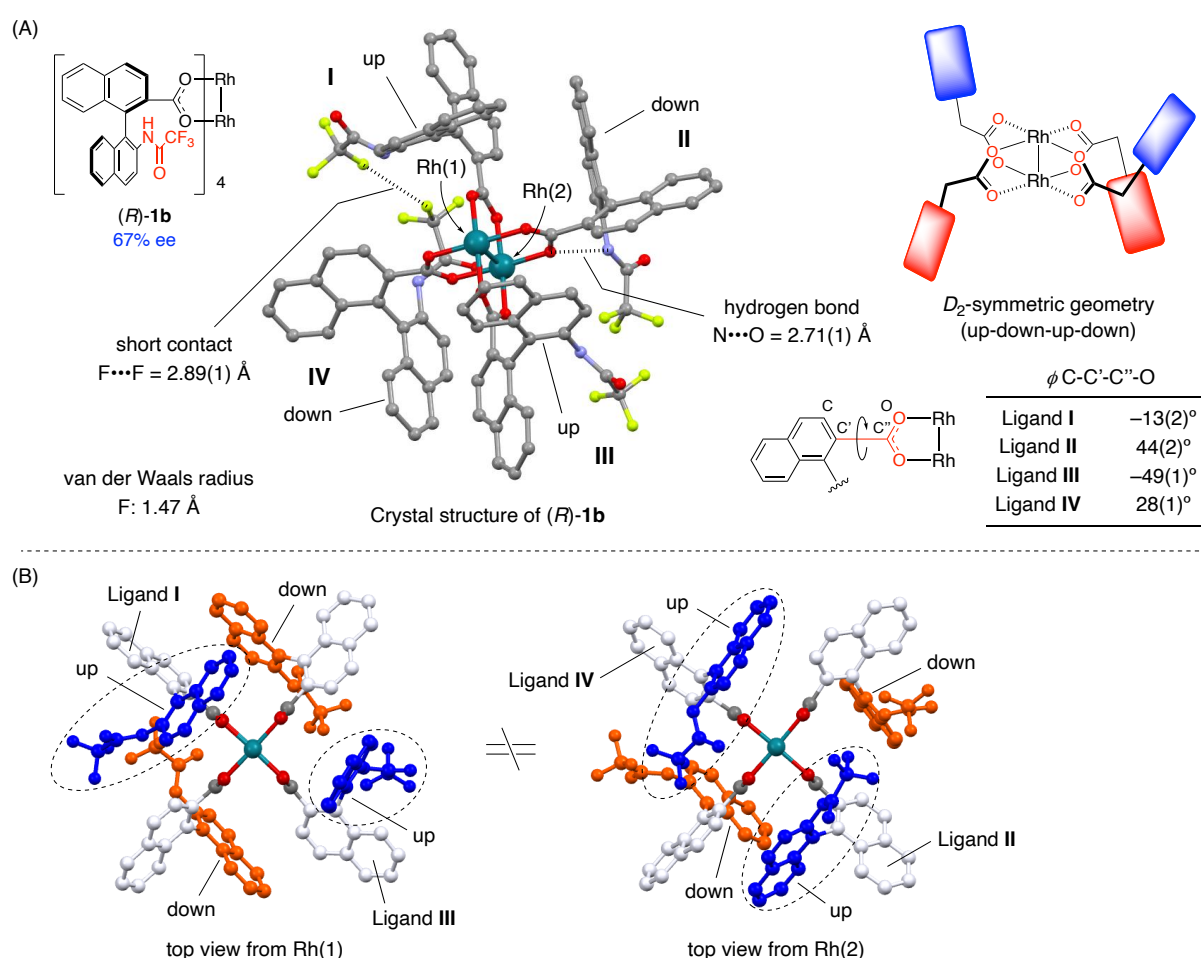


Figure 23. Crystal Structure of Complex (*R*)-**1b**. Hydrogen atoms and solvent molecules coordinated at the axial positions are omitted for clarity. In the top views of the complex (B), the pairs of amide-substituted naphthyl rings located at the upper or lower side relative to the indicated Rh center are shown in blue and orange, respectively.

次いで、錯体 (*R*)-**1b** の双方のロジウム原子周辺の立体構造を比較したところ (Figure 23B)、錯体 (*R*)-**1a** と同様にロジウム中心の上下に非等価な立体環境を形成しており、その要因をカルボキシラート部位の二面角 ($\phi_{\text{C-C}^{\prime}\text{-C}^{\prime\prime}\text{-O}}$) の違いから考察した。Rh(2) 周辺の不斉空間は、配位子 **II** と **IV** のナフチル環 (点線部) によって形成されるが、カルボキシラート部位の二面角は 16° ほど異なっていた (配位子 **II** : $44(2)^\circ$ v.s. 配位子 **IV** : $28(1)^\circ$)。一方で、Rh(1) 周辺の不斉空間を形成する配位子 **I** と **III** の二面角の違いは 36° と大きく (配位子 **I** : $-13(2)^\circ$ v.s. 配位子 **IV** : $-49(1)^\circ$)、2つのナフチル環 (点線部) が Rh(1) を均等に囲んでないことがわかった (Figure 23B)。このような二面角の違いにより、双方のロジウム原子が等しく覆われず、ロジウム中心の上下が非対称な擬 D_2 対称構造を形成したと考えられる。以上のように、ビナフチル型の配位子を有するロジウム二核錯体は、いずれもカルボキシラート部位の配座制御が不十分であり、ロジウム中心の上下で非対称な不斉環境を形成していることがわかった。錯体 (*R*)-**1b** は、これらの錯体の中では基質 **11a** の分子内 C-H 挿入反応の不斉誘起に優れる錯体であるが (67% ee)、その不斉誘起の程度の違いは C_2 対称か D_2 対称であるかの対称性の違いによる影響が大きいと考えられる。

最後に、高い立体選択性を示したトリフルオロアセトアミド基を有するナフトチオフェン型の錯体 (*S*)-**10b** の立体構造について考察した (Figure 24)。錯体 (*R*)-**1b** と同様に、錯体 (*S*)-**10b** はアミド基が置換したナフトチオフェン環がロジウム中心に対してそれぞれ up-down-up-down に並んだ D_2 対称構造を有することがわかった (Figure 24A)。実際に、錯体 (*S*)-**10b** が形成可能な4つの対称構造について DFT 計算を行ったところ、結晶構造から確認された D_2 対称構造が最安定配座であることが裏付けられた (Figure S19)。また、錯体 (*S*)-**10b** の配位子 **III** と **IV** のトリフルオロメチル基のフッ素原子同士も相互作用可能な距離に位置しており (フッ素原子同士の距離 : $2.85(2)$ Å)、トリフルオロアセトアミド基の導入が D_2 対称構造形成の主要因であるという仮説を支持した。メチルカルバメート基を有するナフトチオフェン型の錯体 (*R*)-**10a** の結晶構造は未だ明らかになっていないが、トリフルオロアセトアミド基を持たないためにフッ素原子間の相互作用を形成できず、 D_2 対称構造ではなく本触媒系の不斉誘起に適さない C_2 対称構造を形成したことが、中程度の不斉誘起しか示さない要因として考えられる。

さらに、錯体 (*S*)-**10b** のそれぞれのロジウム原子周辺の立体構造を比較したところ (Figure 24B)、ビナフチル型の錯体とは異なり、ロジウム中心の上下に類似した不斉環境を形成していることが見て取れた。実際に、ビナフチル型の錯体 (*R*)-**1b** とは異なり、錯体 (*S*)-**10b** のカルボキシラート部位の二面角 ($\phi_{\text{S-C-C-O}}$) はいずれも 10° 前後にとどまっており (Figure 24C)、それぞれのロジウム原子周辺に不斉空間を形成する配位子同士に大きな差は見られなかった。すなわち、Rh(1) 周辺の不斉空間を形成する配位子 **I** と **III**、及び Rh(2) 周辺の不斉空間を形成する配位子 **II** と **IV** では、カルボキシラート部位の二面角 ($\phi_{\text{S-C-C-O}}$) の差はそれぞれ 3° と 4° にとどまっていた (配位子 **I** : $7(2)^\circ$ v.s. 配位子 **III** : $4(2)^\circ$ 、配位子 **II** : $-12(2)^\circ$ v.s. 配位子 **IV** : $-16(2)^\circ$)。以上のように、それぞれのロジウム原子が2つのナフトチオフェン環 (点線部) によって等しく囲まれるため、錯体 (*S*)-**10b** はロジウム中心の上下の不斉環境が類似した高度な D_2 対称構造を形成したと考えられる。

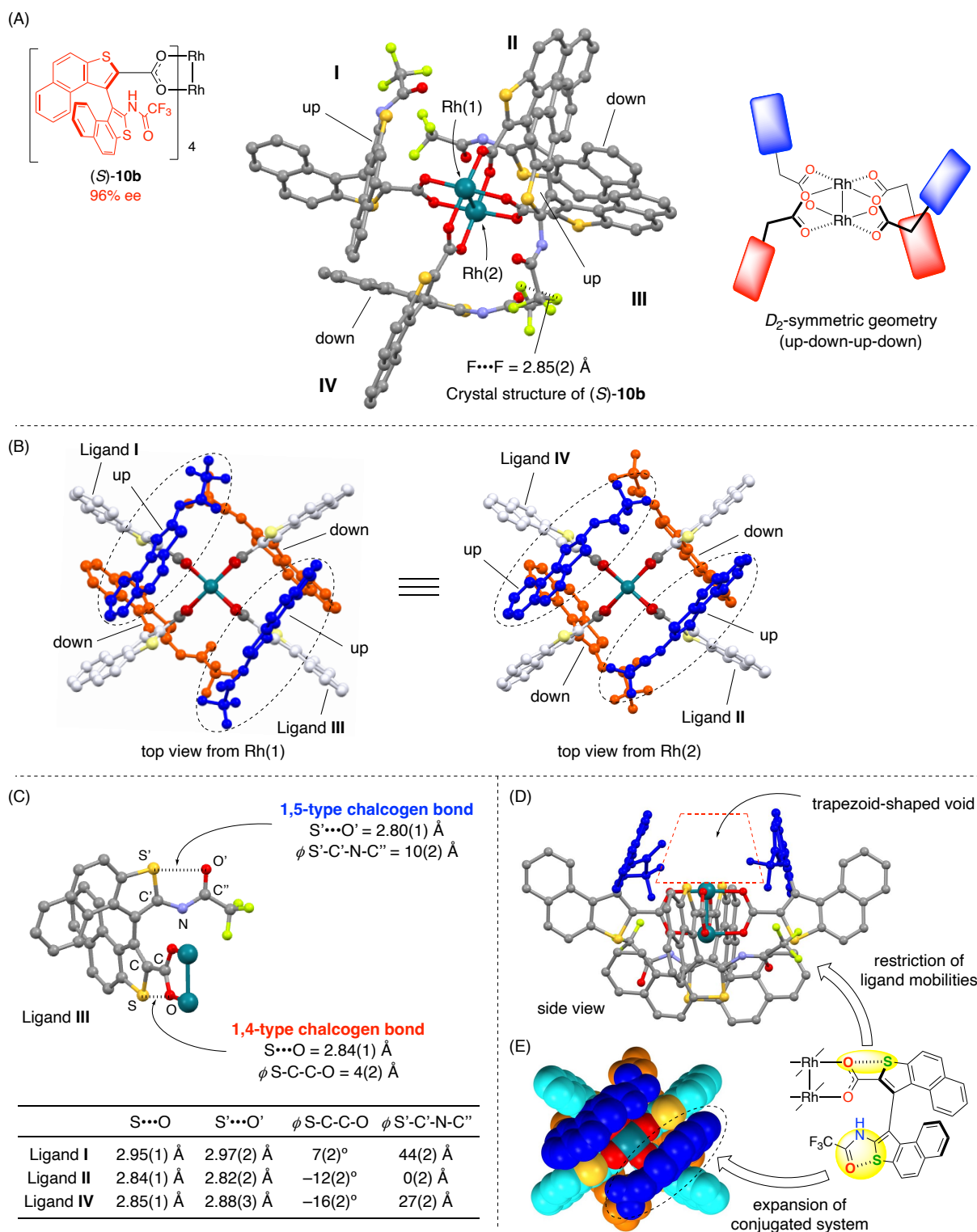
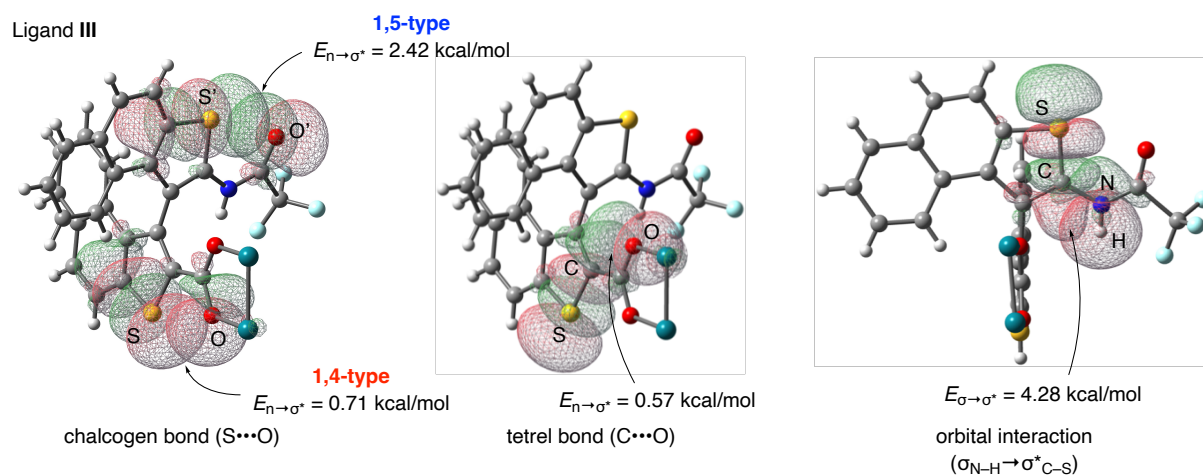


Figure 24. Crystal Structure of Complex (S)-10b. Hydrogen atoms and solvent molecules coordinated at the axial positions are omitted for clarity. In the top views of the complex (B), the pairs of amide-substituted naphthyl rings located at the upper or lower side relative to the indicated Rh center are shown in blue and orange, respectively. (C) Dihedral angles of S-C-C-O and S'-C'-N-C'', as well as the S...O and S'...O' distances of each ligand; the locations of these angles and distances are illustrated using Ligand III. (E) Space-filling models of the top view from Rh(2).

このように、錯体 (**S**)-**10b** はカルボキシラート部位の配座が制御され、ロジウム中心の上下に等価な不斉環境を有することが明らかになったので、各配位子の硫黄-酸素原子間の距離も精査した。このとき、錯体 (**S**)-**10b** の 1 分子は別の分子と相互作用していないことが確認されており、単体の結晶構造中の相互作用のみを議論することとした。Figure 24C に示すように、カルボキシラート部位 ($\text{S}\cdots\text{O}$) 及びアミド部位 ($\text{S}'\cdots\text{O}'$) のいずれの硫黄-酸素原子間の距離もファンデルワールス半径の和である 3.32 \AA よりも短く、硫黄および酸素原子がカルコゲン結合を形成可能な距離に位置していることがわかった。上述したように、カルボキシラート部位の二面角はいずれも 10° 前後の値を示し、カルボキシ基が芳香環とほぼ同一平面上に位置することも考え合わせると、それぞれの配位子において 1,4 型のカルコゲン結合がカルボキシ基の配座制御に寄与していると考えられた。このようにカルボキシラート部位が配座制御されると、3 位に置換したナフトチオフェン環は錯体の内側に傾くことになるが、筆者が期待した通り、これがロジウム原子周辺に効果的な不斉場を形成した要因であると考えられる (Figure 24D)。

さらに、アミド部位の構造制御についても調べたところ、配位子 **II** と **III** のアミド基は芳香環とほぼ同一平面上に配座制御されていることがわかった ($\phi \text{S}'\text{-C}'\text{-N-C}'' = 0(2)^\circ, 10(2)^\circ$)。一方で、配位子 **I** と **IV** のアミド基は芳香環との同一平面上から大きく逸れてはいるものの ($\phi \text{S}'\text{-C}'\text{-N-C}'' = 44(2)^\circ, 27(2)^\circ$)、硫黄-酸素原子間距離はいずれもファンデルワールス半径の和よりも短く、1,5 型のカルコゲン結合を形成していることが示唆された。Space-filling モデルからも確認できるように、この 1,5 型のカルコゲン結合によってナフトチオフェン環の共役系が拡張したような大きな平面構造が形成されており、触媒活性中心を囲む大きな不斉空間が構築されていることがわかった (Figure 24E)。なお、配位子 **I** と **IV** のアミド基は、アキシアル位に配位したエタノール分子と N-H 結合を介した水素結合を形成していることが確認され、この水素結合がナフトチオフェン環の同一平面からアミド基が外れた要因であると考えられる。

次に、錯体 (*S*)-**10b** の結晶構造から示唆された“カルコゲン結合を介した配座制御”を評価すべく、結晶構造に基づいたNBO解析を行った (Figure 25、汎関数と基底関数:M06/6-31G+(d,p)-LanL2DZ(Rh))。本解析では、二次摂動エネルギーが0.50 kcal/molを上回る相互作用のみが評価対象となっているため、配位子 **II** のカルボキシラート部位ではカルコゲン結合の形成が確認されなかったが、その他の硫黄-酸素原子間にはいずれもカルコゲン結合が形成されていることがわかった。特に、配位子 **III** では最も強い軌道相互作用が確認され、カルボキシラート部位には0.71 kcal/molほどの1,4型のカルコゲン結合が、アミド部位には2.42 kcal/molほどの1,5型のカルコゲン結合が形成されていることがわかった。また、カルコゲン元素を有するビアリールジカルボン酸 (Figure 14) やジペプチド *rac*-**9** のエステル部位 (Figure 17A) で確認された炭素-酸素原子間のテトレル結合についても評価したところ、配位子 **III** と **IV** においてそれぞれ0.57 kcal/mol、及び0.54 kcal/molほどのテトレル結合を形成していることが確認された。このように、カルボキシラート部位に形成されているカルコゲン結合やテトレル結合はいずれも強力な軌道相互作用ではないが、共役系に対して付加的に作用することでカルボキシラート部位が配座制御されており、ロジウム中心の上下に等価な不斉環境を有する高度な D_2 対称構造の構築に寄与していることがわかった。さらに、アミド部位では、1,5型のカルコゲン結合だけでなく、ジペプチド *rac*-**9** (Figure 17A) において確認された N-H 結合の結合性軌道 σ_{N-H} と C-S 結合の反結合性軌道 σ^*_{C-S} 間の軌道相互作用も形成されており ($E_{\sigma \rightarrow \sigma^*} = 2.82\text{--}4.64$ kcal/mol)、ナフトチオフェン環とアミド基にまたがる大きな平面構造の構築に寄与していることがわかった。



	chalcogen bond		tetrel bond	orbital interaction
	$E_{S \cdots O}$ (kcal/mol)	$E_{S \cdots O^*}$ (kcal/mol)	$E_{C \cdots O}$ (kcal/mol)	$E_{\sigma \rightarrow \sigma^*}$ (kcal/mol)
Ligand I	0.68	2.34	<0.50	4.64
Ligand II	<0.50	0.58	<0.50	2.82
Ligand IV	0.66	1.22	0.54	4.06

Threshold for printing: 0.50 kcal/mol.

Figure 25. NBO Analysis for Complex (*S*)-**10b**. NBO overlaps between the oxygen lone pairs (n_O) or the bonding orbital of the N-H bond (σ_{N-H}) and the antibonding orbitals of the S-C bonds (σ^*_{S-C} and σ^*_{C-S}), together with the corresponding second order perturbation energies for Ligand **III** in the crystal structure of (*S*)-**10b**. The second order perturbation energies for Ligand **I**, **II** and **IV** are shown in the table.

また、ナフトチオフェン型の錯体 (*S*)-**10b**、及びカルコゲン結合を形成しない酸素原子を導入したナフトフラン型の錯体 (*S*)-**52** の立体構造をそれぞれ最適化し、硫黄原子を導入したことの重要性を評価した (Figure 26、汎関数と基底関数 : M06/6-31G(d,p)-LanL2DZ(Rh))。その結果、ナフトフラン型の錯体 (*S*)-**52** では、ナフトチオフェン型の錯体 (*S*)-**10b** と比べて対称性が大きく崩れていることが見てとれた (Figure 26A)。この違いはカルボキシレート部位およびアミド部位の二面角の違いからも確認でき、ナフトフラン型の錯体 (*S*)-**52** ではそれぞれの官能基を芳香環との同一平面上に配座制御できていないことがわかる (Figure 26B、カルボキシレート部位の二面角 ($\phi_{\text{O-C-C-O}}$) の絶対値 : 15.0–30.4°、アミド部位の二面角 ($\phi_{\text{O-C-N-C}}$) の絶対値 : 8.8–50.0°)。この計算結果からも、硫黄原子を導入したことで形成されるカルコゲン結合が高度な D_2 対称構造の構築に寄与していることが示された。

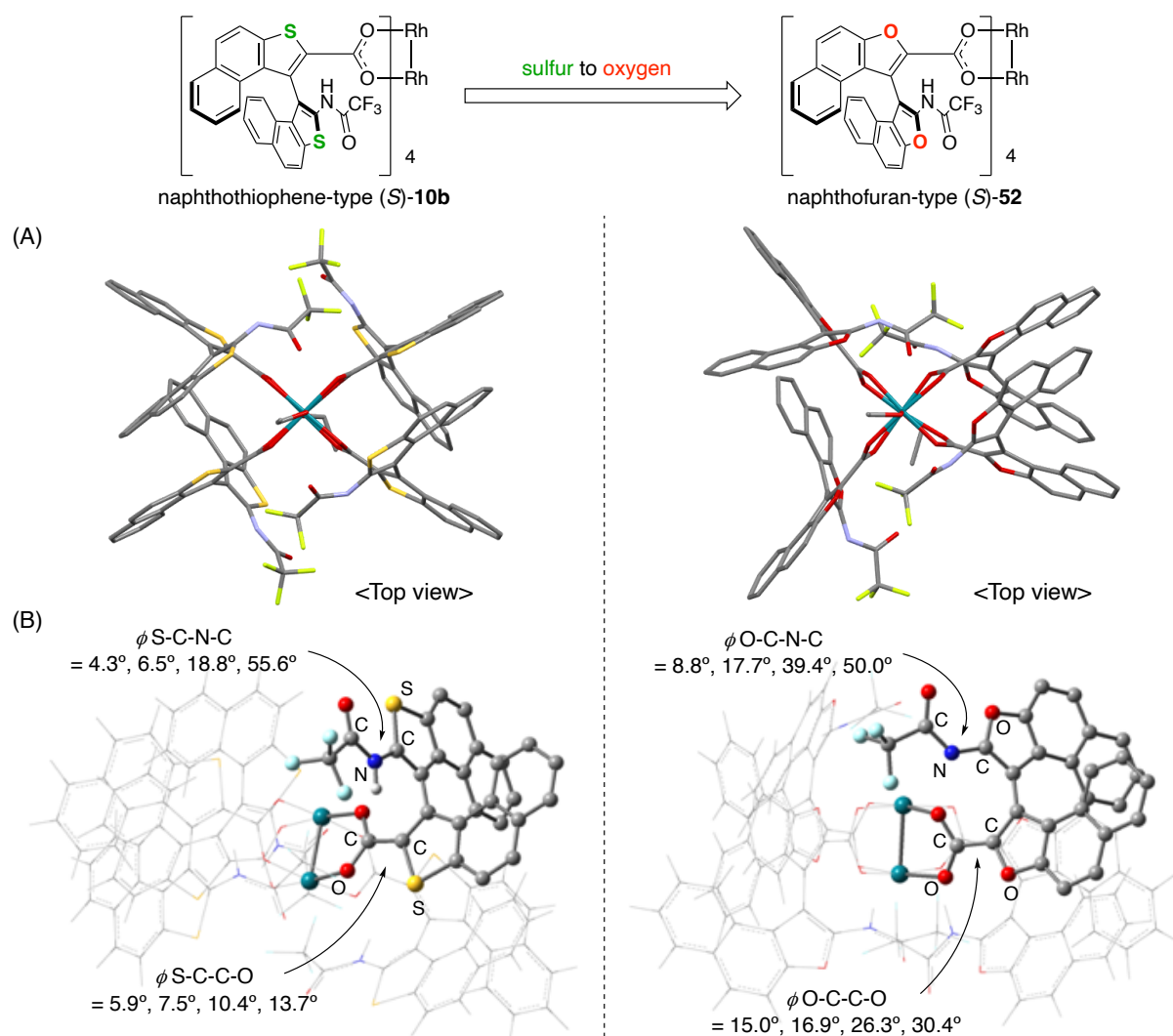
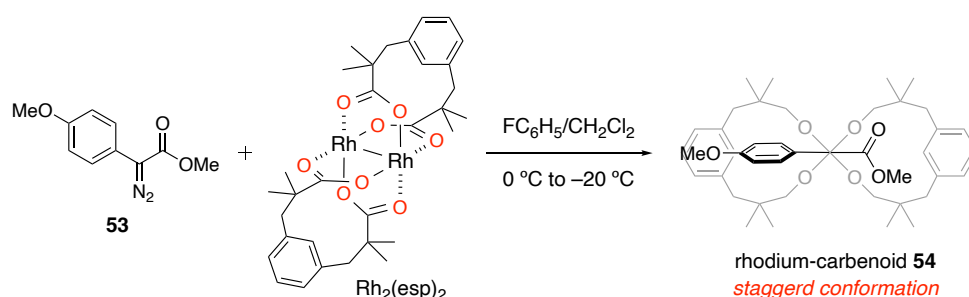


Figure 26. Optimized Structures of Naphthothiophene-Type Complex (*S*)-**10b** and Naphthofuran-Type Complex (*S*)-**52**. The structures of these complexes with coordination of two EtOH molecules as the axial ligands were optimized by M06/6-31G(d,p)-LanL2DZ(Rh). Hydrogen atoms are omitted for clarity. (A) Top view. (B) The absolute values of the dihedral angles of carboxylate and amide moieties for each ligand are shown in the figure.

最後に、基質 **11b** をモデルとして、錯体 **10b** がエナンチオ、ジアステロ選択的に *cis*-(3*S*,4*R*)-**12b** を与える立体選択性の発現機構について、結晶構造をもとに考察した。

先に Fürstner らは、 α -アリール- α -ジアゾ酢酸エステル **53** と錯体 $\text{Rh}_2(\text{esp})_2$ から得られるロジウムカルベノイド種 **54** の X 線結晶構造解析により、 α -アリールエステル部位が O-Rh-O 部位に対してねじれ配座を取ることを明らかにしている (Scheme 17)。⁴⁴ このとき、カルベノイド炭素に直結したアリール基は、電子供与性の共鳴効果によってロジウムカルベノイドの求電子性を低下させるように炭素-ロジウム結合と同一平面上に位置し、エステル基はロジウムカルベノイドの求電子性を向上させないように炭素-ロジウム結合に対して直交することがわかっている。この知見を考慮すると、基質 **11b** と錯体 (*S*)-**10b** から得られるロジウムカルベノイド中間体は、Figure 27 に示す中間体 **A** と **B** の 2 つに限定できると考えられる。すなわち、錯体 (*S*)-**10b** の立体構造を O-Rh-O 軸ごとに I-IV の 4 つの象限に分割して考えると、 α -アリールエステル部位が第 I 象限と第 III 象限にまたがる中間体 **A** と、第 II 象限と第 IV 象限にまたがる中間体 **B** の 2 つに限られる。このとき、中間体 **B** では α -アリール基とナフトチオフェン環との間に立体障害を生じるため、中間体 **A** からの反応が優先すると考えた。また、炭素-ロジウム結合に対して直交するエステル基の向きによって中間体 **A-I** と **A-II** が考えられるが、エステル部位のアルキル基と配位子との間に立体障害を生じない中間体 **A-I** のみで反応が進行すると考えられる。この中間体 **A-I** では、第 III 象限、および第 IV 象限側の空間が立体的に空いているため、第 III、第 IV 象限側のエナンチオ面で C-H 挿入反応が進行すると考えられる (エナンチオ選択性の決定段階)。



Scheme 17. Structure of Reactive Donor/Acceptor Rhodium(II) Carbene **54** in the Solid State.

続く C-H 挿入段階では、エステル部位のベンゼン環を上側に向ける *cis* 体を生じる遷移状態と、ベンゼン環を下側に向ける *trans* 体を生じる遷移状態の 2 つの遷移状態が考えられる (ジアステロ選択性の決定段階)。このうち、*trans* 体を生じる遷移状態は、下側に向けたベンゼン環とロジウムカルボキシレート部位との間に立体障害を生じるため、不利な遷移状態であると考察した。したがって、中間体 **A-I** から *cis* 体を生じる遷移状態を経て C-H 挿入反応が進行した際の生成物 *cis*-(3*S*,4*R*)-**12b** がジアステロ選択的に得られ、*trans* 体を生じる遷移状態から得られる生成物 *trans*-(3*S*,4*S*)-**12b** は全く確認されなかったと考えられる。以上のような立体選択性の発現機構により、錯体 (*S*)-**10b** を触媒とする分子内 C-H 挿入反応では、エナンチオ・ジアステロ選択的に 3*S*,4*R* の絶対配置を有する α,β -ジアリール γ -ラクトン *cis*-**12** が得られると考えられる。この *inside* 型分子内 C-H 挿入反応は、これまで立体制御が困難であった反応系であるが、カルコゲン結合を介して配座制御したナフトチオ

フェン型のロジウム二核錯体 **10b** は、エナンチオ選択性の決定段階における立体配座を加熱条件下でも強く制御できたことが優れた不斉誘起の要因として考えられる。

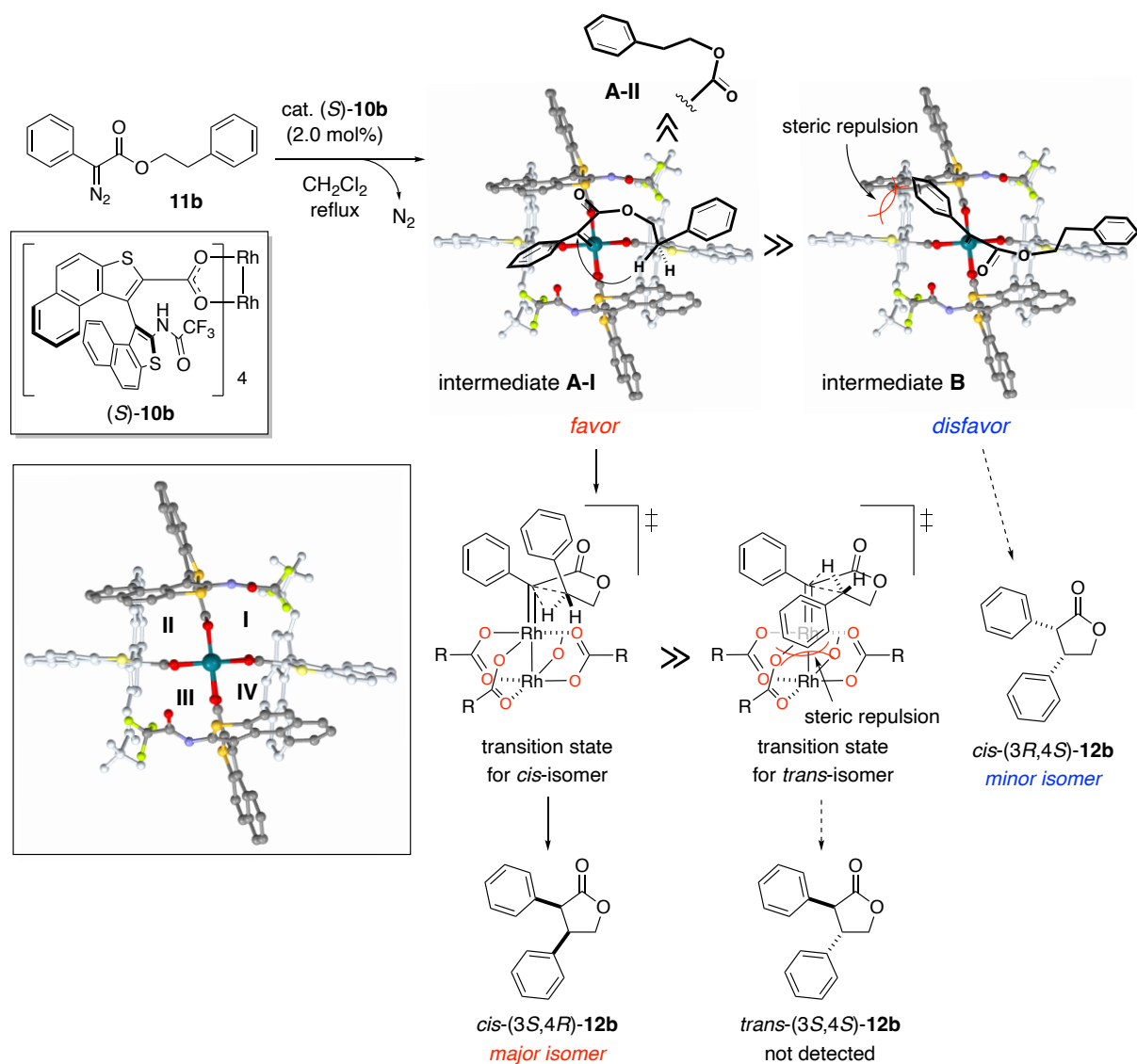


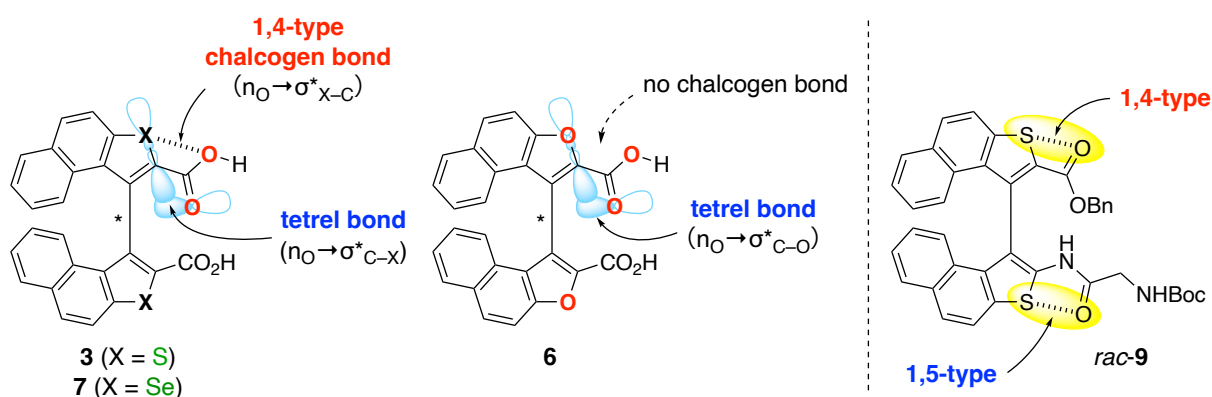
Figure 27. Models to Rationalize the Stereoselectivity with Naphthothiophene-Type Complex **(S)-10b**.

結論

筆者は、カルコゲン結合を介してカルボキシラート部位、及びアミド部位を配座制御したナフトチオフェン型のロジウム二核錯体 **10b** を創製し、この錯体が基質 **11** の分子内 C-H 挿入反応を高収率・高立体選択的に触媒することを見出した。このカルコゲン結合を介した配座制御は本触媒系における立体選択性向上の主要因であることが示唆されたため、硫黄原子を酸素やセレン原子に変換した錯体を用いた検討が今後の課題である。以下に、本研究の成果を要約する。

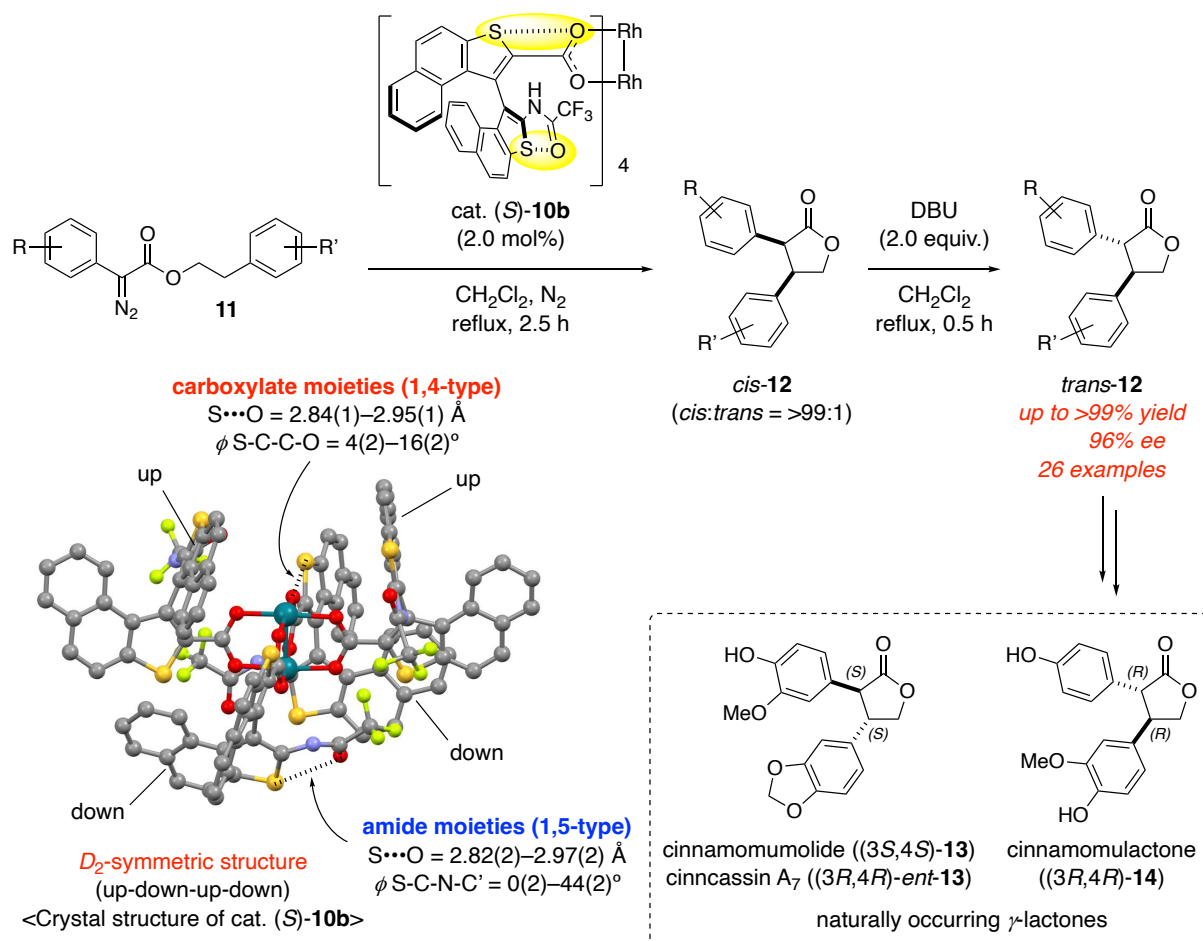
(1) カルコゲン元素を有するビアリールジカルボン酸、及びナフトチオフェン型軸性不斉 δ -アミノ酸誘導体の合成と構造解析

筆者の所属研究室で以前報告したナフトチオフェン型のビアリールジカルボン酸 **3** の硫黄原子を酸素やセレン原子に変えたジカルボン酸 **6** と **7** を合成し、X 線結晶構造解析及び NBO 解析を行うことで“カルコゲン結合を介したカルボキシ基の配座制御”を評価した。その結果、ナフトチオフェン型のジカルボン酸 **3**、及びナフトセレンフェン型のジカルボン酸 **7** では、酸素-カルコゲン原子間の 1,4 型のカルコゲン結合だけでなく、炭素原子を介したテトレル結合も確認され、共役系に対して付加的に働く相互作用としてカルコゲン結合の配座制御に寄与していることを明らかにした。一方で、ナフトフラン型のジカルボン酸 **6** では、予想通り酸素原子同士の間には働くカルコゲン結合は確認されなかったが、テトレル結合を介してカルボキシ基が芳香環とほぼ同一平面上に配座制御されていることを見出した。さらに、ナフトチオフェン型のロジウム二核錯体の創製に向けて、軸性不斉 δ -アミノ酸誘導体の合成を検討した。このうち、ジペプチド *rac*-**9** の結晶構造からは、エステル部位の 1,4 型のカルコゲン結合に加えて、アミド部位に 1,5 型のカルコゲン結合が確認され、これらのカルコゲン結合を介した配座制御が明確な立体構造の形成に寄与していることを明らかにした。



(2) 立体選択的な分子内 C-H 挿入反応の開発と天然 γ -ラク톤の不斉合成

合成したナフトチオフェン型のロジウム二核錯体 **10b** が、基質 **11** の分子内 C-H 挿入反応を高収率・高立体選択的に触媒することを見出し、その結果として天然 γ -ラクトン類の短工程での不斉合成も可能になった。錯体 (*S*)-**10b** の X 線結晶構造解析の結果、カルボキシレート部位、及びアミド部位の硫黄-酸素原子間に複数のカルコゲン結合が確認され、このカルコゲン結合を介した配座制御によって構築された明確かつ意図した立体構造が、優れた不斉誘起を示した主要因であることが示唆された。



実験の部

実験項

General Information

Uncorrected melting points were measured by using a Yanagimoto micro melting point apparatus or a Büchi Melting Point M-565. NMR spectra were obtained with a JEOL ECX-400 PKT, a JEOL ECA-600, a Bruker UltraShield 300, or a Bruker Ascend 500 spectrometer. Chemical shifts are given in units of ppm (^1H NMR in CDCl_3 : tetramethylsilane as the internal standard at 0 ppm, and CDCl_3 as the internal standard at 7.26 ppm; ^{13}C NMR in CDCl_3 : CDCl_3 as the internal standard at 77.16 ppm; ^{31}P NMR in CDCl_3 : H_3PO_4 as the internal standard at 0 ppm; ^1H NMR in acetone- d_6 : acetone- d_6 as the internal standard at 2.05 ppm; ^{13}C NMR in acetone- d_6 : acetone- d_6 as the internal standard at 29.84 ppm and 206.26 ppm; ^1H NMR in methanol- d_4 : methanol- d_4 as the internal standard at 3.31 ppm; ^{13}C NMR in methanol- d_4 : methanol- d_4 as the internal standard at 49.00 ppm; ^1H NMR in $\text{DMSO}-d_6$: $\text{DMSO}-d_6$ as the internal standard at 2.50 ppm; ^{13}C NMR in $\text{DMSO}-d_6$: $\text{DMSO}-d_6$ as the internal standard at 39.52 ppm). Spin–spin coupling constants are given in units of Hz. IR spectra were recorded on a JASCO FT-IR 4200 or a JASCO FT-IR 4600 spectrometer. HRMS was recorded on a JEOL GCmate II (for EI), a JEOL MStation JMS-700 spectrometer (for FAB), on a Bruker Daltonics Impact HD-KC or a Shimadzu LCMS-IT-TOF (for ESI). The specific rotation was recorded on a JASCO P-2200 polarimeter. UV/Vis spectra were recorded with a JASCO V-550 UV/Vis spectrophotometer. CD spectra were recorded with a JASCO J-720W spectropolarimeter. All microwave experiments were performed with a Biotage Initiator⁺.

Column chromatography on silica gel was carried out using silica gel 60 N (spherical, neutral, 63–210 μm , Kanto Chemical Co., Inc.). TLC analyses and preparative TLC analyses were performed on commercial glass plates bearing a 0.25 mm layer or 0.5 mm layer of Merck Kiesel-gel 60 F₂₅₄, respectively. Analytical HPLC was carried out with a JASCO PU-2089 Plus instrument equipped with a Daicel CHIRALPAK IC (4.6 mm \times 250 mm), CHIRALPAK ID (4.6 mm \times 250 mm), CHIRALCEL AD-H (4.6 mm \times 250 mm), a COSMOSIL CHiRAL 5A (4.6 mm \times 250 mm), a COSMOSIL CHiRAL 5B (4.6 mm \times 250 mm), or a COSMOSIL CHiRAL 5C (4.6 mm \times 250 mm), and a JASCO UV-2075 Plus for UV/Vis detector (detection: 254 nm). Or, analytical HPLC was run with a JASCO PU-4180 instrument equipped with a JASCO UV-4075 for UV/Vis detector (detection: 254 nm, 230 nm, or 225 nm). Preparative HPLC was run with a JASCO PU-2086 Plus instrument equipped with a COSMOSIL 5SL-II (20 mm \times 250 mm) and a JASCO UV-2075 Plus for UV/Vis detector (detection: 254 nm). Or, preparative HPLC was run with a YMC Multiple Preparative HPLC LC-forte/R instrument (detection: 254–320 nm).

All chemical reagents were obtained from common commercial sources, and used as received.

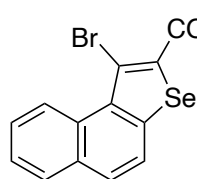
第 1 章に関する実験

Preparation of Axially Chiral Biaryl Dicarboxylic Acids Bearing Chalcogen Atoms

Syntheses of Naphthoselenophene-Type Biaryl Dicarboxylic Acids (*S*)-7 and (*R*)-7 (Scheme 6)

The construction of naphthoselenophene ring was carried out according to the previous report for the construction of selenophene rings by Arsenyan, P. and co-workers.³⁰

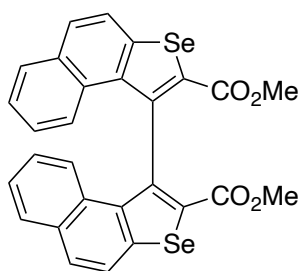
Methyl 1-bromonaphtho[2,1-*b*]selenophene-2-carboxylate (**23**)



Selenium dioxide (8.86 g, 79.8 mmol, 2.00 equiv.) was dissolved in 48 wt% of aqueous hydrogen bromide (39.7 mL, 351 mmol, 8.80 equiv.) at rt. After being stirred at rt for 30 min, a solution of methyl 3-(naphthalen-1-yl)propionate (**22**)³¹ (8.39 g, 39.9 mmol, 1.00 equiv.) and cyclohexene (4.85 mL, 47.9 mmol, 1.20 equiv.) in 1,4-dioxane (200 mL) was added dropwise, and the reaction mixture was stirred at 70 °C for 12 h. Then, the resulting mixture was diluted with AcOEt and water, and extracted with AcOEt. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 9:1), and the obtained solid was further washed with CHCl₃/*n*-hexane to afford **23** (6.49 g, 44% yield).

Pale yellow solid; M.p. 130–131 °C; ¹H NMR (300 MHz, CDCl₃) δ 10.01 (d, *J* = 8.7 Hz, 1H), 8.00–7.89 (m, 1H), 7.89–7.78 (m, 2H), 7.74–7.55 (m, 2H), 3.96 (s, 3H); ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 163.2, 143.2, 133.0, 132.6, 131.9, 129.6, 129.4, 129.3, 126.8, 126.2, 123.3, 123.0, 115.5, 52.8; IR (neat) 1718, 1480, 1212, 1192, 1047, 804, 787, 777, 752, 675 cm⁻¹; HRMS (EI) *m/z*: [M]⁺ Calcd for C₁₄H₉BrO₂Se 367.8951; Found 367.8953.

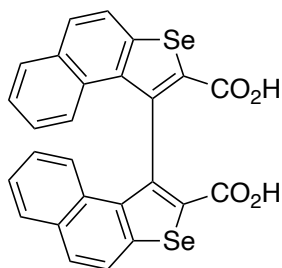
Dimethyl [1,1'-binaphtho[2,1-*b*]selenophene]-2,2'-dicarboxylate (*rac*-**S1**)



A solution of **23** (4.88 g, 13.3 mmol, 1.00 equiv.) and Cu powder (4.21 g, 66.3 mmol, 5.00 equiv.) in DMF (20 mL) was refluxed for 7 h under a N₂ atmosphere. After cooling to rt, the reaction mixture was filtered, washed with CHCl₃ to remove Cu, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 4:1 to CHCl₃ only) to afford **S1** containing DMF (3.70 g, <97% yield). For physical data, the obtained solid was further washed with CHCl₃/*n*-hexane to give pure **S1**.

Pale yellow solid; M.p. 260–261 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.06 (d, *J* = 8.7 Hz, 2H), 7.89–7.81 (m, 4H), 7.42–7.35 (m, 2H), 7.31 (ddd, *J* = 8.1, 7.0, 1.1 Hz, 2H), 7.02 (ddd, *J* = 8.5, 6.9, 1.4 Hz, 2H), 3.57 (s, 6H); ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 163.4, 145.6, 144.0, 135.6, 132.3, 132.2, 131.4, 129.2, 129.1, 127.2, 125.5, 123.6, 122.9, 52.5; IR (neat) 1710, 1486, 1433, 1262, 1223, 1058, 813, 799, 741, 718 cm⁻¹; HRMS (EI) *m/z*: [M]⁺ Calcd for C₂₈H₁₈O₄Se₂ 577.9535; Found 577.9538.

[1,1'-Binaphtho[2,1-*b*]selenophene]-2,2'-dicarboxylic acid (*rac*-**7**)



To a solution of **S1** (3.70 g, 6.42 mmol, 1.00 equiv.) in THF/MeOH/H₂O (2:1:1, 200 mL), KOH (5.00 g, 75.7 mmol, 11.8 equiv.) was added at rt. After being refluxed for 5 h, the reaction mixture was cooled to rt, and washed with CPME. The aqueous layer was acidified with 2 M aq. HCl, and extracted with AcOEt. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was washed with CHCl₃ to afford racemic **7** (3.03 g, 83% yield in 2 steps from **23**).

White solid; M.p. >300 °C; ¹H NMR (300 MHz, acetone-*d*₆) δ 11.20 (br s, 2H), 8.30 (d, *J* = 8.8 Hz, 2H), 8.01–7.92 (m, 4H), 7.43 (dq, *J* = 8.7, 0.8 Hz, 2H), 7.34 (ddd, *J* = 8.1, 7.0, 1.1 Hz, 2H), 7.04 (ddd, *J* = 8.6, 6.9, 1.4 Hz, 2H); ¹³C{¹H} NMR (75 MHz, acetone-*d*₆) δ 164.3, 145.8, 144.8, 136.6, 134.1, 133.3, 133.0, 130.2, 129.4, 127.6, 126.3, 124.8, 123.3; ¹³C{¹H} NMR (126 MHz, CD₃OD) δ 166.21 (COOH); IR (neat) 1672, 1645, 1479, 1435, 1308, 1262, 1199, 796, 709, 455 cm⁻¹; HRMS (EI) *m/z*: [*M*]⁺ Calcd for C₂₆H₁₄O₄Se₂ 549.9222; Found 549.9223.

Optical Resolution of Racemic **7** (Scheme 6)

Optical resolution of *rac*-**7** was conducted according to our previous report for the synthesis of optically active naphthothiophene-type dicarboxylic acid **3**.²⁰

(*S*)-[1,1'-Binaphtho[2,1-*b*]selenophene]-2,2'-dicarboxylic acid ((*S*)-**7**)

Racemic **7** (500 mg, 912 μmol, 1.00 equiv.) was completely dissolved in acetone (100 mL) at rt. To the solution, a solution of (1*S*,2*S*)-1,2-diphenylethylenediamine ((*S,S*)-**5**) (96.8 mg, 456 μmol, 0.500 equiv.) in acetone (10 mL) was added at rt. After being stirred at rt for 21 h, the precipitated solids were collected, and washed with acetone.* The obtained solids were dissolved in acetone/2 M aq. HCl, and the solution was extracted with AcOEt. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was washed with CHCl₃ to afford (*S*)-**7** (124 mg, 25% yield). The enantiomeric excess of (*S*)-**7** was determined to be >99% ee by HPLC analysis; HPLC (CHIRAL 5B (4.6 mm × 250 mm), *n*-hexane/EtOH/TFA = 90/10/0.1, flow rate = 1.0 mL/min, *l* = 254 nm) *t*_R = 12.1 min (for (*R*)-**7**), 17.5 min (for (*S*)-**7**).

CD (MeCN, 0.0240 mM, 25 °C) λ_{ext} (Δε): 345 (−14.8), 329 (−12.7), 293 (−4.25), 271 (−3.48), 246 (83.5), 232 (−93.1), 211 (15.0) nm.

*The filtrate was concentrated *in vacuo* to remove solvent, and the obtained residue was dissolved in acetone/2 M aq. HCl. Then, the solution was extracted with AcOEt. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. Finally, the single crystal of *rac*-**7** was obtained by recrystallization from a solution of the residue in MeOH.

Crystallographic data for the single crystal of *rac*-**7** obtained by recrystallization from MeOH: C₂₆H₁₄O₄Se₂, *M* = 548.29, 0.30 × 0.30 × 0.30 mm³, monoclinic, *P*2₁/*n*, *a* = 10.0447(3) Å, *b* = 10.1059(3) Å, *c* = 25.0609(7) Å, α =

90° , $\beta = 95.305(7)^\circ$, $\gamma = 90^\circ$, $V = 2533.05(13) \text{ \AA}^3$, $Z = 4$, $\rho_{\text{calcd}} = 1.438 \text{ g cm}^{-3}$, $T = 293(2) \text{ K}$, 24413 reflections measured, 4612 unique. The final R_1 and wR were 0.0565 and 0.1386 (all data). These data have been deposited with the Cambridge Crystallographic Data Center as CCDC 2144807.

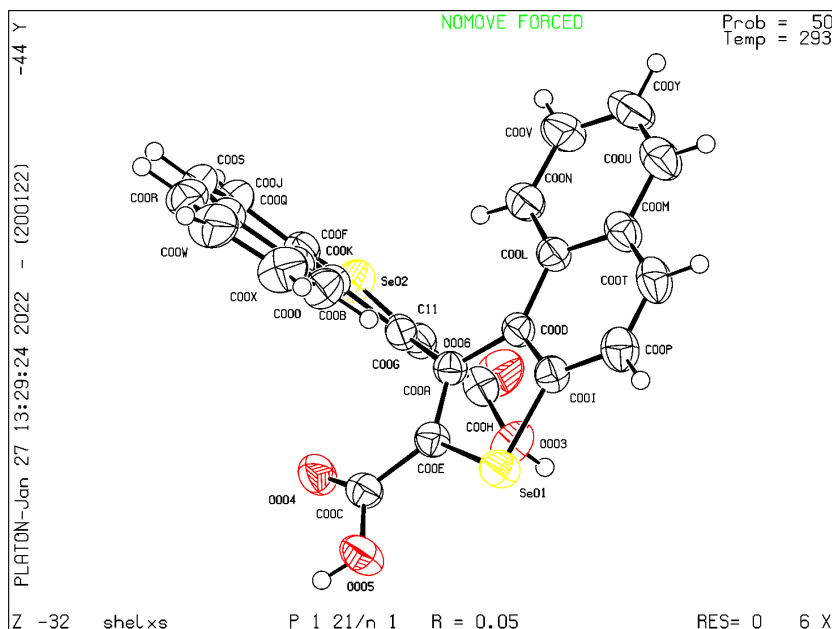


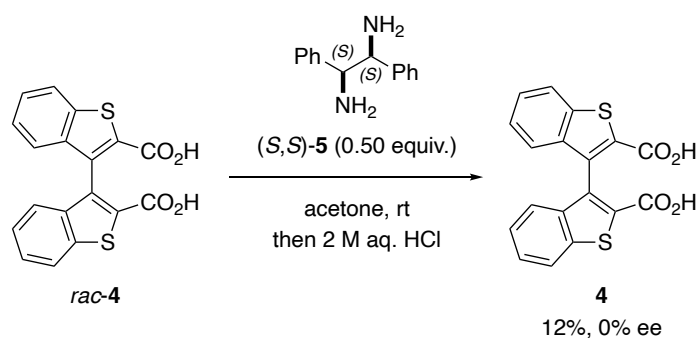
Figure S1. ORTEP Diagram of the Single Crystal of Racemic **7** (50% Probability).

(*R*)-[1,1'-Binaphtho[2,1-*b*]selenophene]-2,2'-dicarboxylic acid ((*R*)-**7**)

(*R*)-**7** was also obtained from *rac*-**7** by using (*R,R*)-**5** instead of (*S,S*)-**5**. Yield: 111 mg (22% from 500 mg of *rac*-**7**, >99% ee).

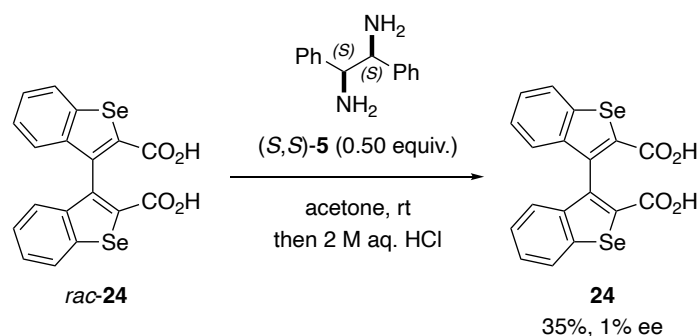
$[\alpha]_{\text{D}}^{19} = +157.9$ (c 0.8, MeOH for (*R*)-isomer (>99% ee)); CD (MeCN, 0.0240 mM, 25 °C) λ_{ext} ($\Delta\epsilon$): 345 (15.6), 330 (13.0), 293 (4.35), 272 (3.89), 246 (−90.0), 232 (98.8), 211 (−18.5) nm; UV (MeCN, 0.0240 mM, 25 °C) λ_{max} ($\log\epsilon$): 338 (4.42), 327 (4.48), 290 (4.23), 236 (4.74), 205 (4.67) nm.

The absolute configuration of each isomer of **7** was determined by comparing Cotton effects of its CD spectrum with those of (*R*)-**3** and (*S*)-**3**.



Scheme S1. Attempt for the Optical Resolution of Benzothiophene-Type *Rac-4*.

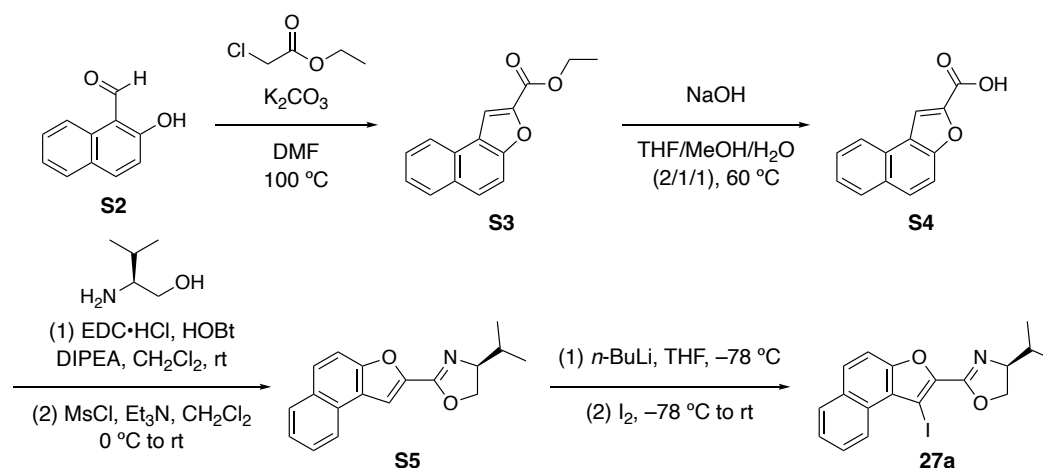
Racemic **4**¹⁸ (500 mg, 1.41 mmol, 1.00 equiv.) was completely dissolved in acetone (20 mL) at rt. To the solution, a solution of (*S,S*)-**5** (150 mg, 705 μmol , 0.500 equiv.) in acetone (10 mL) was added at rt. After being stirred at rt for 7 h, the precipitated solids were collected, and washed with acetone. The obtained solids were dissolved in acetone/2 M aq. HCl, and the solution was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give **4** (58.4 mg, 12% yield). The enantiomeric excess of **4** was determined to be 0% ee by HPLC analysis; HPLC (CHIRAL 5B (4.6 mm \times 250 mm), *n*-hexane/EtOH/TFA = 90/10/0.1, flow rate = 0.5 mL/min, λ = 254 nm) t_R = 15.0 min (for (*R*)-**4**), 20.4 min (for (*S*)-**4**).



Scheme S2. Attempt for the Optical Resolution of Benzoselenophene-Type *Rac-24*.

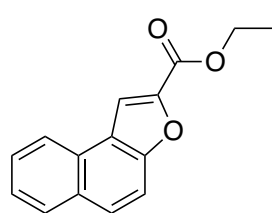
Racemic **24**³² (500 mg, 1.12 mmol, 1.00 equiv.) was completely dissolved in acetone (50 mL) at rt. To the solution, a solution of (*S,S*)-**5** (118 mg, 558 μmol , 0.500 equiv.) in acetone (10 mL) was added at rt. After being stirred at rt for 2 h, the precipitated solids were collected, and washed with acetone. The obtained solids were dissolved in acetone/2 M aq. HCl, and the solution was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give **24** (175 mg, 35% yield). The enantiomeric excess of **24** was determined to be 1% ee by HPLC analysis; HPLC (CHIRAL 5B (4.6 mm \times 250 mm), *n*-hexane/EtOH/TFA = 90/10/0.1, flow rate = 0.5 mL/min, λ = 254 nm) t_R = 16.1 min (for (*R*)-**24**), 21.3 min (for (*S*)-**24**).

Syntheses of Naphthofuran-Type Biaryl Dicarboxylic Acids (*R*)-6 and (*S*)-6 (Scheme 7-2)



Scheme S3. Synthesis of Naphthofuran-Type Coupling Precursor **27a**.

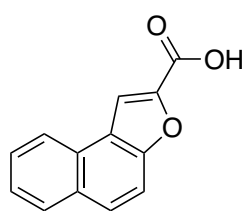
Ethyl naphtho[2,1-*b*]furan-2-carboxylate (**S3**)



To a solution of 2-hydroxy-1-naphthoaldehyde (**S2**) (5.00 g, 29.0 mmol, 1.00 equiv.) and K_2CO_3 (12.0 g, 87.1 mmol, 3.00 equiv.) in DMF (40 mL), ethyl 2-chloroacetate (4.64 mL, 43.6 mmol, 1.50 equiv.) was added at rt under a N_2 atmosphere. After being stirred at 100 °C for 16 h, the reaction mixture was cooled to rt, filtered, and washed with AcOEt. Then, the filtrate was diluted with H_2O , and extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO_2 , n -hexane:AcOEt = 9:1) to afford **S3** (5.24 g, 75% yield).

White solid; M.p. 96–97 °C; 1H NMR (500 MHz, $CDCl_3$) δ 8.18–8.13 (m, 1H), 8.02 (d, J = 1.0 Hz, 1H), 7.98–7.93 (m, 1H), 7.89–7.84 (m, 1H), 7.70 (dd, J = 9.1, 1.0 Hz, 1H), 7.64 (ddd, J = 8.2, 7.0, 1.3 Hz, 1H), 7.54 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H), 4.48 (q, J = 7.1 Hz, 2H), 1.47 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 159.6, 154.1, 145.2, 130.6, 129.2, 129.1, 128.1, 127.4, 125.5, 123.5, 122.9, 112.9, 61.6, 14.5 (One carbon signal was overlapped); IR (neat) 1724, 1551, 1324, 1222, 1168, 1122, 1018, 821, 759, 742 cm^{-1} ; HRMS (EI) m/z : $[M]^+$ Calcd for $C_{15}H_{12}O_3$ 240.0787; Found 240.0783.

Naphtho[2,1-*b*]furan-2-carboxylic acid (**S4**)

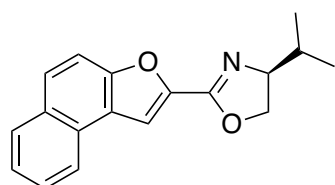


To a solution of **S3** (13.6 g, 56.6 mmol) in THF/MeOH (2:1, 225 mL), 2 M aq. NaOH (75 mL) was added at rt. After being stirred at 60 °C for 39.5 h, the reaction mixture was cooled to rt, and washed with CPME. The aqueous layer was acidified with 2 M aq. HCl, and extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give **S4** (11.9 g, 99% yield).

White solid; M.p. 200–201 °C; 1H NMR (500 MHz, CD_3OD) δ 8.30–8.26 (m, 1H), 8.16 (d, J = 1.0 Hz, 1H),

8.03–7.98 (m, 1H), 7.95 (d, $J = 9.0$ Hz, 1H), 7.72 (dd, $J = 9.1, 1.0$ Hz, 1H), 7.66 (ddd, $J = 8.2, 7.0, 1.3$ Hz, 1H), 7.56 (ddd, $J = 8.2, 7.0, 1.2$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CD_3OD) δ 162.4, 155.3, 146.9, 132.0, 130.3, 130.0, 129.5, 128.4, 126.5, 124.5, 124.1, 113.9, 113.4; IR (neat) 1675, 1552, 1411, 1328, 1174, 798, 756, 741, 577, 419 cm^{-1} ; HRMS (EI) m/z : $[\text{M}]^+$ Calcd for $\text{C}_{13}\text{H}_8\text{O}_3$ 212.0474; Found 212.0473.

(S)-4-Isopropyl-2-(naphtho[2,1-*b*]furan-2-yl)-4,5-dihydrooxazole (**S5**)

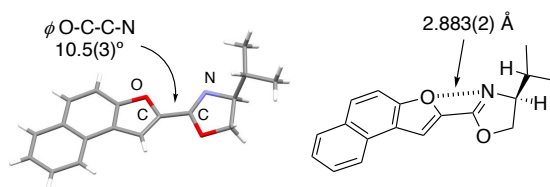


To a solution of **S4** (13.3 g, 62.7 mmol, 1.00 equiv.), EDC•HCl (18.0 g, 94.0 mmol, 1.50 equiv.) and HOBT•H₂O (14.4 g, 94.0 mmol, 1.50 equiv.) in CH_2Cl_2 (200 mL), DIPEA (32.8 mL, 188 mmol, 3.00 equiv.) and L-valinol (10.5 mL, 94.0 mmol, 1.50 equiv.) were added at rt. After being stirred at rt for 21 h, the reaction mixture was quenched with 2 M aq. HCl, and extracted with CHCl_3 .

The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue.

Then, the residue was dissolved in CH_2Cl_2 (200 mL), and Et_3N (26.2 mL, 188 mmol, 3.00 equiv.) and MsCl (8.40 mL, 108 mmol, 1.72 equiv.) were added to the solution at 0 °C under a N_2 atmosphere. After being stirred at rt for 41 h, the reaction mixture was concentrated *in vacuo* to give a residue, and the residue was dissolved in MeOH/2 M aq. NaOH. The mixture was extracted with CPME, and the organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO_2 , *n*-hexane:AcOEt = 9:1 to 17:3 to 4:1 to 3:1) to afford **S5** (7.52 g, 43% yield).

White solid; M.p. 136–137 °C; $[\alpha]_{\text{D}}^{16} = -68.3$ (c 0.7, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 8.14 (d, $J = 8.1$ Hz, 1H), 7.96 (d, $J = 8.1$ Hz, 1H), 7.82 (d, $J = 9.0$ Hz, 1H), 7.79 (s, 1H), 7.72 (d, $J = 9.0$ Hz, 1H), 7.62 (ddd, $J = 8.2, 6.8, 1.3$ Hz, 1H), 7.53 (ddd, $J = 8.1, 6.8, 1.2$ Hz, 1H), 4.54–4.47 (m, 1H), 4.25–4.17 (m, 2H), 2.00–1.90 (m, $J = 6.7$ Hz, 1H), 1.10 (d, $J = 6.7$ Hz, 3H), 0.98 (d, $J = 6.8$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 156.4, 153.8, 143.9, 130.7, 129.1, 128.01, 127.98, 127.1, 125.3, 123.5, 123.2, 112.9, 109.6, 73.2, 70.7, 32.9, 19.3, 18.4; IR (neat) 1671, 1548, 1521, 1369, 1164, 1094, 969, 808, 747, 420 cm^{-1} ; HRMS (EI) m/z : $[\text{M}]^+$ Calcd for $\text{C}_{18}\text{H}_{17}\text{NO}_2$ 279.1259; Found 279.1259.



Crystallographic data for the single crystal of **S5** obtained by recrystallization from CHCl_3 /*n*-hexane: $\text{C}_{18}\text{H}_{16}\text{NO}_2$, $M = 278.32$, $0.30 \times 0.30 \times 0.30$ mm^3 , orthorhombic, $P2_12_12_1$, $a = 6.2140(2)$ Å, $b = 14.4760(5)$ Å, $c = 15.7146(5)$ Å, $\alpha = 90^\circ$, $\beta = 90^\circ$, $\gamma = 90^\circ$, $V = 1413.59(8)$ Å³, $Z = 4$, $\rho_{\text{calcd}} = 1.308$ g cm^{-3} , $T = 296.15$ K, 15579 reflections measured, 2588 unique. The final R_1 and wR were 0.0365 and 0.0815 (all data). These data have been deposited with the Cambridge Crystallographic Data Center as CCDC 2144822.

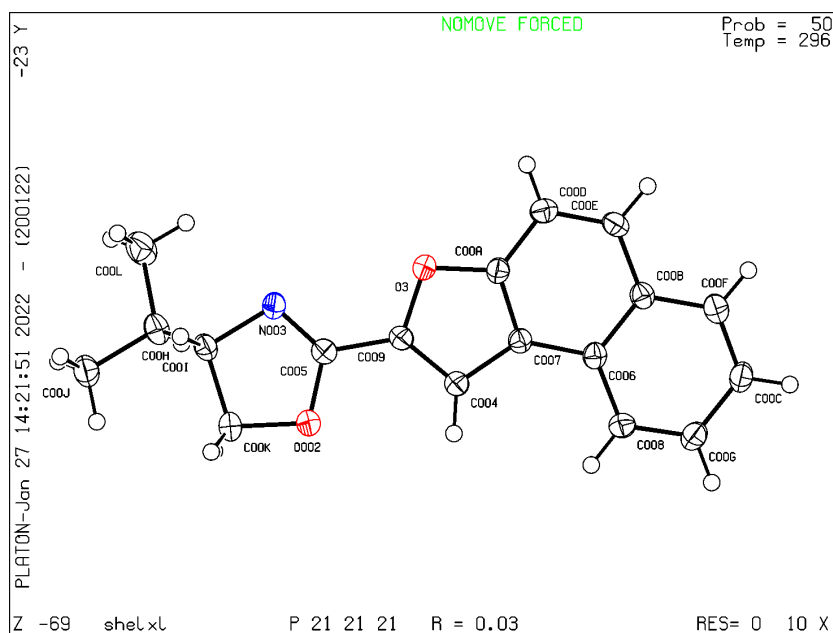
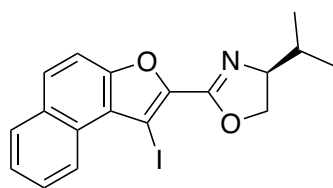


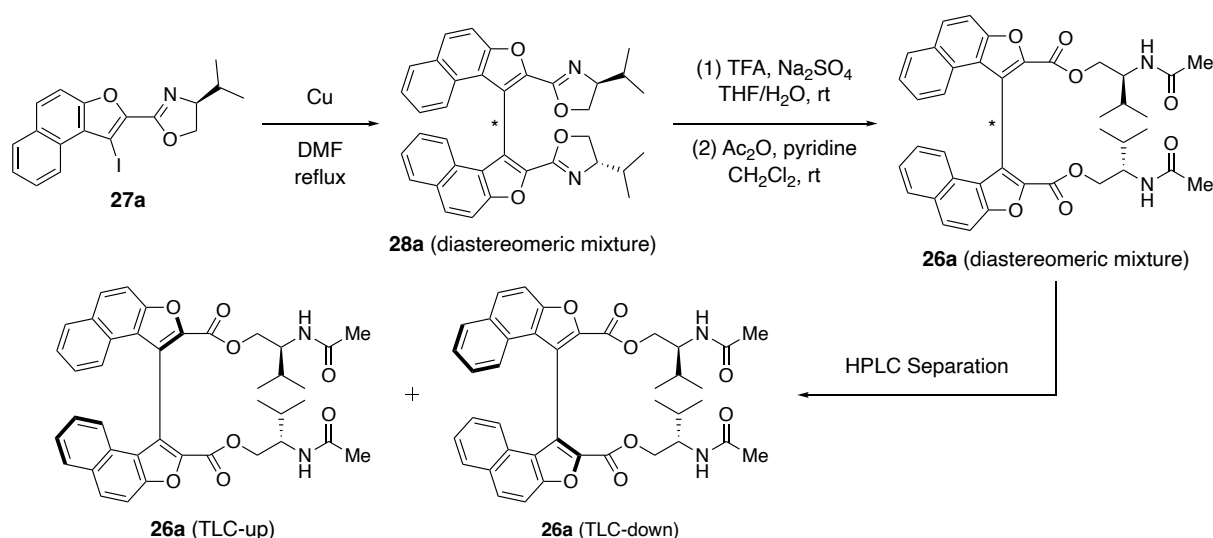
Figure S2. ORTEP Diagram of the Single Crystal of **S5** (50% Probability).

(*S*)-2-(1-Iodonaphtho[2,1-*b*]furan-2-yl)-4-isopropyl-4,5-dihydrooxazole (**27a**)



To a solution of **S5** (652 mg, 2.33 mmol, 1.00 equiv.) in THF (30 mL), *n*-BuLi (1.60 M in *n*-hexane, 1.75 mL, 2.80 mmol, 1.20 equiv.) was added at $-78\text{ }^{\circ}\text{C}$ under a N_2 atmosphere. After being stirred at $-78\text{ }^{\circ}\text{C}$ for 0.5 h, I_2 (889 mg, 3.50 mmol, 1.50 equiv.) was added in one portion. After being stirred at rt for 41 h, the reaction mixture was quenched with sat. aq. $\text{Na}_2\text{S}_2\text{O}_3$, and extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO_2 , *n*-hexane:AcOEt = 9:1) to afford **27a** (769 mg, 81% yield).

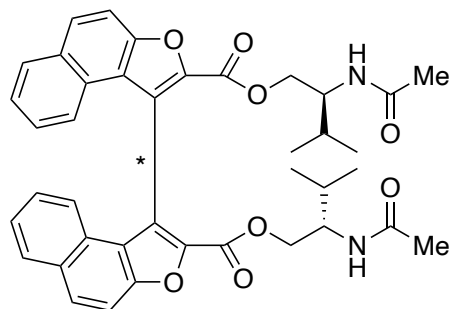
White solid; M.p. $90\text{--}91\text{ }^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{17} = -46.3$ (*c* 0.8, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 9.52 (d, $J = 8.4$ Hz, 1H), 7.99–7.95 (m, 1H), 7.85 (d, $J = 9.0$ Hz, 1H), 7.73–7.67 (m, 2H), 7.57 (ddd, $J = 8.1, 6.9, 1.2$ Hz, 1H), 4.57–4.49 (m, 1H), 4.28–4.19 (m, 2H), 2.01–1.90 (m, 1H), 1.11 (d, $J = 6.8$ Hz, 3H), 1.00 (d, $J = 6.7$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 156.2, 153.1, 143.5, 131.2, 129.4, 129.3, 128.5, 126.7, 125.6, 122.0, 121.4, 112.5, 73.1, 70.7, 66.4, 33.0, 19.2, 18.4; IR (neat) 1638, 1195, 1120, 994, 963, 808, 795, 743, 685, 611 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{18}\text{H}_{17}\text{INO}_2$ 406.0299; Found 406.0325.



Scheme S4. Synthesis and HPLC Separation of Diastereomeric Mixture of **26a**.

(*R*_a)- or (*S*_a)-Bis((*S*)-2-acetamido-3-methylbutyl) [1,1'-binaphtho[2,1-*b*]furan]-2,2'-dicarboxylate

((*R*_a)- or (*S*_a)-**26a**)



A solution of **27a** (4.96 g, 12.2 mmol, 1.00 equiv.) and Cu powder (6.22 g, 97.9 mmol, 8.00 equiv.) in DMF (40 mL) was refluxed for 10 h under a N₂ atmosphere. After cooling to rt, the reaction mixture was filtered, and washed with AcOEt to remove Cu. The filtrate was diluted with H₂O, and extracted with AcOEt. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated in *vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 7:3 to 3:2) to afford diastereomeric mixture of **28a** (1.88 g).

The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 7:3 to 3:2) to afford diastereomeric mixture of **28a** (1.88 g).

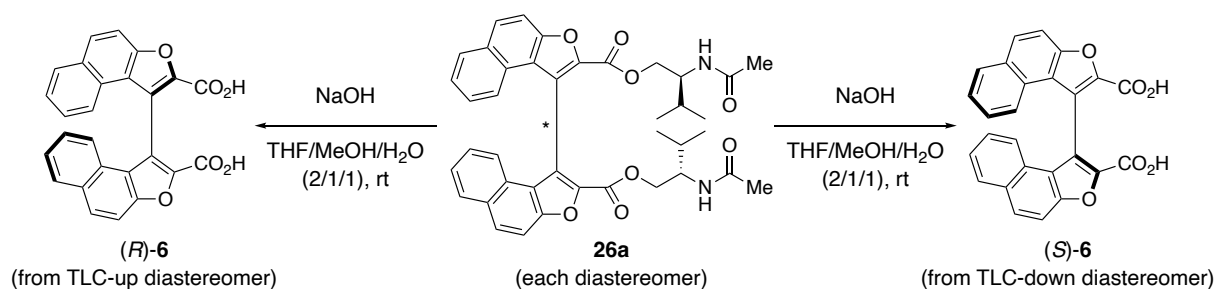
To a solution of diastereomeric mixture of **28a** (1.88 g, 3.38 mmol, 1.00 equiv.) in THF (20 mL), TFA (10.0 mL, 130 mmol), H₂O (2.00 mL, 111 mmol) and Na₂SO₄ (20.0 g, 141 mmol) were added at rt. After being stirred at rt for 15 min, the reaction mixture was filtered, and concentrated *in vacuo* to give a residue. Then, to a solution of the residue in CH₂Cl₂ (20 mL), pyridine (10.0 mL, 124 mmol) and Ac₂O (10.0 mL, 106 mmol) were added at rt under a N₂ atmosphere. After being stirred at rt for 12 h, the reaction mixture was quenched with 2 M aq. HCl, and extracted with CHCl₃. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, CHCl₃:MeOH = 10:1) to afford diastereomeric mixture of **26a**. This diastereomeric mixture of **26a** was separated by recycled prep. HPLC to give 1.10 g of **26a** (TLC-up, 27% yield in 3 steps from **27a**) and 849 mg of **26a** (TLC-down, 21% yield in 3 steps from **27a**); HPLC (COSMOSIL 5SL-II (20 mm × 250 mm), CHCl₃/acetone = 10/1, flow rate = 20 mL/min, λ = 254 nm).

26a (TLC-up, (*R*_a)-isomer)

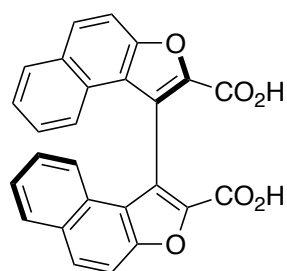
Pale yellow amorphous solid; $[\alpha]_D^{17} = -116.2$ (*c* 0.7, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 8.10–8.03 (m, 2H), 8.03–7.97 (m, 2H), 7.94 (d, *J* = 9.1 Hz, 2H), 7.59–7.52 (m, 2H), 7.48 (ddd, *J* = 8.3, 7.1, 1.3 Hz, 2H), 7.30 (ddd, *J* = 8.3, 7.0, 1.3 Hz, 2H), 4.12 (qd, *J* = 11.6, 2.8 Hz, 4H), 3.91 (d, *J* = 9.3 Hz, 2H), 3.50 (tt, *J* = 9.4, 2.8 Hz, 2H), 1.24 (s, 6H), 0.67 (d, *J* = 6.6 Hz, 6H), 0.56 (d, *J* = 6.6 Hz, 6H), 0.38 (dq, *J* = 9.7, 6.6 Hz, 2H); ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 169.4, 159.1, 154.1, 141.3, 131.2, 130.9, 129.7, 128.5, 128.2, 126.3, 122.3, 121.5, 120.7, 113.2, 65.9, 53.0, 28.5, 22.6, 19.3, 19.0; IR (neat) 1715, 1649, 1530, 1318, 1279, 1154, 806, 746, 517, 422 cm⁻¹; HRMS (FAB) *m/z*: [M+H]⁺ Calcd for C₄₀H₄₁N₂O₈ 677.2863; Found 677.2870.

26a (TLC-down, (*S*_a)-isomer)

Pale yellow amorphous solid; $[\alpha]_D^{18} = -174.5$ (*c* 0.5, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 8.05 (d, *J* = 9.1 Hz, 2H), 8.01–7.94 (m, 2H), 7.90 (d, *J* = 9.1 Hz, 2H), 7.53 (dd, *J* = 8.3, 1.1 Hz, 2H), 7.45 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 2H), 7.29–7.20 (m, 2H), 4.89 (d, *J* = 9.0 Hz, 2H), 4.21–4.01 (m, 4H), 3.60–3.46 (m, 2H), 1.92 (s, 6H), 0.51–0.41 (m, 6H), 0.37–0.16 (m, 8H); ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 170.1, 159.5, 153.9, 141.1, 131.2, 131.1, 129.5, 128.5, 128.2, 126.1, 122.4, 121.8, 120.9, 112.6, 66.1, 53.2, 28.2, 23.1, 19.2, 18.7; IR (neat) 1715, 1649, 1530, 1320, 1279, 1153, 1067, 805, 746, 425 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₄₀H₄₀NaN₂O₈ 699.2677; Found 699.2669.



Scheme S5. Hydrolysis of Each Diastereomer of **26a**.

(*R*)-[1,1'-Binaphtho[2,1-*b*]furan]-2,2'-dicarboxylic acid ((*R*)-6)

To a solution of **26a** (TLC-up diastereomer) (1.10 g, 1.63 mmol) in THF/MeOH (2:1, 30 mL), 2 M aq. NaOH (10 mL) was added at rt. After being stirred at rt for 11 h, the reaction mixture was washed with CPME. The aqueous layer was acidified with 2 M aq. HCl, and extracted with AcOEt. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was washed with CHCl₃/*n*-hexane (1:9) to afford (*R*)-**6** (565 mg, 82% yield). The enantiomeric excess of (*R*)-**6** was determined to be >99% ee by HPLC analysis; HPLC (CHIRAL 5A (4.6 mm × 250 mm), *n*-hexane/EtOH/TFA = 90/10/0.1, flow rate = 0.5 mL/min, *l* = 254 nm) *t*_R = 18.3 min (for (*S*)-**6**), 22.3 min (for (*R*)-**6**).

Pale yellow solid (decomposed during the measurement of melting point); ^1H NMR (500 MHz, CD_3OD) δ 8.02 (d, J = 9.1 Hz, 2H), 7.94 (d, J = 8.1 Hz, 2H), 7.87 (d, J = 9.1 Hz, 2H), 7.54–7.48 (m, 2H), 7.34 (ddd, J = 8.1, 6.9, 1.2 Hz, 2H), 7.12 (ddd, J = 8.3, 6.9, 1.2 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CD_3OD) δ 162.1, 154.9, 143.1, 132.5, 131.2, 130.3, 129.9, 128.3, 126.4, 123.2, 122.9, 122.5, 113.6; IR (neat) 2955, 1682, 1541, 1434, 1170, 1007, 954, 803, 744, 421 cm^{-1} ; HRMS (EI) m/z : $[\text{M}]^+$ Calcd for $\text{C}_{26}\text{H}_{14}\text{O}_6$ 422.0790; Found 422.0789; CD (MeCN, 0.0240 mM, 25 $^\circ\text{C}$) λ_{ext} ($\Delta\epsilon$): 338 (–29.2), 325 (–17.2), 313 (–6.59), 301 (15.2), 292 (21.3), 250 (43.7), 225 (–336), 215 (220), 201 (–28.5) nm; UV (MeCN, 0.0240 mM, 25 $^\circ\text{C}$) λ_{max} ($\log\epsilon$): 336 (4.38), 322 (4.35), 304 (4.50), 293 (4.46), 242 (4.52), 223 (4.82), 203 (4.73) nm.

Crystallographic data for the single crystal of (*R*)-**6** obtained by recrystallization from CHCl_3/n -hexane (One CHCl_3 molecule is included in the crystal): $\text{C}_{27}\text{H}_{15}\text{Cl}_3\text{O}_6$, $M = 541.74$, $0.20 \times 0.10 \times 0.020 \text{ mm}^3$, monoclinic, $P2_1$, $a = 10.297(6) \text{ \AA}$, $b = 11.221(6) \text{ \AA}$, $c = 11.547(7) \text{ \AA}$, $\alpha = 90^\circ$, $\beta = 90.256(6)^\circ$, $\gamma = 90^\circ$, $V = 1334.2(13) \text{ \AA}^3$, $Z = 2$, $\rho_{\text{calcd}} = 1.349 \text{ g cm}^{-3}$, $T = 100(2) \text{ K}$, 22784 reflections measured, 6402 unique. The final R_1 and wR were 0.1054 and 0.2533 (all data). These data have been deposited with the Cambridge Crystallographic Data Center as CCDC 2144806.

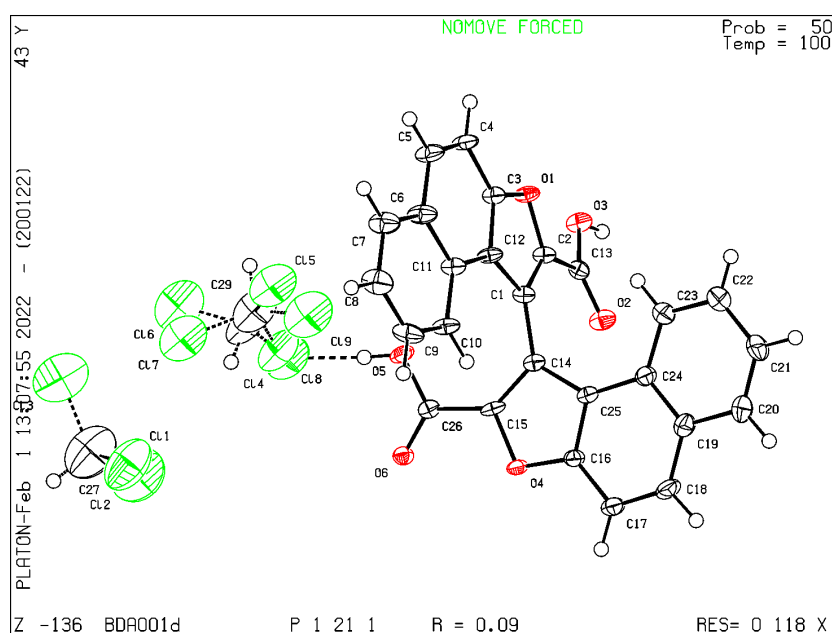
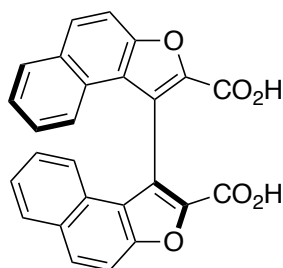


Figure S3. ORTEP Diagram of the Single Crystal of (*R*)-**6** (50% Probability).

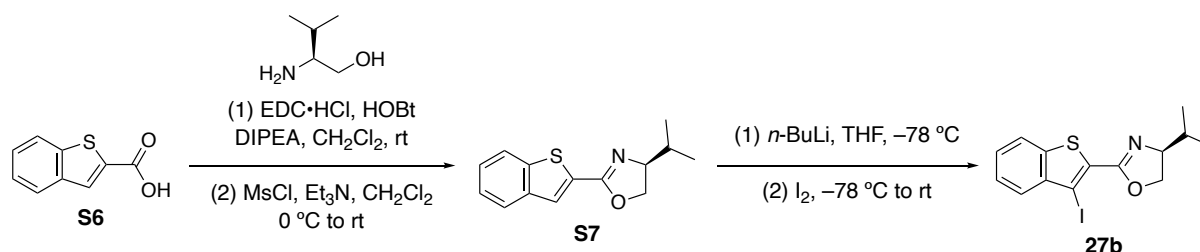
(*S*)-[1,1'-Binaphtho[2,1-*b*]furan]-2,2'-dicarboxylic acid ((*S*)-**6**)



To a solution of **26a** (TLC-down diastereomer) (1.16 g, 1.71 mmol) in THF/MeOH (2:1, 30 mL), 2 M aq. NaOH (10 mL) was added at rt. After being stirred at rt for 8 h, the reaction mixture was washed with CPME. The aqueous layer was acidified with 2 M aq. HCl, and extracted with AcOEt. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was washed with CHCl₃/*n*-hexane (1:9) to afford (*S*)-**6** (621 mg, 86% yield, >99% ee).

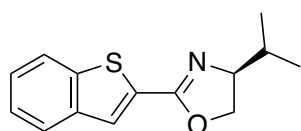
[α]_D¹⁹ = +205.5 (*c* 0.7, MeOH for (*S*)-isomer (>99% ee)); CD (MeCN, 0.0240 mM, 25 °C) λ_{ext} ($\Delta\epsilon$): 338 (30.5), 325 (17.1), 314 (6.30), 300 (−18.2), 292 (−23.8), 250 (−46.7), 225 (352), 215 (−229), 201 (28.2) nm.

Syntheses of Benzothiophene-Type Biaryl Dicarboxylic Acids (*R*)-**4** and (*S*)-**4** (Scheme 7-2)



Scheme S6. Synthesis of Benzothiophene-Type Coupling Precursor **27b**.

(*S*)-2-(Benzo[*b*]thiophen-2-yl)-4-isopropyl-4,5-dihydrooxazole (**S7**)

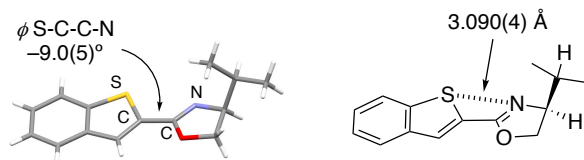


To a solution of benzo[*b*]thiophene-2-carboxylic acid (**S6**) (10.0 g, 56.1 mmol, 1.00 equiv.), EDC·HCl (13.4 g, 70.1 mmol, 1.25 equiv.) and HOBT·H₂O (10.7 g, 70.1 mmol, 1.25 equiv.) in CH₂Cl₂ (100 mL), DIPEA (29.3 mL, 168 mmol, 3.00 equiv.) and L-valinol (7.81 mL, 70.1 mmol, 1.25 equiv.) were added at rt. After being stirred at rt for 119 h, the reaction mixture was quenched with 2 M aq. HCl, and extracted with CHCl₃. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue.

Then, the residue was dissolved in CH₂Cl₂ (200 mL), and Et₃N (23.5 mL, 168 mmol, 3.00 equiv.) and MsCl (6.56 mL, 84.2 mmol, 1.50 equiv.) were added to the solution at 0 °C under a N₂ atmosphere. After being stirred at rt for 108 h, the reaction mixture was concentrated *in vacuo* to give a residue, and the residue was dissolved in MeOH/2 M aq. NaOH. The mixture was extracted with CPME, and the organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 9:1 to 5:1) to afford **S7** (10.4 g, 75% yield).

White solid; M.p. 89–90 °C; [α]_D¹⁸ = −66.0 (*c* 0.9, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 7.89–7.78 (m, 3H), 7.44–7.33 (m, 2H), 4.52–4.38 (m, 1H), 4.24–4.09 (m, 2H), 1.99–1.82 (m, 1H), 1.04 (d, *J* = 6.7 Hz, 3H), 0.94 (d, *J*

= 6.7 Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3) δ 159.5, 141.3, 139.3, 130.7, 127.2, 126.2, 124.9, 124.8, 122.6, 73.1, 70.8, 32.9, 19.1, 18.2; IR (neat) 1643, 1440, 1363, 1175, 1029, 944, 876, 751, 729, 433 cm^{-1} ; HRMS (EI) m/z : $[\text{M}]^+$ Calcd for $\text{C}_{14}\text{H}_{15}\text{NOS}$ 245.0874; Found 245.0874.



Crystallographic data for the single crystal of **S7** obtained by recrystallization from CHCl_3/n -hexane: $\text{C}_{14}\text{H}_{15}\text{NOS}$, $M = 245.33$, $0.30 \times 0.30 \times 0.20 \text{ mm}^3$, orthorhombic, $P2_12_12_1$, $a = 8.2440(2) \text{ \AA}$, $b = 11.7093(3) \text{ \AA}$, $c = 12.8710(3) \text{ \AA}$, $\alpha = 90^\circ$, $\beta = 90^\circ$, $\gamma = 90^\circ$, $V = 1242.46(6) \text{ \AA}^3$, $Z = 4$, $\rho_{\text{calcd}} = 1.311 \text{ g cm}^{-3}$, $T = 296 \text{ K}$, 13763 reflections measured, 2262 unique. The final R_1 and wR were 0.0256 and 0.0602 (all data). These data have been deposited with the Cambridge Crystallographic Data Center as CCDC 2144821.

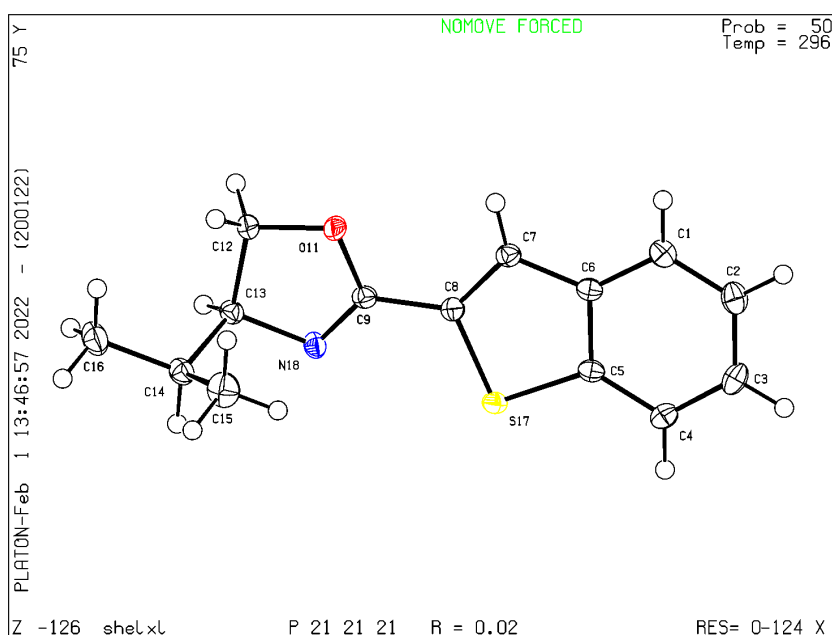
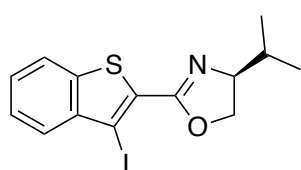


Figure S4. ORTEP Diagram of the Single Crystal of **S7** (50% Probability).

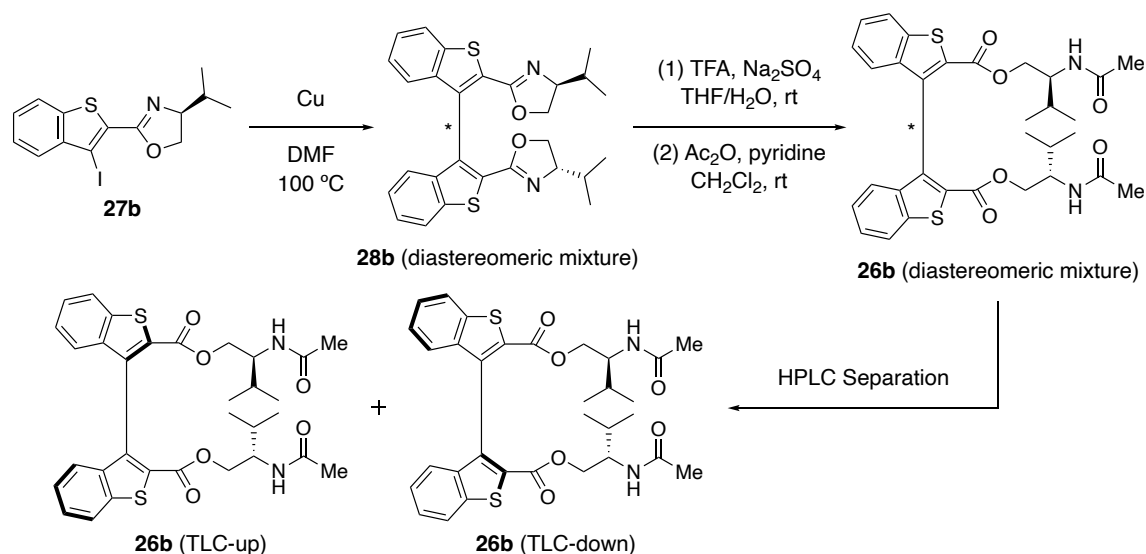
(S)-2-(3-Iodobenzo[*b*]thiophen-2-yl)-4-isopropyl-4,5-dihydrooxazole (27b**)**



To a solution of **S7** (4.00 g, 16.3 mmol, 1.00 equiv.) in THF (150 mL), *n*-BuLi (1.60 M in *n*-hexane, 15.3 mL, 24.5 mmol, 1.50 equiv.) was added at -78°C under a N_2 atmosphere. After being stirred at -78°C for 0.5 h, I_2 (6.21 g, 24.5 mmol, 1.50 equiv.) was added in one portion. After being stirred at rt for 11 h, the reaction mixture was quenched with sat. aq. $\text{Na}_2\text{S}_2\text{O}_3$, and extracted with AcOEt. The organic layer was washed

with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 9:1) to afford **27b** (5.79 g, 96% yield).

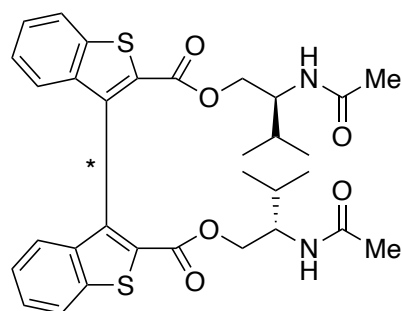
Yellow solid; M.p. 81–82 °C; [α]_D¹⁸ = –38.5 (*c* 1.6, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.93–7.86 (m, 1H), 7.82–7.77 (m, 1H), 7.50–7.42 (m, 2H), 4.51–4.46 (m, 1H), 4.26–4.15 (m, 2H), 1.97–1.86 (m, *J* = 6.6 Hz, 1H), 1.07 (d, *J* = 6.7 Hz, 3H), 0.98 (d, *J* = 6.7 Hz, 3H); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 158.6, 142.1, 139.3, 129.5, 127.6, 127.2, 125.8, 122.4, 83.7, 72.9, 70.8, 33.0, 19.0, 18.4; IR (neat) 1623, 1353, 1258, 1029, 1017, 945, 770, 759, 722, 710 cm^{–1}; HRMS (EI) *m/z*: [M]⁺ Calcd for C₁₄H₁₄INOS 370.9841; Found 370.9839.



Scheme S7. Synthesis and HPLC Separation of Diastereomeric Mixture of **26b**.

(*R*_a)- or (*S*_a)-Bis((*S*)-2-acetamido-3-methylbutyl) [3,3'-bibenzo[*b*]thiophene]-2,2'-dicarboxylate

((*R*_a)- or (*S*_a))-**26b**)



A solution of **27b** (8.00 g, 21.5 mmol, 1.00 equiv.) and Cu powder (11.0 g, 172 mmol, 8.00 equiv.) in DMF (40 mL) was stirred at 100 °C for 21 h under a N₂ atmosphere. After cooling to rt, the reaction mixture was filtered, and washed with AcOEt to remove Cu. The filtrate was diluted with H₂O and extracted with AcOEt. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to

give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 4:1 to 7:3) to afford diastereomeric mixture of **28b** (4.34 g).

To a solution of diastereomeric mixture of **28b** (4.34 g, 8.88 mmol, 1.00 equiv.) in THF (50 mL), TFA (10.0 mL, 130 mmol), H₂O (2.00 mL, 111 mmol) and Na₂SO₄ (20.0 g, 141 mmol) were added at rt. After being stirred at rt for 30 min, the reaction mixture was filtered, and concentrated *in vacuo* to give a residue. Then, to a solution of

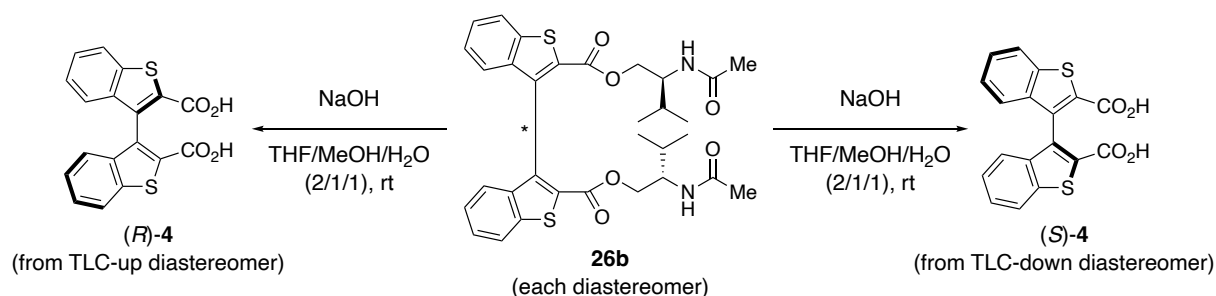
the residue in CH₂Cl₂ (50 mL), pyridine (10.0 mL, 124 mmol) and Ac₂O (10.0 mL, 106 mmol) were added at rt under a N₂ atmosphere. After being stirred at rt for 26 h, the reaction mixture was quenched with 2 M aq. HCl, and extracted with CHCl₃. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, CHCl₃:MeOH = 10:1) to afford diastereomeric mixture of **26b**. This diastereomeric mixture of **26b** was separated by recycled prep. HPLC to give 1.34 g of **26b** (TLC-up, 21% yield in 3 steps from **27b**) and 2.60 g of **26b** (TLC-down, 40% yield in 3 steps from **27b**); HPLC (COSMOSIL 5SL-II (20 mm × 250 mm), CHCl₃/acetone = 20/1, flow rate = 20 mL/min, λ = 254 nm).

26b (TLC-up, (*R*_a)-isomer)

White amorphous solid; $[\alpha]_D^{18} = -77.7$ (*c* 0.8, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 8.00 (dt, *J* = 8.2, 0.9 Hz, 2H), 7.55 (ddd, *J* = 8.2, 6.9, 1.4 Hz, 2H), 7.36 (ddd, *J* = 8.0, 6.9, 1.0 Hz, 2H), 7.32–7.27 (m, 2H), 4.45 (d, *J* = 9.3 Hz, 2H), 4.22 (dd, *J* = 11.5, 3.5 Hz, 2H), 3.99 (dd, *J* = 11.6, 3.1 Hz, 2H), 3.64 (tt, *J* = 9.1, 3.3 Hz, 2H), 1.67 (s, 6H), 0.96–0.79 (m, 2H), 0.79–0.65 (m, 12H); ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 169.5, 162.4, 140.6, 139.9, 135.5, 131.6, 127.9, 125.6, 124.8, 123.1, 66.3, 53.0, 28.6, 23.2, 19.2, 19.1; IR (neat) 3274, 1718, 1697, 1641, 1546, 1372, 1276, 1229, 1113, 757, 734 cm⁻¹; HRMS (FAB) *m/z*: [M+H]⁺ Calcd for C₃₂H₃₇N₂O₆S₂ 609.2093; Found 609.2103.

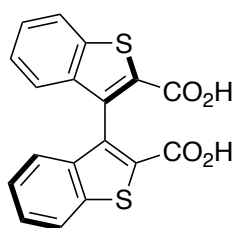
26b (TLC-down, (*S*_a)-isomer)

White solid; M.p. 184–185 °C; $[\alpha]_D^{18} = -171.6$ (*c* 0.8, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 7.97 (dt, *J* = 8.2, 0.9 Hz, 2H), 7.54 (ddd, *J* = 8.3, 7.0, 1.4 Hz, 2H), 7.34 (ddd, *J* = 8.1, 6.9, 1.0 Hz, 2H), 7.29–7.23 (m, 2H), 5.06 (d, *J* = 9.2 Hz, 2H), 4.20–4.00 (m, 4H), 3.59 (tt, *J* = 9.3, 3.2 Hz, 2H), 1.94 (s, 6H), 0.57 (d, *J* = 6.6 Hz, 6H), 0.47 (d, *J* = 6.6 Hz, 6H), 0.40–0.22 (m, 2H); ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 170.0, 162.8, 140.1, 140.0, 135.7, 131.0, 128.1, 125.9, 125.0, 122.9, 66.7, 53.0, 27.9, 23.2, 19.2, 19.1; IR (neat) 1693, 1632, 1555, 1496, 1374, 1283, 1241, 1091, 758, 733 cm⁻¹; HRMS (FAB) *m/z*: [M+H]⁺ Calcd for C₃₂H₃₇N₂O₆S₂ 609.2093; Found 609.2112.



Scheme S8. Hydrolysis of Each Diastereomer of **26b**.

(R)-[3,3'-Bibenzo[*b*]thiophene]-2,2'-dicarboxylic acid ((R)-4)

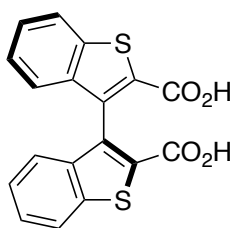


To a solution of **26b** (TLC-up diastereomer) (253 mg, 416 μmol) in THF/MeOH (2:1, 15 mL), 2 M aq. NaOH (5.0 mL) was added at rt. After being stirred at rt for 2.5 h, the reaction mixture was washed with CPME. The aqueous layer was acidified with 2 M aq. HCl, and extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give **(R)-4** (137 mg, 93% yield).

The enantiomeric excess of **(R)-4** was determined to be >99% ee by HPLC analysis; HPLC (CHIRAL 5B (4.6 mm \times 250 mm), *n*-hexane/EtOH/TFA = 90/10/0.1, flow rate = 0.5 mL/min, $\lambda = 254$ nm) $t_R = 15.0$ min (for **(R)-4**), 20.4 min (for **(S)-4**).

White solid (decomposed during the measurement of melting point); $[\alpha]_D^{19} = +80.3$ (c 0.7, MeOH for **(R)**-isomer (>99% ee)); ^1H NMR (300 MHz, acetone- d_6) δ 11.42 (br s, 2H), 8.10 (dt, $J = 8.2, 0.9$ Hz, 2H), 7.56 (ddd, $J = 8.2, 7.0, 1.3$ Hz, 2H), 7.37 (ddd, $J = 8.1, 6.9, 1.0$ Hz, 2H), 7.28 (ddd, $J = 8.2, 1.3, 0.8$ Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, acetone- d_6) δ 163.3, 141.2, 140.7, 137.2, 131.8, 128.2, 126.0, 125.3, 123.7; $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CD_3OD) δ 165.2 (COOH); IR (neat) 2852, 1666, 1498, 1430, 1245, 1091, 754, 729, 582, 422 cm^{-1} ; HRMS (EI) m/z : $[\text{M}]^+$ Calcd for $\text{C}_{18}\text{H}_{10}\text{O}_4\text{S}_2$ 354.0021; Found 354.0021; CD (MeCN, 0.0240 mM, 25 $^\circ\text{C}$) λ_{ext} ($\Delta\epsilon$): 337 (−3.73), 315 (5.94), 286 (36.2), 263 (−10.1), 245 (−8.54), 210 (−200), 200 (154) nm; UV (MeCN, 0.0240 mM, 25 $^\circ\text{C}$) λ_{max} (log ϵ): 316 (3.88), 283 (4.31), 233 (4.48), 205 (4.58) nm.

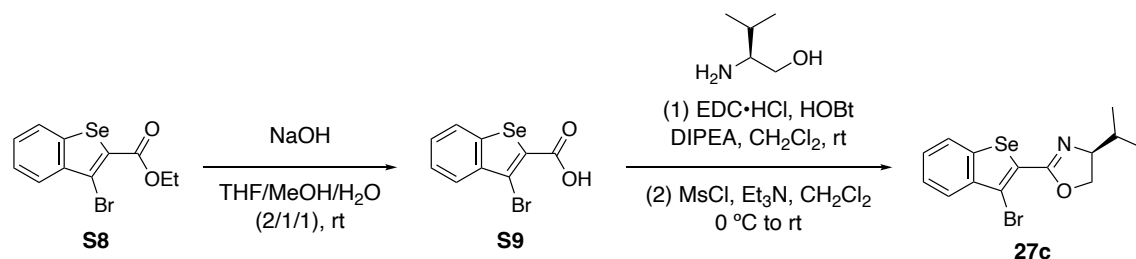
(S)-[3,3'-Bibenzo[*b*]thiophene]-2,2'-dicarboxylic acid ((S)-4)



To a solution of **26b** (TLC-down diastereomer) (398 mg, 654 μmol) in THF/MeOH (2:1, 15 mL), 2 M aq. NaOH (5.0 mL) was added at rt. After being stirred at rt for 3.5 h, the reaction mixture was washed with CPME. The aqueous layer was acidified with 2 M aq. HCl, and extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give **(S)-4** Yield: (217 mg, 94% yield, >99% ee).

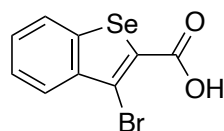
CD (MeCN, 0.0240 mM, 25 $^\circ\text{C}$) λ_{ext} ($\Delta\epsilon$): 338 (4.34), 313 (−4.74), 285 (−32.9), 263 (8.50), 245 (6.87), 210 (180), 200 (−138) nm.

Syntheses of Benzoselenophene-Type Biaryl Dicarboxylic Acids (*R*)-24 and (*S*)-24 (Scheme 7-2)



Scheme S9. Synthesis of Benzoselenophene-Type Coupling Precursor **27c**.

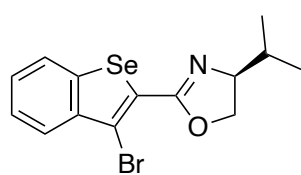
3-Bromobenzo[*b*]selenophene-2-carboxylic acid (**S9**)



To a solution of ethyl 3-bromobenzo[*b*]selenophene-2-carboxylate (**S8**)³⁰ (2.16 g, 6.50 mmol) in THF/MeOH (2:1, 30 mL), 2 M aq. NaOH (10 mL) was added at rt. After being stirred at rt for 5 h, the reaction mixture was washed with CPME. The aqueous layer was acidified with 2 M aq. HCl, and extracted with AcOEt. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give **S9** (1.80 g, 91% yield).

White solid; M.p. 278–288 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.23–8.15 (m, 1H), 8.03–7.96 (m, 1H), 7.63–7.50 (m, 2H); ¹³C{¹H} NMR (75 MHz, DMSO-*d*₆) δ 163.4, 140.3, 140.1, 131.8, 128.2, 127.0, 126.7, 126.3, 114.4; IR (neat) 1651, 1513, 1244, 899, 792, 749, 713, 607, 452, 416 cm⁻¹; HRMS (EI) *m/z*: [M]⁺ Calcd for C₉H₅BrO₂Se 308.8638; Found 308.8640.

(*S*)-2-(3-Bromobenzo[*b*]selenophen-2-yl)-4-isopropyl-4,5-dihydrooxazole (**27c**)

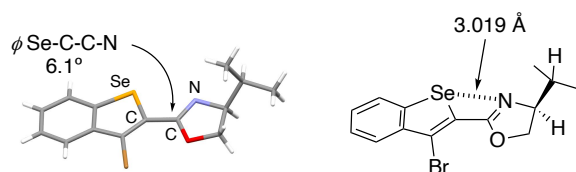


To a solution of **S9** (13.2 g, 43.3 mmol, 1.00 equiv.), EDC·HCl (10.4 g, 54.1 mmol, 1.25 equiv.) and HOBT·H₂O (8.29 g, 54.1 mmol, 1.25 equiv.) in CH₂Cl₂ (150 mL), DIPEA (22.6 mL, 130 mmol, 3.00 equiv.) and L-valinol (6.03 mL, 70.1 mmol, 1.25 equiv.) were added at rt. After being stirred at rt for 71 h, the reaction mixture was quenched with 2 M aq. HCl, and extracted with CHCl₃. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue.

Then, the residue was dissolved in CH₂Cl₂ (300 mL), and Et₃N (18.1 mL, 130 mmol, 3.00 equiv.) and MsCl (5.06 mL, 64.9 mmol, 1.50 equiv.) were added to the solution at 0 °C under a N₂ atmosphere. After being stirred at rt for 72 h, the reaction mixture was concentrated *in vacuo* to give a residue, and the residue was dissolved in MeOH/2 M aq. NaOH. The mixture was extracted with CPME, and the organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 9:1) to afford **27c**. This product was further purified by recrystallization from CHCl₃/*n*-hexane. Yield: 8.82 g (55%).

White prism; M.p. 111–112 °C; [α]_D¹⁸ = –34.1 (*c* 1, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 8.04–7.96 (m, 1H),

7.89–7.81 (m, 1H), 7.52–7.37 (m, 2H), 4.48 (dd, $J = 9.5, 8.1$ Hz, 1H), 4.27–4.09 (m, 2H), 2.00–1.82 (m, $J = 6.7$ Hz, 1H), 1.05 (d, $J = 6.8$ Hz, 3H), 0.96 (d, $J = 6.8$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3) δ 159.9, 141.0, 139.7, 127.6, 127.4, 127.3, 125.8, 125.5, 112.5, 72.8, 71.0, 32.9, 19.0, 18.2; IR (neat) 1619, 1523, 1351, 1278, 1256, 1007, 943, 754, 717, 427 cm^{-1} ; HRMS (EI) m/z : $[\text{M}]^+$ Calcd for $\text{C}_{14}\text{H}_{14}\text{BrNOSe}$ 370.9424; Found 370.9423.



Crystallographic data for the single crystal of **27c** obtained by recrystallization from CHCl_3/n -hexane: $\text{C}_{14}\text{H}_{14}\text{BrNOSe}$, $M = 371.13$, $0.30 \times 0.050 \times 0.050 \text{ mm}^3$, monoclinic, $I121$, $a = 9.6453(5) \text{ \AA}$, $b = 6.3804(3) \text{ \AA}$, $c = 23.2083(17) \text{ \AA}$, $\alpha = 90^\circ$, $\beta = 98.391(7)^\circ$, $\gamma = 90^\circ$, $V = 1412.97(15) \text{ \AA}^3$, $Z = 4$, $\rho_{\text{calcd}} = 1.745 \text{ g cm}^{-3}$, $T = 296 \text{ K}$, 7282 reflections measured, 2270 unique. The final R_1 and wR were 0.0513 and 0.0897 (all data). These data have been deposited with the Cambridge Crystallographic Data Center as CCDC 2144808.

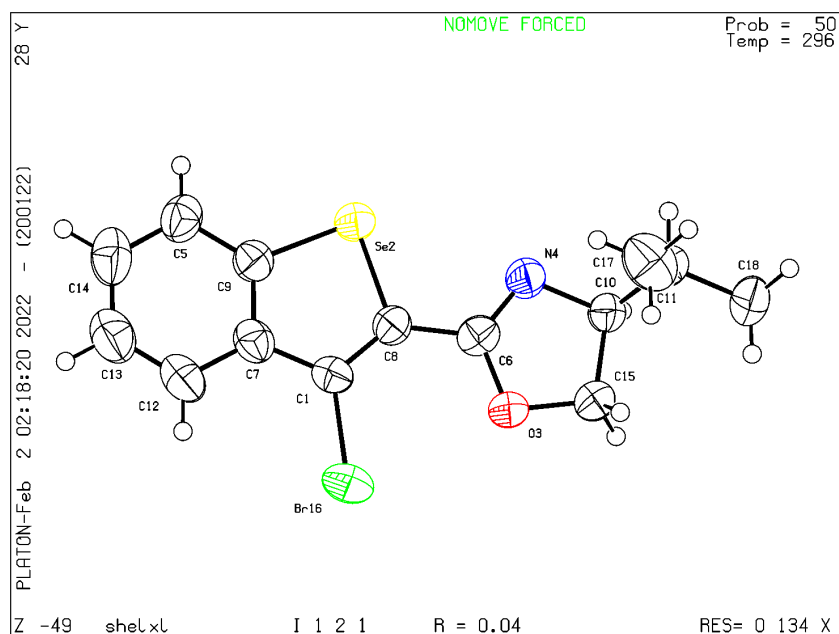
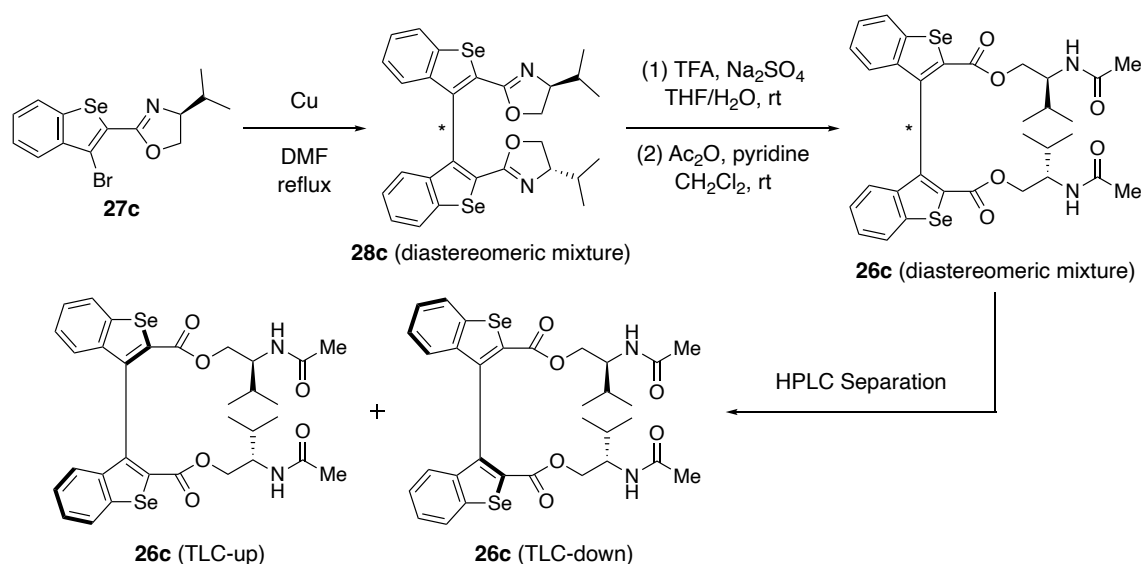


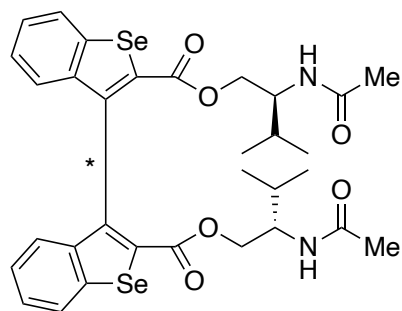
Figure S5. ORTEP Diagram of the Single Crystal of **27c** (50% Probability).



Scheme S10. Synthesis and HPLC Separation of Diastereomeric Mixture of **26c**.

(*R_a*)- or (*S_a*)-Bis((*S*)-2-acetamido-3-methylbutyl) [3,3'-bibenzo[*b*]selenophene]-2,2'-dicarboxylate

((*R_a*)- or (*S_a*))-**26c**)



In a microwave vial, **27c** (3.07 g, 8.27 mmol, 1.00 equiv.), Cu powder (4.21 g, 66.2 mmol, 8.00 equiv.) and DMF (15 mL) were added, and the resulting mixture was degassed with a N₂ gas and securely sealed. The vial was placed into microwave reactor, and heated 200 °C for 4 h. Then, the reaction mixture was filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂,

n-hexane:AcOEt = 4:1) to afford diastereomeric mixture of **28c** (1.16 g).

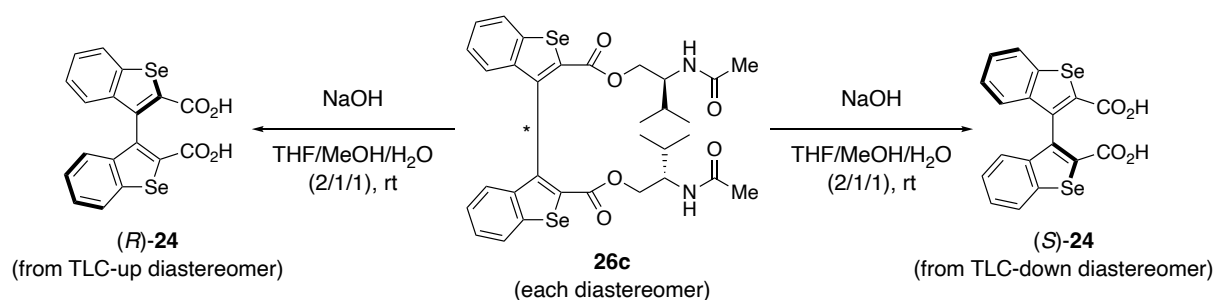
To a solution of diastereomeric mixture of **28c** (1.16 g, 1.99 mmol, 1.00 equiv.) in THF (20 mL), TFA (10.0 mL, 130 mmol), H₂O (2.00 mL, 111 mmol) and Na₂SO₄ (20.0 g, 141 mmol) were added at rt. After being stirred at rt for 25 min, the reaction mixture was filtered, and concentrated *in vacuo* to give a residue. Then, to a solution of the residue in CH₂Cl₂ (20 mL), pyridine (10.0 mL, 124 mmol) and Ac₂O (10.0 mL, 106 mmol) were added at rt under a N₂ atmosphere. After being stirred at rt for 12 h, the reaction mixture was quenched with 2 M aq. HCl, and extracted with CHCl₃. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, CHCl₃:MeOH = 20:1) to afford diastereomeric mixture of **26c**. This diastereomeric mixture of **26c** was separated by recycled prep. HPLC to give 441 mg of **26c** (TLC-up, 15% yield in 3 steps from **27c**) and 738 mg of **26c** (TLC-down, 25% yield in 3 steps from **27c**); HPLC (COSMOSIL 5SL-II (20 mm × 250 mm), CHCl₃/acetone = 15/1, flow rate = 20 mL/min, λ = 254 nm).

26c (TLC-up, (*R*_a)-isomer)

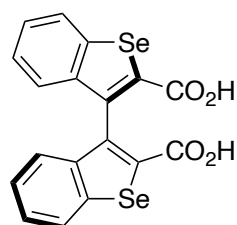
White amorphous solid; $[\alpha]_{\text{D}}^{19} = -64.1$ (*c* 0.8, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 8.03 (dt, *J* = 8.0, 0.9 Hz, 2H), 7.48 (ddd, *J* = 8.2, 7.0, 1.4 Hz, 2H), 7.33 (ddd, *J* = 8.1, 7.0, 1.1 Hz, 2H), 7.28–7.21 (m, 2H), 4.46 (d, *J* = 9.4 Hz, 2H), 4.21 (dd, *J* = 11.6, 3.5 Hz, 2H), 3.97 (dd, *J* = 11.6, 3.1 Hz, 2H), 3.66 (tt, *J* = 9.3, 3.3 Hz, 2H), 1.66 (s, 6H), 1.08–0.91 (m, 2H), 0.79–0.69 (m, 12H); ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 169.5, 163.6, 142.3, 142.1, 140.2, 134.7, 128.0, 127.0, 126.1, 125.8, 66.5, 53.1, 28.7, 23.2, 19.3, 19.2; IR (neat) 1715, 1687, 1640, 1543, 1370, 1276, 1220, 1103, 756, 727 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₃₂H₃₆NaN₂O₆Se₂ 727.0803; Found 727.0777.

26c (TLC-down, (*S*_a)-isomer)

White amorphous solid; $[\alpha]_{\text{D}}^{19} = -169.9$ (*c* 0.9, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 8.00 (dt, *J* = 8.1, 0.9 Hz, 2H), 7.47 (ddd, *J* = 8.2, 7.1, 1.4 Hz, 2H), 7.32 (ddd, *J* = 8.1, 7.0, 1.1 Hz, 2H), 7.22 (ddd, *J* = 8.1, 1.4, 0.6 Hz, 2H), 5.08 (d, *J* = 9.2 Hz, 2H), 4.17 (dd, *J* = 11.6, 3.2 Hz, 2H), 4.02 (dd, *J* = 11.6, 2.9 Hz, 2H), 3.58 (tt, *J* = 9.4, 3.0 Hz, 2H), 1.95 (s, 6H), 0.57 (d, *J* = 6.6 Hz, 6H), 0.46 (d, *J* = 6.6 Hz, 6H), 0.33–0.18 (m, 2H); ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 170.0, 163.9, 142.5, 141.6, 140.4, 133.9, 128.2, 127.2, 126.0, 125.9, 66.9, 53.1, 27.8, 23.2, 19.4, 19.2; IR (neat) 3276, 1689, 1649, 1507, 1370, 1271, 1217, 1068, 755, 728 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₃₂H₃₆NaN₂O₆Se₂ 727.0803; Found 727.0782.



Scheme S11. Hydrolysis of Each Diastereomer of **26c**.

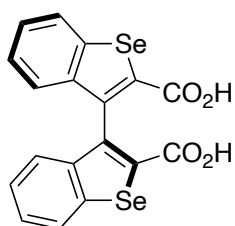
(R)-[3,3'-Bibenzo[*b*]selenophene]-2,2'-dicarboxylic acid (*(R)*-**24**)

To a solution of **26c** (TLC-up diastereomer) (441 mg, 628 μ mol) in THF/MeOH (2:1, 15 mL), 2 M aq. NaOH (5.0 mL) was added at rt. After being stirred at rt for 66 h, the reaction mixture was washed with CPME. The aqueous layer was acidified with 2 M aq. HCl, and extracted with AcOEt. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was

washed with CHCl₃/*n*-hexane (1:9) to afford *(R)*-**24** (233 mg, 83% yield). The enantiomeric excess of *(R)*-**24** was determined to be >99% ee by HPLC analysis; HPLC (CHIRAL 5B (4.6 mm \times 250 mm), *n*-hexane/EtOH/TFA = 90/10/0.1, flow rate = 0.5 mL/min, λ = 254 nm) *t*_R = 16.1 min (for *(R)*-**24**), 21.3 min (for *(S)*-**24**).

Pale yellow solid; M.p. 269–271 °C; ^1H NMR (500 MHz, acetone- d_6) δ 11.34 (br s, 2H), 8.17 (d, J = 8.0 Hz, 2H), 7.52–7.42 (m, 2H), 7.37–7.28 (m, 2H), 7.21 (dd, J = 8.1, 1.1 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, acetone- d_6) δ 164.4, 143.2, 142.8, 142.1, 134.5, 128.1, 127.2, 126.9, 126.1; $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CD_3OD) δ 166.3 (COOH); IR (neat) 2851, 1659, 1506, 1275, 1246, 756, 744, 724, 445, 420 cm^{-1} ; HRMS (EI) m/z : $[\text{M}]^+$ Calcd for $\text{C}_{18}\text{H}_{10}\text{O}_4\text{Se}_2$ 449.8909; Found 449.8909; CD (MeCN, 0.0240 mM, 25 °C) λ_{ext} ($\Delta\epsilon$): 351 (–5.97), 324 (7.64), 295 (26.0), 242 (3.32), 215 (–201), 204 (148) nm; UV (MeCN, 0.0240 mM, 25 °C) λ_{max} (log ϵ): 341 (3.96), 334 (3.95), 285 (4.33), 241 (4.49), 208 (4.58) nm.

(*S*)-[3,3'-Bibenzo[*b*]selenophene]-2,2'-dicarboxylic acid ((*S*)-**24**)



To a solution of **26c** (TLC-down diastereomer) (738 mg, 1.05 mmol) in THF/MeOH (2:1, 15 mL), 2 M aq. NaOH (5.0 mL) was added at rt. After being stirred at rt for 68 h, the reaction mixture was washed with CPME. The aqueous layer was acidified with 2 M aq. HCl, and extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue. The residue was washed with CHCl_3/n -hexane (1:9) to afford (*S*)-**24** (380 mg, 81% yield, >99% ee).

$[\alpha]_{\text{D}}^{19} = -104.7$ (c 0.2, MeOH for (*S*)-isomer (>99% ee)); CD (MeCN, 0.0240 mM, 25 °C) λ_{ext} ($\Delta\epsilon$): 352 (5.09), 325 (–8.92), 295 (–27.3), 241 (–3.87), 215 (201), 204 (–153) nm.

Crystallographic data for the single crystal of (*S*)-**24** obtained by recrystallization from THF/AcOEt/*n*-hexane: $\text{C}_9\text{H}_5\text{O}_2\text{Se}$, $M = 224.09$, $0.30 \times 0.30 \times 0.30 \text{ mm}^3$, orthorhombic, $C222_1$, $a = 11.9700(5) \text{ \AA}$, $b = 12.8292(6) \text{ \AA}$, $c = 13.9262(5) \text{ \AA}$, $\alpha = 90^\circ$, $\beta = 90^\circ$, $\gamma = 90^\circ$, $V = 2138.59(15) \text{ \AA}^3$, $Z = 8$, $\rho_{\text{calcd}} = 1.392 \text{ g cm}^{-3}$, $T = 296(2) \text{ K}$, 11536 reflections measured, 1966 unique. The final R_1 and wR were 0.0542 and 0.1535 (all data). These data have been deposited with the Cambridge Crystallographic Data Center as CCDC 2144805.

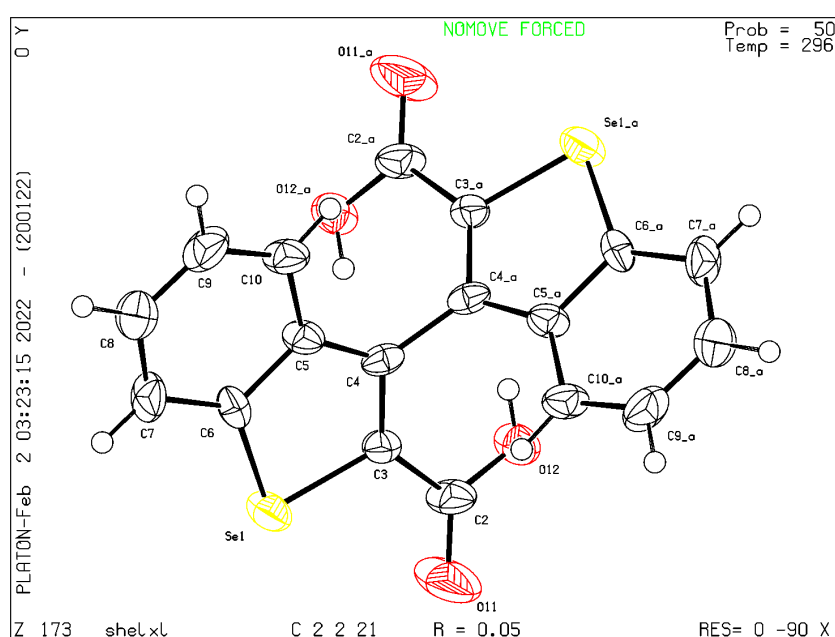
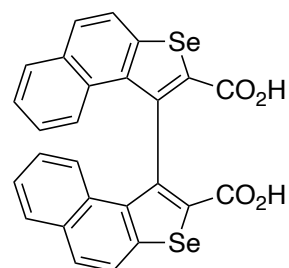
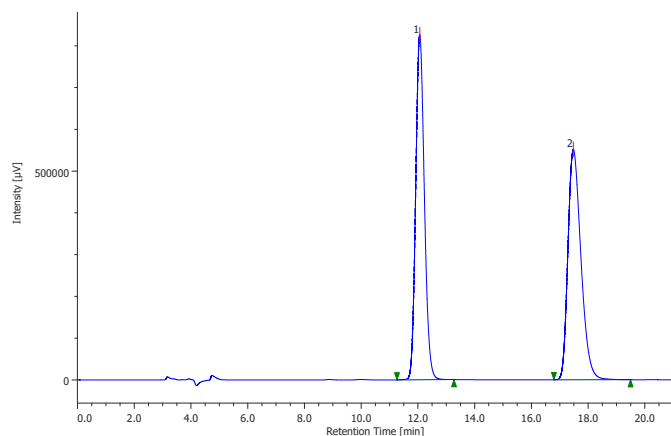


Figure S6. ORTEP Diagram of the Single Crystal of **24** (50% Probability).

HPLC Analysis for Determination of the Optical Purities of Synthetic Biaryl Dicarboxylic Acids

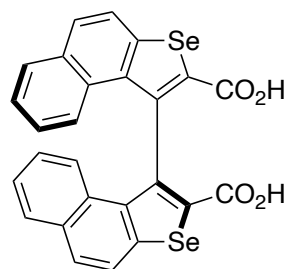
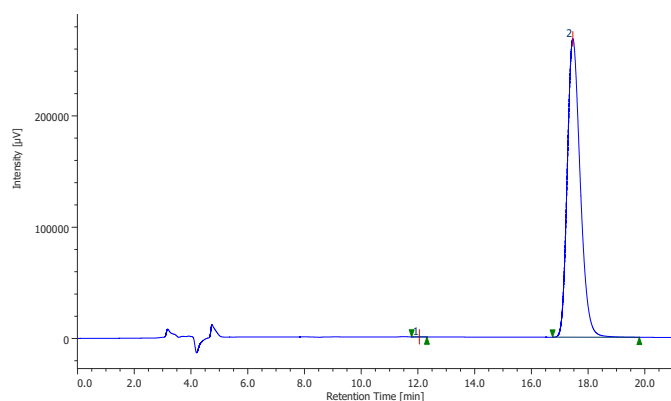
For naphthoselenophene-type biaryl dicarboxylic acid **7**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHiRAL 5B (4.6 mm × 250 mm), *n*-hexane/EtOH/TFA = 90/10/0.1, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of *rac*-**7**



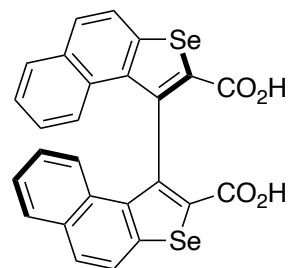
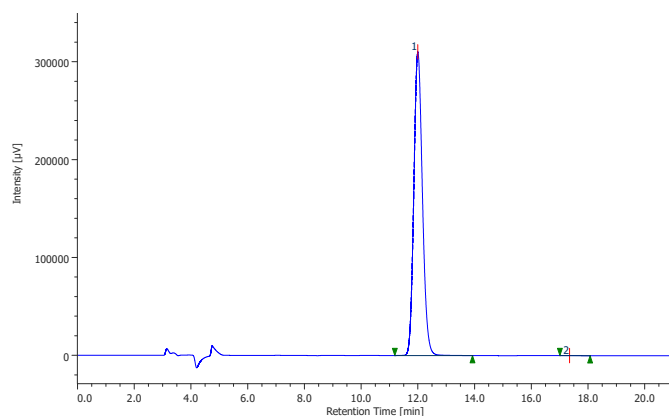
	Retention time (min)	Peak area (%)
1	12.1	49.96
2	17.5	50.04

(2) Chromatogram of (*S*)-**7** (>99% ee)



	Retention time (min)	Peak area (%)
1	12.0	0.03
2	17.5	99.97

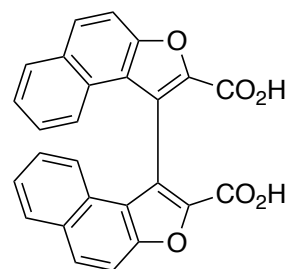
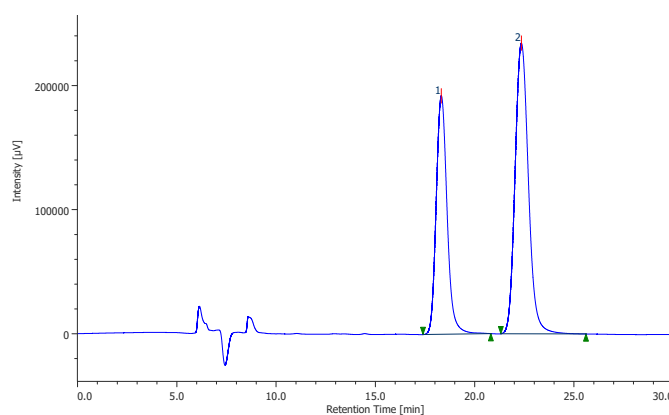
(3) Chromatogram of (*R*)-**7** (>99% ee)



	Retention time (min)	Peak area (%)
1	12.0	99.94
2	17.3	0.06

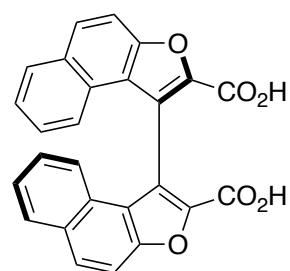
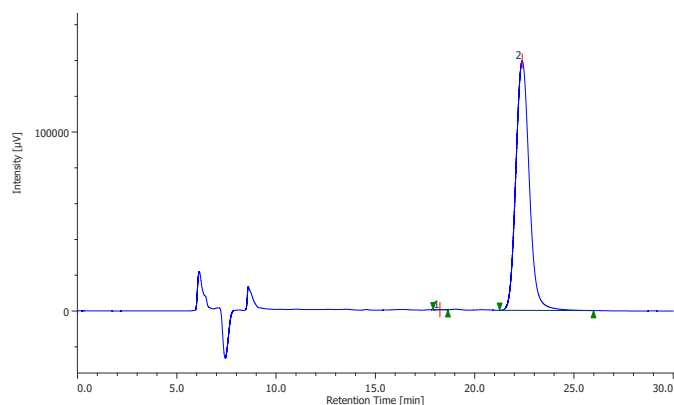
For naphthofuran-type biaryl dicarboxylic acid **6**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHIRAL 5A (4.6 mm \times 250 mm), *n*-hexane/EtOH/TFA = 90/10/0.1, flow rate = 0.5 mL/min, λ = 254 nm).

(1) Chromatogram of mixture of (*R*)-**6** and (*S*)-**6** (20% ee)



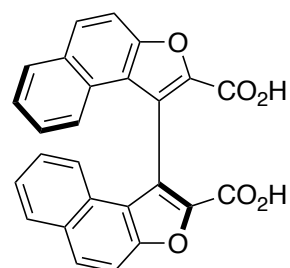
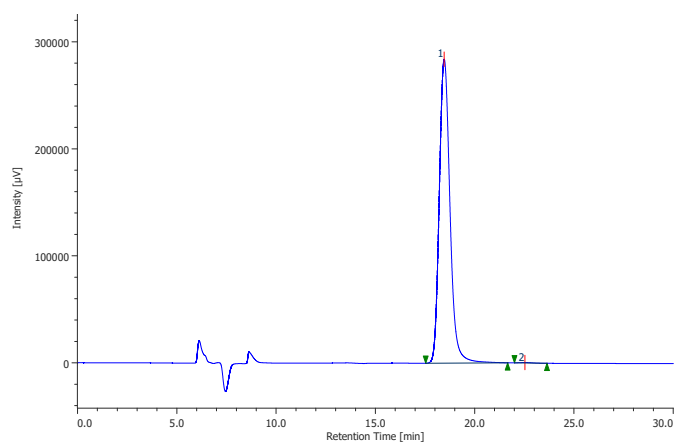
	Retention time (min)	Peak area (%)
1	18.3	40.245
2	22.3	59.755

(2) Chromatogram of (*R*)-**6** (>99% ee)



	Retention time (min)	Peak area (%)
1	18.3	0.02
2	22.4	99.98

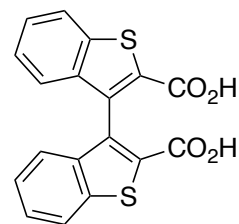
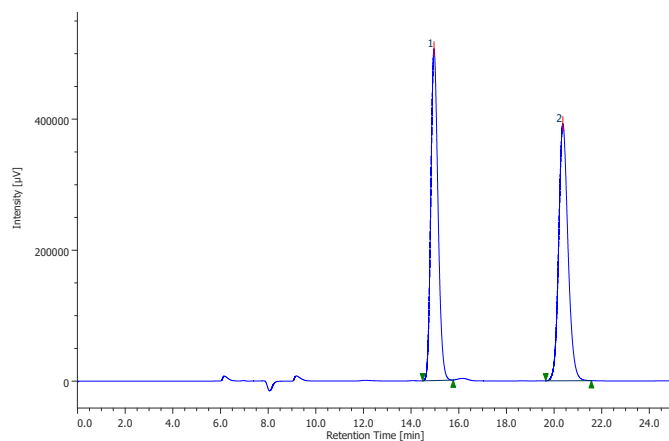
(3) Chromatogram of (*S*)-**6** (>99% ee)



	Retention time (min)	Peak area (%)
1	18.5	99.84
2	22.5	0.16

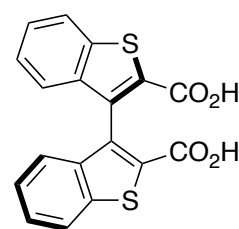
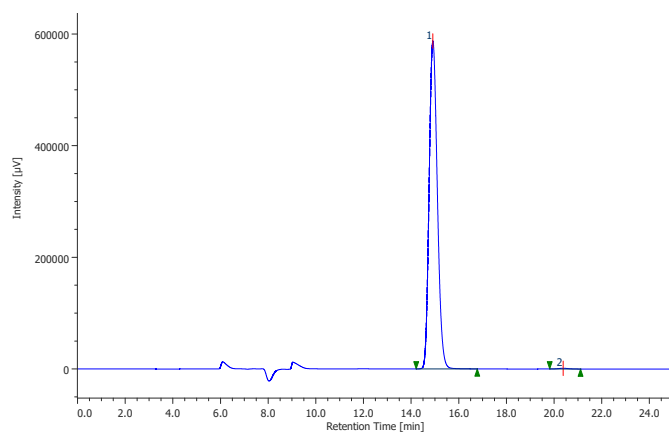
For benzothiophene-type biaryl dicarboxylic acid **4**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHiRAL 5B (4.6 mm × 250 mm), *n*-hexane/EtOH/TFA = 90/10/0.1, flow rate = 0.5 mL/min, λ = 254 nm).

(1) Chromatogram of *rac*-**4**



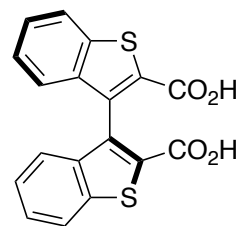
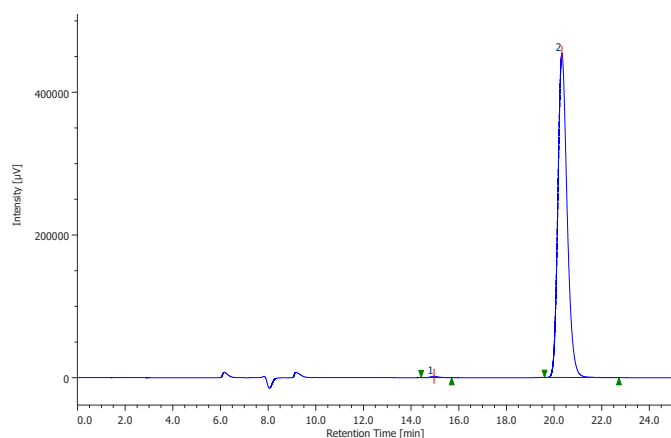
	Retention time (min)	Peak area (%)
1	15.0	49.91
2	20.4	50.09

(2) Chromatogram of (*R*)-**4** (>99% ee)



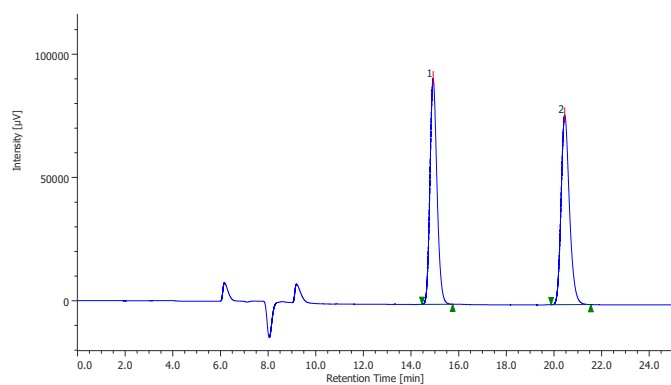
	Retention time (min)	Peak area (%)
1	14.9	99.74
2	20.4	0.26

(3) Chromatogram of (*S*)-**4** (>99% ee)



	Retention time (min)	Peak area (%)
1	15.0	0.365
2	20.3	99.635

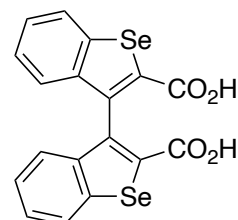
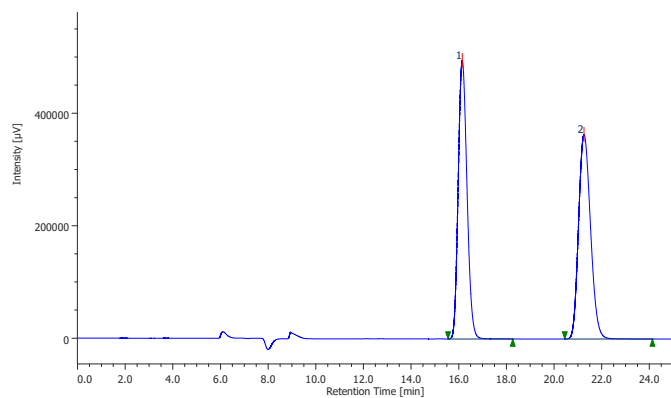
(4) Chromatogram of **4** (Scheme S1, 0% ee)



	Retention time (min)	Peak area (%)
1	14.9	50.01
2	20.4	49.99

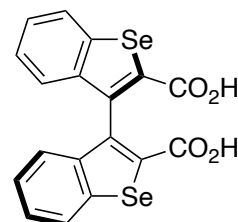
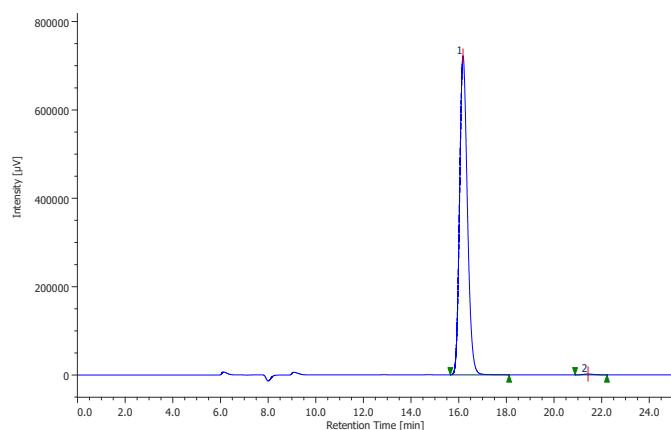
For benzoselenophene-type biaryl dicarboxylic acid **24**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHIRAL 5B (4.6 mm × 250 mm), *n*-hexane/EtOH/TFA = 90/10/0.1, flow rate = 0.5 mL/min, λ = 254 nm).

(1) Chromatogram of *rac*-**24**



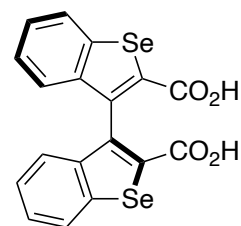
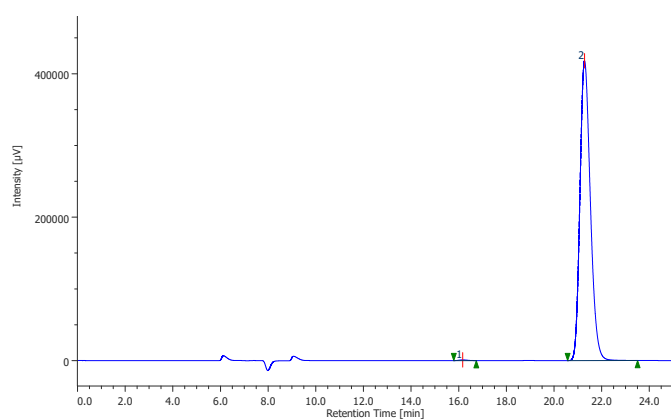
	Retention time (min)	Peak area (%)
1	16.1	49.98
2	21.3	50.02

(2) Chromatogram of (*R*)-**24** (>99% ee)



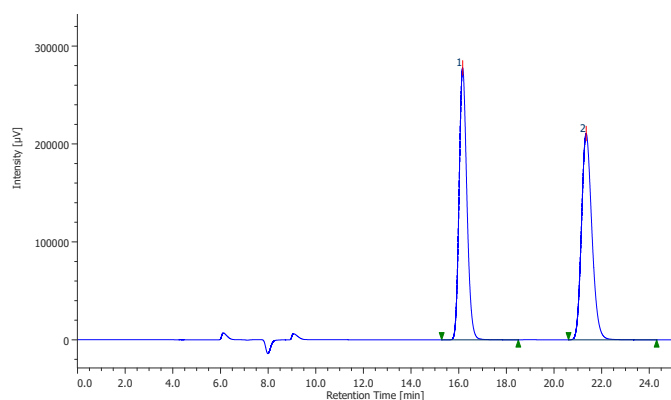
	Retention time (min)	Peak area (%)
1	16.2	99.64
2	21.4	0.36

(3) Chromatogram of (*S*)-**24** (>99% ee)



	Retention time (min)	Peak area (%)
1	16.1	0.19
2	21.3	99.81

(4) Chromatogram of **24** (Scheme S2, 1% ee)



	Retention time (min)	Peak area (%)
1	16.2	49.48
2	21.3	50.52

Determination of Racemization Barriers for **4** and **24**

The racemization barrier was determined by heating each biaryl dicarboxylic acid in chlorobenzene (boiling point: 132 °C) under reflux conditions. By monitoring the ee values at continuous time points, the plots of $\ln(ee_0/ee_t)$ to time for (*S*)-**4** and (*R*)-**24** were obtained as shown in Figure S7 and S8, respectively. Then, the racemization barrier energy ΔG_{rac}^\ddagger was calculated by the following Eyring equation.

$$\Delta G_{rac}^\ddagger = -RT \ln \left(\frac{hk_{rac}}{\kappa T k_B} \right)$$

Where,

k_{rac} : racemization rate constant, ΔG_{rac}^\ddagger : energy barrier for racemization,

T : temperature (405.15 K),

R : gas constant (8.314472 J/K•mol), h : Planck constant (6.63×10^{-34} J•s),

k_B : Boltzmann constant (1.38×10^{-23} J/K),

κ : kappa, transmission coefficient (which is usually unity for this calculation).

(1) For **4** ((*S*)-**4** was used for measurement).

Time (min)	% ee	$\ln(ee_0/ee_t)$
0	99.302	0
30	97.718	0.01608
60	94.954	0.044773
90	92.09	0.075399
120	89.572	0.103123
150	85.61	0.148364
180	82.824	0.181448
210	78.554	0.234379
840	36.152	1.010433

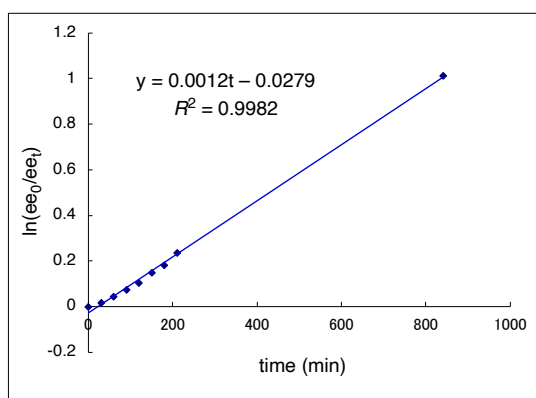


Figure S7. Racemization Rate Constant (k_{rac}) Measurement for (*S*)-**4** (in Chlorobenzene).

The first-order plot was shown as $\ln(ee_0/ee_t) = 0.0012t - 0.0279$ ($R^2 = 0.9982$). After calculation, the racemization rate constant was resulted as $k_{rac} = 1.0242 \times 10^{-5}$ (s^{-1}). Then, the racemization barrier energy ΔG_{rac}^\ddagger was figured out as 33.198 kcal/mol.

(2) For **24** ((*R*)-**24** was used for measurement).

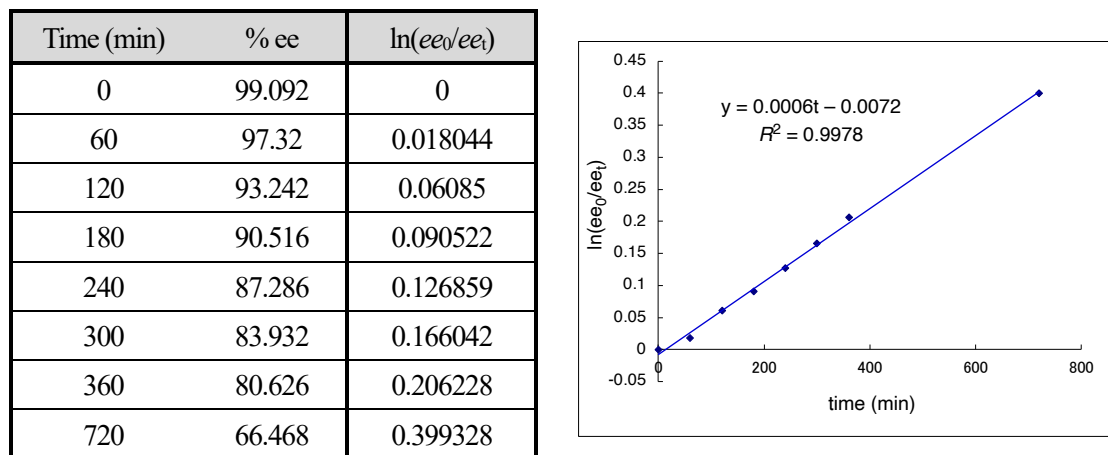


Figure S8. Racemization Rate Constant (k_{rac}) Measurement for (*R*)-**24** (in Chlorobenzene).

The first-order plot was shown as $\ln(ee_0/ee_t) = 0.0006t - 0.0072$ ($R^2 = 0.9978$). After calculation, the racemization rate constant was resulted as $k_{rac} = 4.7384 \times 10^{-6}$ (s^{-1}). Then, the racemization barrier energy ΔG_{rac}^\ddagger was figured out as 33.819 kcal/mol.

Calculation of Racemization Barriers for 4 and 24

Density functional theory (DFT) calculations were performed using the Gaussian 16 software package.⁴⁵ The molecular geometries for the transition states (TS) were first estimated with the *Reaction plus* software package, based on the nudged elastic band method,⁴⁶ and were subsequently re-optimized using the Gaussian 16 software package. Once the stationary points were obtained at ω B97XD/6-31G(d,p) level, the harmonic vibrational frequencies were calculated at the same level to estimate the Gibbs free energy. The nature of the stationary points was characterized via vibrational analysis. All of the Gibbs free energy values reported in this paper were calculated for a temperature of 298.15 K.

Racemization Barrier for 4

The racemization barrier energy of benzothiophene-type biaryl dicarboxylic acid **4** was turned out to be 34.2 kcal/mol by DFT calculation.

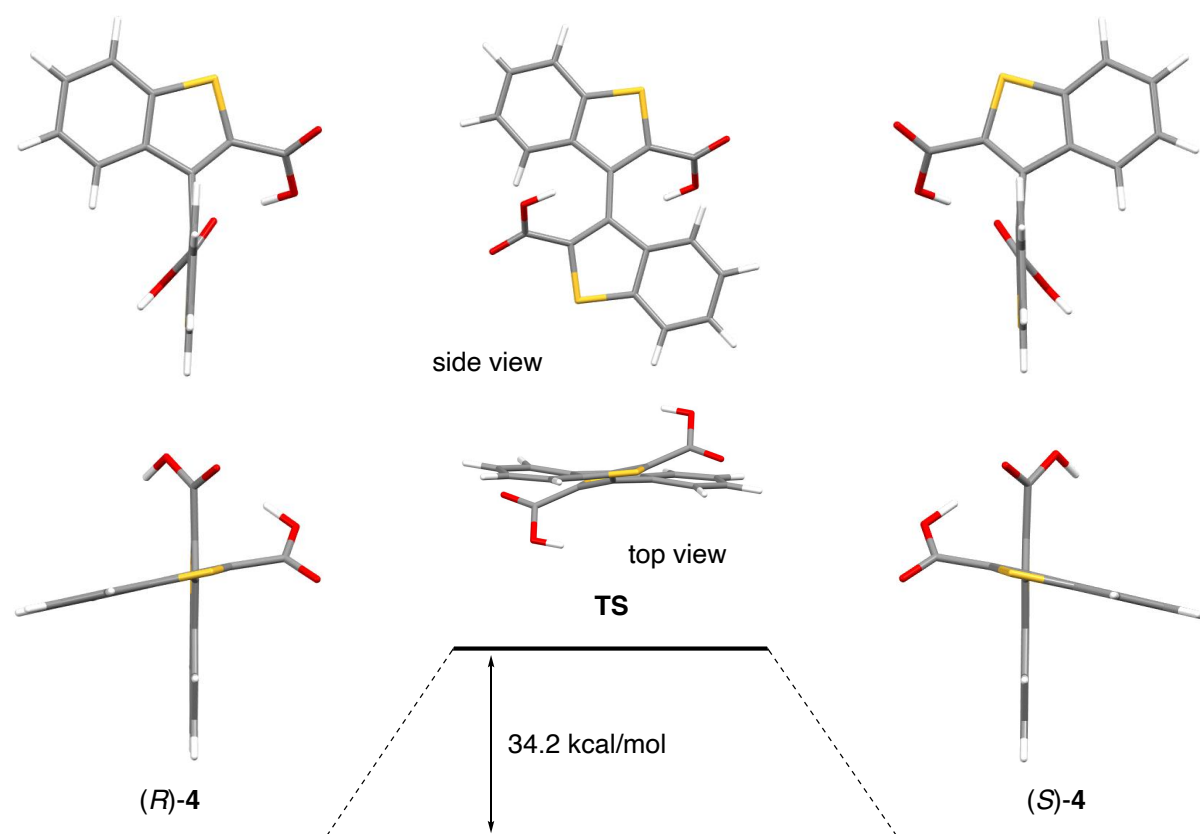
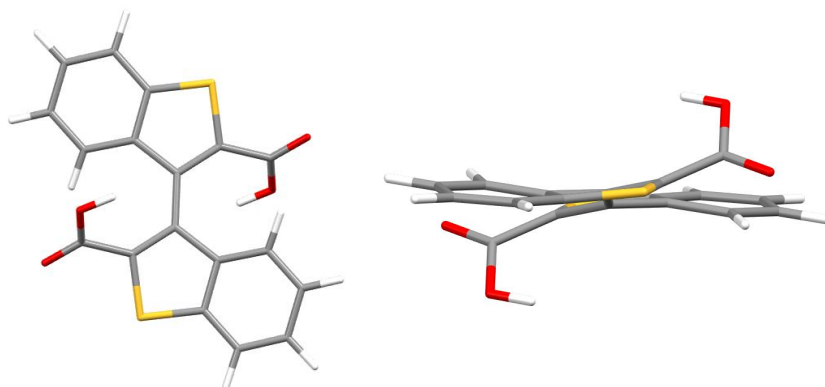


Figure S9. The Optimized Structures for the Ground State and the Transition State (TS) for **4**. Relative Gibbs free energies (kcal/mol) are given.

The Energy and Coordinate of Each Structure for 4

(1) Transition State



Calculation Method = $R\omega B97XD$

Formula = $C_{18}H_{10}O_4S_2$

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

$E(R\omega B97XD) = -1788.8593$ Hartree

Imaginary Freq = 1

Temperature = 298.15 Kelvin

Pressure = 1 atm

Electronic Energy (EE) = -1788.8593 Hartree

Zero-point Energy Correction = 0.242204 Hartree

Thermal Correction to Energy = 0.260384 Hartree

Thermal Correction to Enthalpy = 0.261328 Hartree

Thermal Correction to Free Energy = 0.196597 Hartree

EE + Zero-point Energy = -1788.6171 Hartree

EE + Thermal Energy Correction = -1788.5989 Hartree

EE + Thermal Enthalpy Correction = -1788.598 Hartree

EE + Thermal Free Energy Correction = -1788.6627 Hartree

$E(\text{Thermal}) = 163.393$ kcal/mol

Heat Capacity (C_v) = 72.821 cal/mol-kelvin

Entropy (S) = 136.237 cal/mol-kelvin

01

O	0.31412200	3.94395500	-0.25178900
O	0.96224100	2.70194600	1.46537000
H	0.80564000	1.81573700	1.81216200
C	0.26656800	2.89349200	0.33504000
C	-0.67432700	1.78979900	-0.04461000
C	-0.62066000	0.40908800	0.02452400
C	-1.99364700	-0.12069400	0.10799300
C	-2.96326300	0.86052500	-0.18362800
C	-4.33506900	0.59204600	-0.19329700
H	-5.04527200	1.37041800	-0.45094200
C	-4.76073700	-0.66678200	0.18130500
H	-5.82018200	-0.89889600	0.19274000
C	-3.82839400	-1.62041800	0.61160600
H	-4.17008000	-2.57837000	0.98734300
C	-2.47321000	-1.35592600	0.58648100
H	-1.80535800	-2.09719800	0.99939600
O	-0.96257100	-2.70126900	-1.46605000
O	-0.31318400	-3.94463100	0.24965900
H	-0.80583300	-1.81496500	-1.81252500
C	-0.26627300	-2.89361300	-0.33623800
C	0.67426400	-1.78992900	0.04414700
C	0.62058800	-0.40920700	-0.02495300
C	1.99356900	0.12063900	-0.10777600
C	2.96311200	-0.86047200	0.18439600
C	4.33488700	-0.59185200	0.19466100
H	5.04505400	-1.37011100	0.45274800
C	4.76060400	0.66694600	-0.17999900
H	5.82003600	0.89914100	-0.19102900
C	3.82838100	1.62041100	-0.61095100
H	4.17016400	2.57829200	-0.98678000
C	2.47321000	1.35580900	-0.58637100
H	1.80541900	2.09691100	-0.99975000
S	2.26047800	-2.43347700	0.35668600
S	-2.26060700	2.43346800	-0.35636400

(2) Ground State 1 [(R)-4]



Calculation Method = R ω B97XD

Formula = C₁₈H₁₀O₄S₂

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(R ω B97XD) = -1788.9114 Hartree

Imaginary Freq = 0

Temperature = 298.15 Kelvin

Pressure = 1 atm

Electronic Energy (EE) = -1788.9114 Hartree

Zero-point Energy Correction = 0.2426 Hartree

Thermal Correction to Energy = 0.261698 Hartree

Thermal Correction to Enthalpy = 0.262642 Hartree

Thermal Correction to Free Energy = 0.194151 Hartree

EE + Zero-point Energy = -1788.6688 Hartree

EE + Thermal Energy Correction = -1788.6497 Hartree

EE + Thermal Enthalpy Correction = -1788.6487 Hartree

EE + Thermal Free Energy Correction = -1788.7172 Hartree

E (Thermal) = 164.218 kcal/mol

Heat Capacity (Cv) = 74.068 cal/mol-kelvin

Entropy (S) = 144.153 cal/mol-kelvin

01

O	0.08745200	-2.86645700	1.30492400
O	1.52475500	-2.31184100	2.88441100
H	2.10711500	-1.57660800	3.11235700
C	0.96631000	-2.12247500	1.68543500
C	1.47489700	-0.99398000	0.87482300
C	0.72533400	-0.19306800	0.06490000
C	1.52544000	0.84508200	-0.54642000
C	2.87858600	0.77739500	-0.17269900
C	3.82181100	1.68036800	-0.66920700
H	4.86533600	1.61501300	-0.38172200
C	3.38254700	2.66387600	-1.53793700
H	4.09495700	3.37988900	-1.93388100
C	2.03203100	2.74960600	-1.91666100
H	1.71874300	3.52871700	-2.60288900
C	1.10382400	1.85046100	-1.43058100
H	0.06049600	1.90524600	-1.72334200
O	-0.10125100	-2.90490200	-1.40969700
O	-1.42343800	-2.12076400	-3.01774300
H	-0.06366000	-2.87123800	-0.42853400
C	-1.00267000	-2.05623100	-1.88905200
C	-1.47262100	-0.98873500	-0.94603800
C	-0.74563100	-0.20867400	-0.09642200
C	-1.56296500	0.78507000	0.56499600
C	-2.91300500	0.69744600	0.18018300
C	-3.87834400	1.55382700	0.71858400
H	-4.91838700	1.47595500	0.42061200
C	-3.47256300	2.50534400	1.63716600
H	-4.20585900	3.18111900	2.06463500
C	-2.12545900	2.61057200	2.02276600
H	-1.83364300	3.36707000	2.74347000
C	-1.17263200	1.76065800	1.49588400
H	-0.13097000	1.84035400	1.79157800
S	-3.15789500	-0.55443000	-1.00370800
S	3.17141900	-0.55263700	0.91647300

(3) Ground State 2 [(S)-4]



Calculation Method = R ω B97XD

Formula = C₁₈H₁₀O₄S₂

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(R ω B97XD) = -1788.9114 Hartree

RMS Gradient Norm = 5.92e-07 Hartree/Bohr

Imaginary Freq = 0

Temperature = 298.15 Kelvin

Pressure = 1 atm

Electronic Energy (EE) = -1788.9114 Hartree

Zero-point Energy Correction = 0.2426 Hartree

Thermal Correction to Energy = 0.261698 Hartree

Thermal Correction to Enthalpy = 0.262642 Hartree

Thermal Correction to Free Energy = 0.194151 Hartree

EE + Zero-point Energy = -1788.6688 Hartree

EE + Thermal Energy Correction = -1788.6497 Hartree

EE + Thermal Enthalpy Correction = -1788.6487 Hartree

EE + Thermal Free Energy Correction = -1788.7172 Hartree

E (Thermal) = 164.218 kcal/mol

Heat Capacity (Cv) = 74.068 cal/mol-kelvin

Entropy (S) = 144.152 cal/mol-kelvin

01

O	1.42376900	2.12098100	3.01758200
O	0.10132900	2.90495700	1.40966100
H	0.06360600	2.87121300	0.42850800
C	1.00283600	2.05634400	1.88895900
C	1.47266900	0.98879600	0.94595800
C	0.74562700	0.20878600	0.09634200
C	1.56290000	-0.78498300	-0.56510800
C	2.91295000	-0.69744600	-0.18032200
C	3.87822200	-1.55388100	-0.71876200
H	4.91827800	-1.47608300	-0.42081200
C	3.47236100	-2.50535200	-1.63735500
H	4.20560500	-3.18116600	-2.06485400
C	2.12524400	-2.61048900	-2.02293200
H	1.83336500	-3.36695000	-2.74364800
C	1.17248400	-1.76052500	-1.49600900
H	0.13081000	-1.84014000	-1.79168600
O	-1.52527400	2.31199000	-2.88421200
O	-0.08761600	2.86643700	-1.30498100
H	-2.10769400	1.57678700	-3.11210000
C	-0.96659200	2.12252800	-1.68536100
C	-1.47504600	0.99401500	-0.87470700
C	-0.72535400	0.19314800	-0.06486100
C	-1.52531400	-0.84509500	0.54648100
C	-2.87849400	-0.77753100	0.17286900
C	-3.82158400	-1.68060800	0.66944000
H	-4.86514100	-1.61534900	0.38205300
C	-3.38214600	-2.66409500	1.53810800
H	-4.09445100	-3.38018500	1.93409900
C	-2.03158800	-2.74970600	1.91671300
H	-1.71816400	-3.52880500	2.60289200
C	-1.10351700	-1.85045200	1.43057600
H	-0.06015700	-1.90512900	1.72324700
S	-3.17152800	0.55249900	-0.91625100
S	3.15792400	0.55438600	1.00360900

Racemization Barrier of **24**

The racemization barrier energy of benzoselenophene-type biaryl dicarboxylic acid **24** was turned out to be 37.3 kcal/mol by DFT calculation.

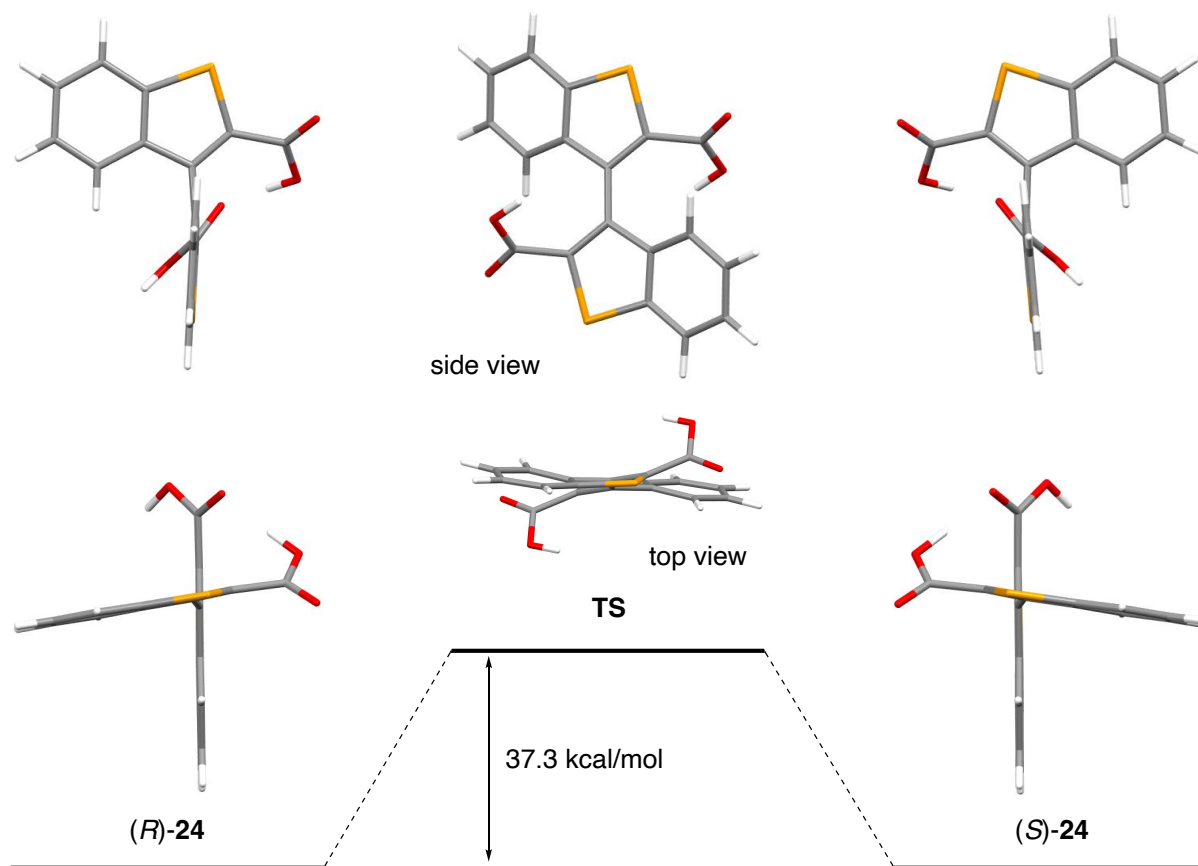
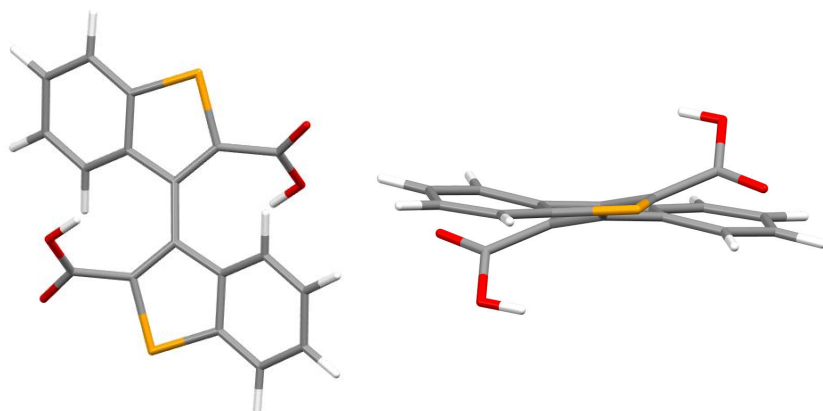


Figure S10. The Optimized Structures for the Ground State and the Transition State (TS) for **24**. Relative Gibbs free energies (kcal/mol) are given.

The Energy and Coordinate of Each Structure for 24

(1) Transition State



Calculation Method = $R\omega B97XD$

Formula = $C_{18}H_{10}O_4Se_2$

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

$E(R\omega B97XD) = -5791.309$ Hartree

Imaginary Freq = 1

Temperature = 298.15 Kelvin

Pressure = 1 atm

Electronic Energy (EE) = -5791.309 Hartree

Zero-point Energy Correction = 0.240049 Hartree

Thermal Correction to Energy = 0.259037 Hartree

Thermal Correction to Enthalpy = 0.259981 Hartree

Thermal Correction to Free Energy = 0.192535 Hartree

EE + Zero-point Energy = -5791.069 Hartree

EE + Thermal Energy Correction = -5791.05 Hartree

EE + Thermal Enthalpy Correction = -5791.0491 Hartree

EE + Thermal Free Energy Correction = -5791.1165 Hartree

$E(\text{Thermal}) = 162.548$ kcal/mol

Heat Capacity (C_v) = 74.379 cal/mol-kelvin

Entropy (S) = 141.954 cal/mol-kelvin

01

O	1.23200800	-3.77782400	-0.03702400
O	0.05974800	-2.80983500	1.57335900
H	-0.17427100	-1.91900100	1.85937300
C	0.83147200	-2.76364300	0.47860700
C	1.28943700	-1.40718000	0.04744000
C	0.72788000	-0.14587900	0.05404700
C	1.78299100	0.88506600	0.15648200
C	3.08452700	0.41017100	-0.10688000
C	4.20322900	1.24504400	-0.09135400
H	5.18576300	0.84990500	-0.32726600
C	4.04652300	2.56585300	0.28289800
H	4.90575900	3.22720800	0.31121500
C	2.79057900	3.02541300	0.69484800
H	2.67956300	4.03489400	1.07456600
C	1.68194200	2.20289500	0.64163900
H	0.75093500	2.58113500	1.03771900
O	-0.05878300	2.80835600	-1.57458700
O	-1.23169700	3.77776400	0.03448000
H	0.17484000	1.91726200	-1.86011000
C	-0.83105900	2.76313000	-0.48018900
C	-1.28924500	1.40708100	-0.04794200
C	-0.72798900	0.14561800	-0.05402500
C	-1.78333200	-0.88509000	-0.15577600
C	-3.08471800	-0.40976200	0.10755500
C	-4.20354600	-1.24449100	0.09309200
H	-5.18596400	-0.84898600	0.32887800
C	-4.04715000	-2.56563800	-0.28010200
H	-4.90644200	-3.22696400	-0.30735600
C	-2.79140800	-3.02571100	-0.69211000
H	-2.68067800	-4.03548200	-1.07113800
C	-1.68262200	-2.20332600	-0.63988700
H	-0.75191000	-2.58190200	-1.03639400
Se	-3.12778800	1.43998500	0.27048800
Se	3.12799700	-1.43948700	-0.27135200

(2) Ground State 1 [(R)-24]



Calculation Method = R ω B97XD

Formula = C₁₈H₁₀O₄Se₂

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(R ω B97XD) = -5791.3665 Hartree

Imaginary Freq = 0

Temperature = 298.15 Kelvin

Pressure = 1 atm

Electronic Energy (EE) = -5791.3665 Hartree

Zero-point Energy Correction = 0.241049 Hartree

Thermal Correction to Energy = 0.260855 Hartree

Thermal Correction to Enthalpy = 0.261799 Hartree

Thermal Correction to Free Energy = 0.190615 Hartree

EE + Zero-point Energy = -5791.1255 Hartree

EE + Thermal Energy Correction = -5791.1057 Hartree

EE + Thermal Enthalpy Correction = -5791.1047 Hartree

EE + Thermal Free Energy Correction = -5791.1759 Hartree

E (Thermal) = 163.689 kcal/mol

Heat Capacity (Cv) = 75.192 cal/mol-kelvin

Entropy (S) = 149.819 cal/mol-kelvin

01

O	-0.27830600	-2.81920100	-1.29876400
O	-1.79572100	-2.15898500	-2.76201800
H	-2.35769600	-1.38942800	-2.91940800
C	-1.15190100	-2.03272400	-1.59643800
C	-1.57093300	-0.92210000	-0.71738200
C	-0.73104300	-0.15227600	0.02231700
C	-1.40336400	0.88453400	0.77910000
C	-2.79670600	0.92183100	0.60747800
C	-3.58389500	1.85831000	1.27768600
H	-4.66048700	1.88035700	1.14857700
C	-2.95720500	2.76452500	2.11658200
H	-3.55341000	3.50219300	2.64331700
C	-1.56563200	2.74062600	2.29644800
H	-1.09905300	3.45653300	2.96408300
C	-0.78814000	1.80943800	1.63625600
H	0.28830400	1.77327300	1.77166500
O	0.25626300	-2.83382100	1.39192900
O	1.79691400	-2.07156100	2.80408400
H	0.08372500	-2.80025000	0.42567800
C	1.22078200	-1.99185100	1.74561300
C	1.57068000	-0.92651900	0.75715100
C	0.74915500	-0.17072000	-0.01725100
C	1.43593500	0.83095400	-0.80921900
C	2.82978200	0.84691200	-0.62401200
C	3.63581800	1.74334100	-1.32909600
H	4.71162400	1.75080600	-1.18928700
C	3.03784600	2.62727600	-2.21053700
H	3.65322700	3.32942700	-2.76332400
C	1.64669900	2.62717700	-2.39622600
H	1.19790000	3.32959800	-3.09046800
C	0.84738300	1.73851000	-1.70358200
H	-0.23016700	1.73289700	-1.84026500
Se	3.36202000	-0.42076900	0.63686900
Se	-3.37433500	-0.42277000	-0.55574400

(3) Ground State 2 [(S)-24]



Calculation Method = R ω B97XD

Formula = C₁₈H₁₀O₄Se₂

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(R ω B97XD) = -5791.3665 Hartree

Imaginary Freq = 0

Temperature = 298.15 Kelvin

Pressure = 1 atm

Electronic Energy (EE) = -5791.3665 Hartree

Zero-point Energy Correction = 0.241049 Hartree

Thermal Correction to Energy = 0.260855 Hartree

Thermal Correction to Enthalpy = 0.261799 Hartree

Thermal Correction to Free Energy = 0.190615 Hartree

EE + Zero-point Energy = -5791.1255 Hartree

EE + Thermal Energy Correction = -5791.1057 Hartree

EE + Thermal Enthalpy Correction = -5791.1047 Hartree

EE + Thermal Free Energy Correction = -5791.1759 Hartree

E (Thermal) = 163.689 kcal/mol

Heat Capacity (Cv) = 75.192 cal/mol-kelvin

Entropy (S) = 149.82 cal/mol-kelvin

01

O	-1.79606600	-2.07100400	2.80454200
O	-0.25624600	-2.83396400	1.39187300
H	-0.08385300	-2.80042700	0.42558500
C	-1.22039400	-1.99168300	1.74579100
C	-1.57055900	-0.92656400	0.75717900
C	-0.74915500	-0.17076600	-0.01734500
C	-1.43606600	0.83081300	-0.80931900
C	-2.82989700	0.84668400	-0.62399500
C	-3.63606600	1.74300600	-1.32906000
H	-4.71186000	1.75039800	-1.18915300
C	-3.03823800	2.62693900	-2.21060300
H	-3.65372100	3.32901400	-2.76337400
C	-1.64710800	2.62693300	-2.39640900
H	-1.19842000	3.32935100	-3.09072500
C	-0.84766400	1.73836300	-1.70378300
H	0.22987400	1.73282800	-1.84055500
O	1.79595500	-2.15911400	-2.76187300
O	0.27831900	-2.81916000	-1.29878100
H	2.35800800	-1.38960700	-2.91923100
C	1.15201500	-2.03275800	-1.59637200
C	1.57101000	-0.92210800	-0.71733100
C	0.73103800	-0.15221500	0.02220100
C	1.40327900	0.88471600	0.77889600
C	2.79663400	0.92202800	0.60737200
C	3.58374800	1.85861300	1.27751700
H	4.66035000	1.88067000	1.14849000
C	2.95696900	2.76492300	2.11624300
H	3.55311300	3.50268100	2.64292100
C	1.56538300	2.74101000	2.29600900
H	1.09873500	3.45699400	2.96351400
C	0.78796500	1.80971300	1.63588500
H	-0.28848700	1.77353500	1.77121800
Se	3.37438500	-0.42273600	-0.55561500
Se	-3.36193800	-0.42095200	0.63702600

NBO Analyses for the Optimized Structures of the Transition State in Racemization Pathway for **4** and **24**

We performed the natural bond orbital (NBO) analyses for the optimized structures of the transition state in racemization pathway for biaryl dicarboxylic acids **4** and **24** as mentioned above at the ω B97XD/6-311G(d,p) level, using the Gaussian 16 software package.⁴⁵

(1) Benzothiophene-type biaryl dicarboxylic acid **4**

We couldn't detect any orbital interactions in the optimized structure of the transition state in racemization pathway for biaryl dicarboxylic acid **4** probably because of the threshold for printing (0.50 kcal/mol).

(2) Benzoselenophene-type biaryl dicarboxylic acid **24**

Second order perturbation theory analysis of Fock matrix in NBO basis

Donor NBO (i)	Acceptor NBO (j)	E(2) kcal/mol	E(j) – E(i) a.u.	F(i,j) a.u.
LP(2) O1 (#99)	BD*(1) C8–Se34 (#512)	0.70	0.58	0.019
LP(2) O18 (#105)	BD*(1) C24–Se33 (#620)	0.71	0.58	0.019

Threshold for printing: 0.50 kcal/mol

NBO Analyses for Biaryl Dicarboxylic Acids Containing Chalcogen Bonds (Figure 14)

We performed NBO analyses for biaryl dicarboxylic acids containing chalcogen atoms to investigate intramolecular chalcogen and tetrel bonding interactions at the ω B97XD/6-311G(d,p) level, using the Gaussian 16 software package.⁴⁵

(1) Naphthothiophene-type biaryl dicarboxylic acid **3**: We performed the NBO analysis based on the structure of (*S*)-**3** in the crystal structure of *rac*-**3** (Figure 14B, CCDC 1863131).²⁰

Second order perturbation theory analysis of Fock matrix in NBO basis

Donor NBO (i)	Acceptor NBO (j)	E(2) kcal/mol	E(j) – E(i) a.u.	F(i,j) a.u.
LP(2) O2 (#107)	BD*(1) C5–S6 (#617)	1.09	0.64	0.024
LP(1) O3 (#108)	BD*(1) S6–C7 (#620)	0.96	1.00	0.028
LP(1) O44 (#114)	BD*(1) S26–C27 (#650)	0.54	0.99	0.021
LP(2) O46 (#117)	BD*(1) C25–S26 (#648)	1.07	0.64	0.024

Threshold for printing: 0.50 kcal/mol

(2) Naphthofuran-type biaryl dicarboxylic acid **6**: We performed the NBO analysis based on the crystal structure of (*R*)-**6** (Figure 14A, CCDC 2144806).

Second order perturbation theory analysis of Fock matrix in NBO basis

Donor NBO (i)	Acceptor NBO (j)	E(2) kcal/mol	E(j) – E(i) a.u.	F(i,j) a.u.
LP(2) O15 (#101)	BD*(1) C2–S3 (#600)	1.22	0.76	0.028
LP(1) O31 (#106)	BD*(1) C18–C19 (#632)	0.78	1.09	0.026

Threshold for printing: 0.50 kcal/mol

(3) Naphthoselenophene-type biaryl dicarboxylic acid **7**: We performed the NBO analysis based on the structure of (*R*)-**7** in the crystal structure of *rac*-**7** (Figure 14C, CCDC 2144807).

Second order perturbation theory analysis of Fock matrix in NBO basis

Donor NBO (i)	Acceptor NBO (j)	E(2) kcal/mol	E(j) – E(i) a.u.	F(i,j) a.u.
LP(1) O3 (#128)	BD*(1) Se2–C16 (#650)	0.63	0.90	0.021
LP(2) O5 (#131)	BD*(1) Se1–C14 (#648)	1.14	0.57	0.023
LP(1) O6 (#132)	BD*(1) Se1–C18 (#649)	1.18	0.92	0.029
LP(2) O8 (#135)	BD*(1) Se2–C20 (#651)	1.16	0.59	0.024

Threshold for printing: 0.50 kcal/mol

(4) Benzothiophene-type biaryl dicarboxylic acid **4**: We performed the NBO analysis based on the crystal structure of (*R*)-**4** reported by Svoboda, J. and co-workers (Figure S11, CCDC 196033).¹⁸

Second order perturbation theory analysis of Fock matrix in NBO basis

Donor NBO (i)	Acceptor NBO (j)	E(2) kcal/mol	E(j) – E(i) a.u.	F(i,j) a.u.
LP(2) O3 (#85)	BD*(1) S1–C22 (#463)	0.57	0.65	0.018
LP(1) O4 (#86)	BD*(1) S1–C7 (#462)	0.80	0.95	0.025
LP(2) O5 (#89)	BD*(1) S2–C24 (#465)	0.55	0.65	0.017
LP(1) O6 (#90)	BD*(1) S2–C14 (#464)	0.68	1.00	0.023

Threshold for printing: 0.50 kcal/mol

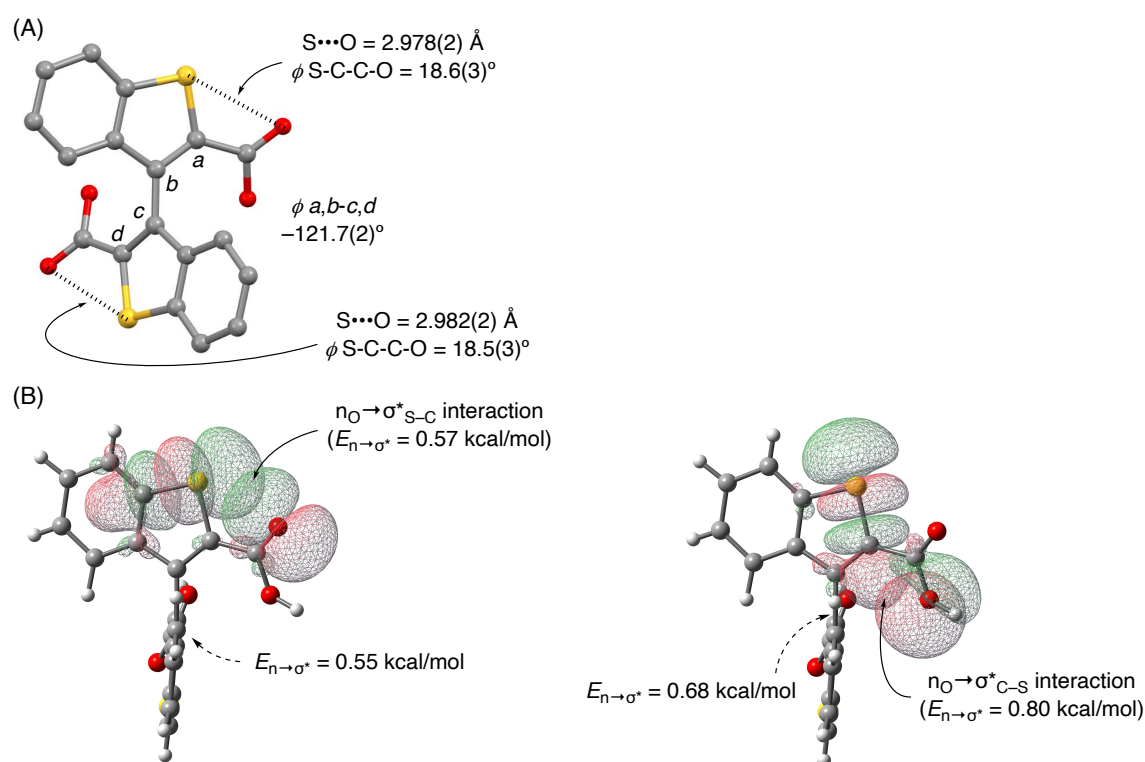


Figure S11. (A) Crystal Structure of Benzothiophene-Type Biaryl Dicarboxylic Acid (*R*)-**4**. (B) NBO Analysis for (*R*)-**4**. NBO overlaps between the oxygen lone pairs (n_O) and the antibonding orbitals of the C–S bonds (σ^*_{S-C} and σ^*_{C-S}), together with the corresponding second order perturbation energies ($E_{n \rightarrow \sigma^*}$).

(5) Benzoselenophene-type biaryl dicarboxylic acid **24**: We performed the NBO analysis based on the crystal structure of (*S*)-**24** (Figure S12, CCDC 2144805).

Second order perturbation theory analysis of Fock matrix in NBO basis

Donor NBO (i)	Acceptor NBO (j)	E(2) kcal/mol	E(j) – E(i) a.u.	F(i,j) a.u.
LP(2) O2 (#101)	BD*(1) Se1–C9 (#499)	1.01	0.57	0.022
LP(2) O19 (#107)	BD*(1) Se18–C26 (#523)	1.01	0.57	0.022

Threshold for printing: 0.50 kcal/mol

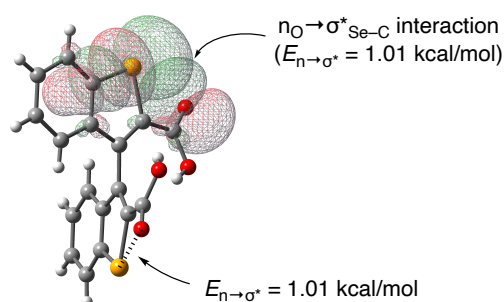


Figure S12. NBO Analysis for Benzoselenophene-Type Biaryl Dicarboxylic Acid (*S*)-**24**. NBO overlaps between the oxygen lone pairs (n_O) and the antibonding orbitals of the C–Se bonds ($\sigma^*_{\text{Se-C}}$), together with the corresponding second order perturbation energies ($E_{n \rightarrow \sigma^*}$).

We also performed the NBO analysis for compound **27c** based on its crystal structure (Figure S13, CCDC 2144808).

Second order perturbation theory analysis of Fock matrix in NBO basis

Donor NBO (i)	Acceptor NBO (j)	E(2) kcal/mol	E(j) – E(i) a.u.	F(i,j) a.u.
LP(1) N4 (#91)	BD*(1) Se2–C10 (#424)	1.41	0.69	0.028

Threshold for printing: 0.50 kcal/mol

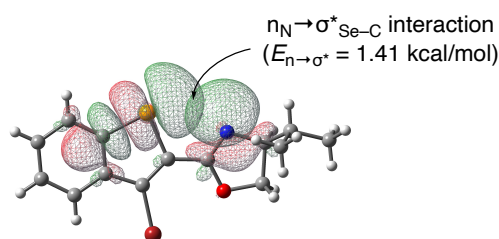
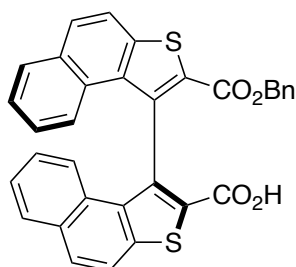


Figure S13. NBO Analysis for **27c**. NBO overlap between the nitrogen lone pair (n_N) and the antibonding orbital of the C–Se bonds ($\sigma^*_{\text{Se-C}}$), together with the corresponding second order perturbation energies ($E_{n \rightarrow \sigma^*}$).

Synthesis of Axially Chiral δ -Amino Acid (*S*)-21 (Scheme 8A)

(*S*)-2'-((Benzyloxy)carbonyl)-[1,1'-binaphtho[2,1-*b*]thiophene]-2-carboxylic acid ((*S*)-30)

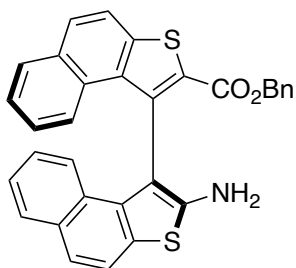


To a solution of (*S*)-[1,1'-binaphtho[2,1-*b*]thiophene]-2,2'-dicarboxylic acid ((*S*)-3)²⁰ (6.11 g, 13.4 mmol, 1.00 equiv., >99% ee), Ag₂CO₃ (1.85 g, 6.72 mmol, 0.500 equiv.), and TBAI (14.9 g, 40.3 mmol, 3.00 equiv.), benzyl bromide (4.80 mL, 40.3 mmol, 3.00 equiv.) was added at rt. After being stirred at 40 °C for 17 h, the reaction mixture was quenched with 2 M aq. HCl, and extracted with AcOEt.

The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 4:1 to 7:3 to 1:1) to afford (*S*)-30 (1.84 g, 25% yield).

Yellow prisms (*n*-hexane/AcOEt); M.p. 110–112 °C; [α]_D²⁰ = –86.6 (*c* 0.6, CHCl₃); ¹H NMR (600 MHz, CDCl₃) δ 7.97 (d, *J* = 8.9 Hz, 1H), 7.89–7.81 (m, 5H), 7.33 (ddd, *J* = 8.0, 6.9, 1.1 Hz, 1H), 7.29–7.23 (m, 2H), 7.22–7.18 (m, 1H), 7.18–7.15 (m, 1H), 7.14–7.10 (m, 2H), 7.03 (ddd, *J* = 8.5, 6.9, 1.4 Hz, 1H), 6.96 (ddd, *J* = 8.5, 6.9, 1.4 Hz, 1H), 6.86–6.82 (m, 2H), 4.95 (d, *J* = 12.4 Hz, 1H), 4.93 (d, *J* = 12.4 Hz, 1H); ¹³C{¹H} NMR (151 MHz, CDCl₃) δ 167.4, 162.3, 141.6, 141.5, 141.0, 139.4, 135.0, 133.7, 133.6, 131.98, 131.96, 130.63, 130.58, 129.6, 129.3, 129.19, 129.16, 129.1, 128.4, 128.1, 128.0, 127.9, 127.5, 127.4, 125.8, 125.7, 122.6, 122.5, 120.8, 67.2 (One carbon signal was overlapped); IR (KBr) 3059, 2602, 1681, 1481, 1434, 1316, 1271, 1227, 907, 733 cm^{–1}; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₃₃H₂₀NaO₄S₂ 567.0695; Found 567.0693.

(*S*)-Benzyl 2'-amino-[1,1'-binaphtho[2,1-*b*]thiophene]-2-carboxylate ((*S*)-8)



To a solution of (*S*)-30 (100 mg, 184 μ mol, 1.00 equiv.) and Et₃N (76.0 μ L, 551 μ mol, 3.00 equiv.) in toluene (20 mL), DPPA (59.2 μ L, 275 μ mol, 1.50 equiv.) was added at rt under an Ar atmosphere. After being stirred at 90 °C for 1 h, water (331 μ L, 18.4 mmol, 100 equiv.) was added. Then, the reaction mixture was stirred at 90 °C for 15 h. The reaction mixture was quenched with sat. aq. NH₄Cl, and extracted with AcOEt. The organic layer was washed with brine, dried over

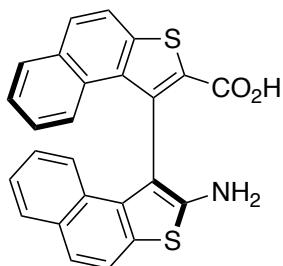
Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 4:1) to afford (*S*)-8 (53.0 mg, 56% yield, >99% ee). The optical purity of (*S*)-8 was determined to be >99% ee by HPLC analysis; HPLC (CHIRAL 5B (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, λ = 320 nm) *t*_R = 6.7 min (for (*S*)-8), 8.9 min (for (*R*)-8).

*For HPLC analysis, (*R*)-8 was also synthesized by following this procedure.

Yellow amorphous solid; [α]_D²⁰ = –28.6 (*c* 0.8, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.97 (d, *J* = 8.8 Hz, 1H), 7.93–7.84 (m, 3H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.74 (d, *J* = 8.7 Hz, 1H), 7.61 (d, *J* = 8.6 Hz, 1H), 7.39 (ddd, *J* = 8.1, 7.0, 1.1 Hz, 1H), 7.30–7.12 (m, 6H), 6.97–6.86 (m, 3H), 5.03 (s, 2H), 3.77 (s, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 162.4, 146.8, 141.3, 138.5, 135.2, 134.1, 133.8, 132.3, 132.0, 131.4, 131.1, 129.5, 129.0, 128.7, 128.6, 128.4, 128.0, 127.9, 127.8, 126.0, 125.7, 124.6, 122.9, 122.8, 122.6, 120.7, 120.6, 111.8, 67.2 (One carbon signal was overlapped); IR (neat) 3351, 3055, 1686, 1492, 1406, 1219, 1065, 906, 802, 732 cm^{–1}; HRMS (ESI) *m/z*:

$[M+Na]^+$ Calcd for $C_{32}H_{21}NNaO_2S_2$ 538.0906; Found 538.0913.

(*S*)-2'-Amino-[1,1'-binaphtho[2,1-*b*]thiophene]-2-carboxylic acid ((*S*)-**21**)



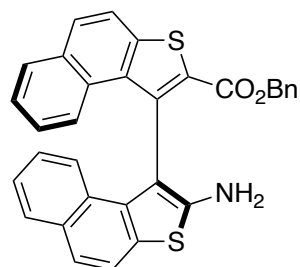
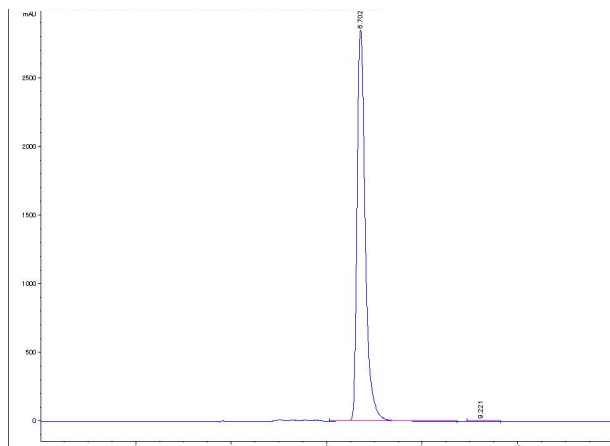
To a solution of (*S*)-**8** (20.0 mg, 38.8 μ mol, 1.00 equiv.) in THF/MeOH/H₂O (2:1:1, 4.0 mL), LiOH•H₂O (6.50 mg, 15.5 mmol, 4.00 equiv.) was added at rt. After being stirred at rt for 12 h, the reaction mixture was quenched with 2 M aq. HCl, and extracted with AcOEt. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by prep. TLC (SiO₂, *n*-hexane:AcOEt = 1:2) to afford (*S*)-**21** (13.6 mg, 82% yield).

Yellow amorphous solid; $[\alpha]_D^{22} = -25.4$ (*c* 0.1, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.90–7.82 (m, 2H), 7.79 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.75–7.65 (m, 3H), 7.53 (d, *J* = 8.7 Hz, 1H), 7.30 (ddd, *J* = 8.0, 7.0, 1.2 Hz, 1H), 7.15–7.03 (m, 3H), 6.82 (t, *J* = 7.8 Hz, 1H); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 165.3, 147.2, 141.7, 139.0, 133.7, 133.6, 132.2, 131.9, 131.0, 130.7, 129.7, 128.9, 128.8, 128.63, 128.59, 127.8, 126.0, 125.8, 124.7, 123.1, 122.6, 122.4, 120.7, 120.4, 110.8; IR (neat) 3443, 3341, 2961, 1657, 1258, 797, 750 cm⁻¹; HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{25}H_{15}NNaO_2S_2$ 448.0436; Found 448.0434.

HPLC Analysis for Determination of the Optical Purity of Synthetic δ -Amino Acid **8**

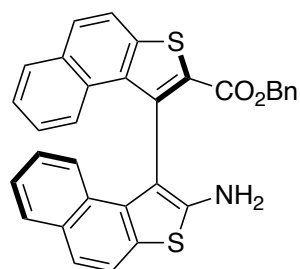
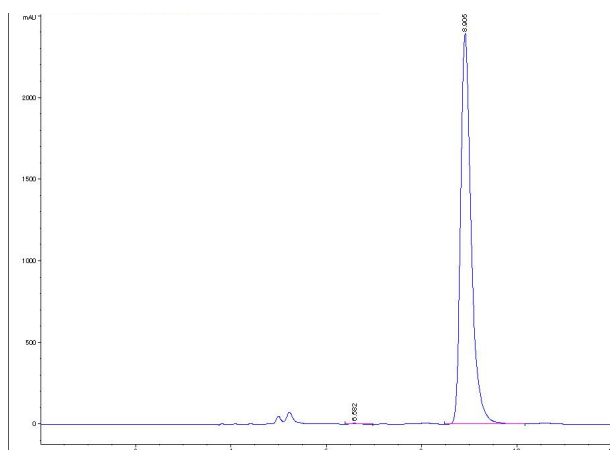
For δ -amino acid **8**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHiRAL 5B (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, λ = 320 nm).

(1) Chromatogram of (*S*)-**8** (>99% ee)



	Retention time (min)	Peak area (%)
1	6.7	99.94
2	9.2	0.06

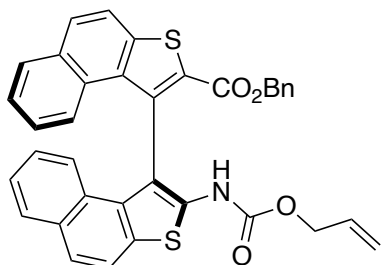
(2) Chromatogram of (*R*)-**8** (>99% ee)



	Retention time (min)	Peak area (%)
1	6.6	0.14
2	8.9	99.86

Transformation to *N*-Protected Axially Chiral δ -Amino Acids **36** (Scheme 9)

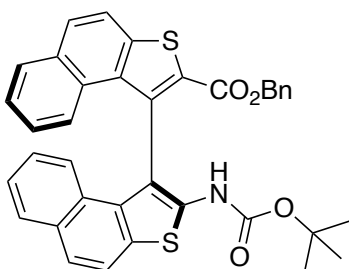
(*S*)-Benzyl 2'-(((allyloxy)carbonyl)amino)-[1,1'-binaphtho[2,1-*b*]thiophene]-2-carboxylate ((*S*)-**35a**)



To a solution of (*S*)-**30** (20.0 mg, 36.7 μ mol, 1.00 equiv.) and Et₃N (30.7 μ L, 220 μ mol, 6.00 equiv.) in allyl alcohol (4.0 mL), DPPA (59.2 μ mol, 275 μ mol, 7.50 equiv.) was added at rt under an Ar atmosphere. After being stirred at 90 °C for 12 h, the reaction mixture was quenched with sat. aq. NH₄Cl, and extracted with AcOEt. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by prep. TLC (SiO₂, *n*-hexane:AcOEt = 3:1) to afford (*S*)-**35a** (9.1 mg, 41% yield). The optical purity of (*S*)-**35a** was determined to be >99% ee by HPLC analysis; HPLC (CHIRALPAK AD-H (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 0.5 mL/min, λ = 254 nm) t_R = 31.9 min (for (*R*)-**35a**), 36.2 min (for (*S*)-**35a**).

Yellow prisms (*n*-hexane/AcOEt); M.p. 83–84 °C; $[\alpha]_D^{20}$ = –58.0 (*c* 1.6, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.98 (d, *J* = 8.8 Hz, 1H), 7.93 (d, *J* = 8.8 Hz, 1H), 7.91–7.82 (m, 3H), 7.72 (d, *J* = 8.7 Hz, 1H), 7.61 (d, *J* = 8.6 Hz, 1H), 7.38 (ddd, *J* = 8.1, 7.0, 1.2 Hz, 1H), 7.31–7.25 (m, 1H), 7.25–7.19 (m, 1H), 7.19–7.07 (m, 4H), 6.96 (ddd, *J* = 8.5, 6.9, 1.4 Hz, 1H), 6.88 (d, *J* = 7.2 Hz, 2H), 6.82 (br s, 1H), 5.93–5.73 (m, 1H), 5.35–5.15 (m, 2H), 5.05–4.95 (m, 2H), 4.65–4.50 (m, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 162.1, 152.7, 141.5, 136.9, 136.5, 134.9, 133.5, 132.2, 132.1, 132.0, 131.8, 131.7, 131.4, 130.8, 129.8, 129.2, 129.1, 128.9, 128.4, 128.2, 128.0, 126.2, 124.9, 124.5, 122.7, 122.4, 120.7, 120.6, 119.6, 115.1, 67.4, 67.1 (Two carbon signals were overlapped); IR (KBr) 3405, 3279, 3058, 1722, 1577, 1543, 1499, 1209, 1065, 908, 733 cm^{–1}; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₃₆H₂₅NNaO₄S₂ 622.1117; Found 622.1116.

(*S*)-Benzyl 2'-(((*tert*-butoxycarbonyl)amino)-[1,1'-binaphtho[2,1-*b*]thiophene]-2-carboxylate ((*S*)-**35b**)

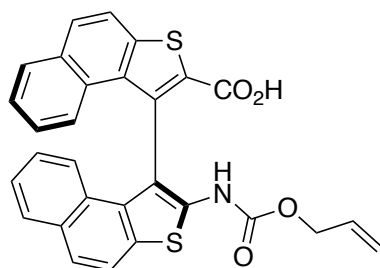


To a solution of (*S*)-**30** (100 mg, 184 μ mol, 1.00 equiv.) in *t*BuOH (10 mL), DPPA (59.2 μ mol, 275 μ mol, 1.50 equiv.) and Et₃N (76.8 μ L, 551 μ mol, 3.00 equiv.) were added at rt under an Ar atmosphere. After being stirred at 90 °C for 12 h, the reaction mixture was quenched with sat. aq. NH₄Cl, and extracted with AcOEt. The organic layer was washed with water and brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by prep. TLC (SiO₂, *n*-hexane:AcOEt = 3:1) to afford (*S*)-**35b** (93.0 mg, 83% yield). The optical purity of (*S*)-**35b** was determined to be >99% ee by HPLC analysis; HPLC (CHIRALPAK AD-H (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 8.0 min (for (*S*)-**35b**), 10.3 min (for (*R*)-**35b**).

Yellowish green amorphous solid; $[\alpha]_D^{21}$ = –3.2 (*c* 0.8, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.99 (d, *J* = 8.8 Hz, 1H), 7.93 (d, *J* = 8.8 Hz, 1H), 7.87 (d, *J* = 7.9 Hz, 1H), 7.85 (d, *J* = 8.7 Hz, 1H), 7.82 (d, *J* = 7.9 Hz, 1H), 7.68 (d, *J* = 8.7 Hz, 1H), 7.63 (d, *J* = 8.6 Hz, 1H), 7.37 (ddd, *J* = 8.0, 7.0, 1.2 Hz, 1H), 7.27–7.23 (m, 1H), 7.22–7.17 (m, 1H), 7.15–7.09 (m, 4H), 6.92 (ddd, *J* = 8.4, 6.8, 1.3 Hz, 1H), 6.86 (d, *J* = 7.5 Hz, 2H), 6.57 (br s, 1H), 5.00 (d,

$J = 12.2$ Hz, 1H), 4.95 (d, $J = 12.2$ Hz, 1H), 1.41 (s, 9H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 162.2, 152.0, 141.4, 137.1, 137.0, 134.8, 133.6, 132.1, 131.92, 131.85, 131.3, 130.8, 129.7, 129.1, 128.9, 128.7, 128.4, 128.1, 128.0, 127.9, 126.1, 125.9, 124.6, 124.0, 122.63, 122.55, 120.6, 120.5, 113.9, 82.3, 67.3, 28.2 (One carbon signal was overlapped); IR (KBr) 1721, 1689, 1541, 1496, 1263, 1156, 1066, 804, 757 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{37}\text{H}_{29}\text{NNaO}_4\text{S}_2$ 638.1430; Found 638.1465.

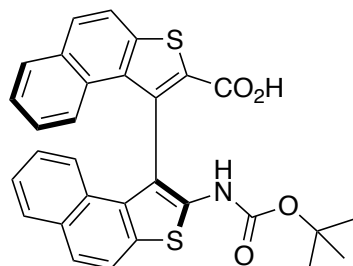
(*S*)-2'-(((Allyloxy)carbonyl)amino)-[1,1'-binaphtho[2,1-*b*]thiophene]-2-carboxylic acid ((*S*)-**36a**)



To a solution of (*S*)-**35a** (71.0 mg, 118 μmol , 1.00 equiv.) in THF/MeOH/ H_2O (2:1:1, 4.0 mL), $\text{LiOH}\cdot\text{H}_2\text{O}$ (19.9 mg, 474 mmol, 4.00 equiv.) was added at rt. After being stirred at rt for 3 h, the reaction mixture was quenched with 2 M aq. HCl, and extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue. The residue was purified by prep. TLC (SiO_2 , *n*-hexane:AcOEt = 1:2) to afford (*S*)-**36a** (31.0 mg, 53% yield).

Yellow amorphous solid; $[\alpha]_{\text{D}}^{21} = -62.5$ (c 1.1, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 7.99–7.87 (m, 3H), 7.85 (d, $J = 8.0$ Hz, 1H), 7.79 (d, $J = 8.1$ Hz, 1H), 7.70 (d, $J = 8.7$ Hz, 1H), 7.51 (d, $J = 8.6$ Hz, 1H), 7.36 (t, $J = 7.5$ Hz, 1H), 7.21 (t, $J = 7.5$ Hz, 1H), 7.08 (t, $J = 7.8$ Hz, 1H), 7.04 (d, $J = 8.5$ Hz, 1H), 6.89 (t, $J = 7.7$ Hz, 1H), 6.81 (br s, 1H), 5.85–5.72 (m, 1H), 5.27–5.10 (m, 2H), 4.54 (s, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 166.1, 152.7, 142.0, 138.2, 136.5, 133.5, 132.2, 132.0, 131.9, 131.6, 131.2, 130.7, 130.1, 129.0, 128.8, 128.0, 126.2, 124.8, 124.5, 122.5, 122.4, 120.6, 120.5, 119.5, 114.7, 67.0 (Three carbon signals were overlapped); IR (KBr) 3282, 2925, 1703, 1680, 1577, 1543, 1501, 1259, 1063, 802 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{29}\text{H}_{19}\text{NNaO}_4\text{S}_2$ 532.0648; Found 532.0645.

(*S*)-2'-((*tert*-Butoxycarbonyl)amino)-[1,1'-binaphtho[2,1-*b*]thiophene]-2-carboxylic acid ((*S*)-**36b**)



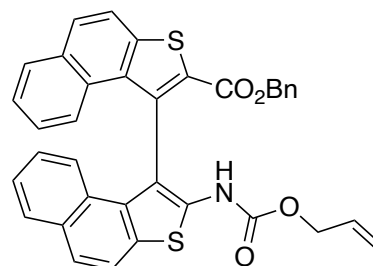
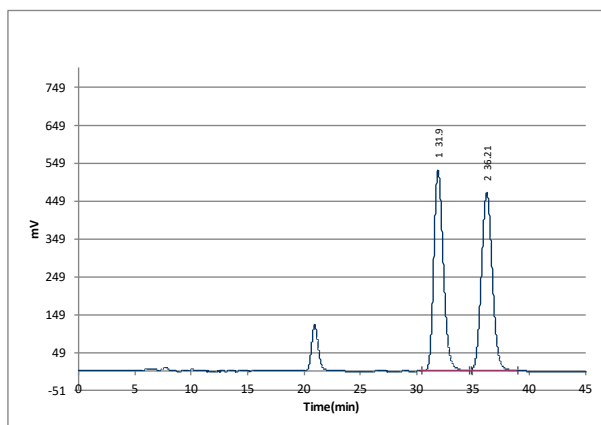
To a solution of (*S*)-**35b** (108 mg, 175 μmol) in MeOH (5.0 mL), Pd/C (10 wt%) was added at rt. After being stirred at rt for 12 h under H_2 atmosphere, the reaction mixture was filtered, and concentrated *in vacuo* to give (*S*)-**36b** (70.4 mg, 72% yield).

Yellow amorphous solid; $[\alpha]_{\text{D}}^{21} = -5.8$ (c 0.5, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 9.89 (br s, 1H), 7.97–7.88 (m, 3H), 7.85 (d, $J = 8.0$ Hz, 1H), 7.80 (d, $J = 8.0$ Hz, 1H), 7.70 (d, $J = 8.7$ Hz, 1H), 7.57 (d, $J = 8.6$ Hz, 1H), 7.37 (t, $J = 7.5$ Hz, 1H), 7.21 (ddd, $J = 8.1$, 6.9, 1.2 Hz, 1H), 7.11 (t, $J = 7.8$ Hz, 1H), 7.04 (d, $J = 8.5$ Hz, 1H), 6.89 (ddd, $J = 8.4$, 6.8, 1.3 Hz, 1H), 6.66 (br s, 1H), 1.43 (s, 9H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 167.0, 152.0, 142.0, 138.7, 136.9, 133.6, 132.0, 131.8, 131.1, 130.7, 130.3, 130.0, 128.9, 128.7, 128.1, 126.1, 126.0, 124.6, 124.1, 122.5, 122.4, 120.52, 120.46, 113.3, 82.4, 28.1 (Two carbon signals were overlapped); IR (KBr) 3412, 2979, 1682, 1572, 1542, 1497, 1432, 1247, 1156, 803, 756 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{30}\text{H}_{23}\text{NNaO}_4\text{S}_2$ 548.0961; Found 548.0980.

HPLC Analysis for Determination of the Optical Purities of *N*-Protected δ -Amino Acids **35**

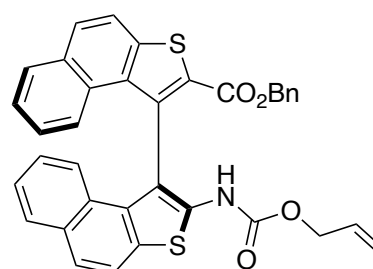
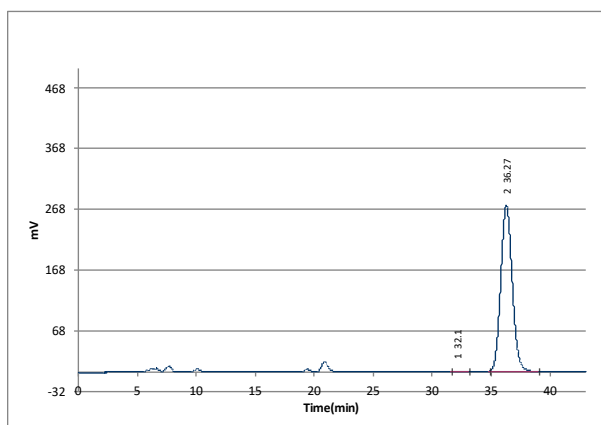
For δ -amino acid **35a**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHIRALPAK AD-H (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 0.5 mL/min, λ = 254 nm).

(1) Chromatogram of *rac*-**35a**



	Retention time (min)	Peak area (%)
1	31.9	49.69
2	36.2	50.31

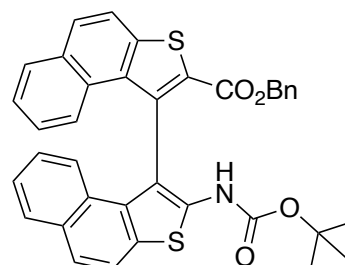
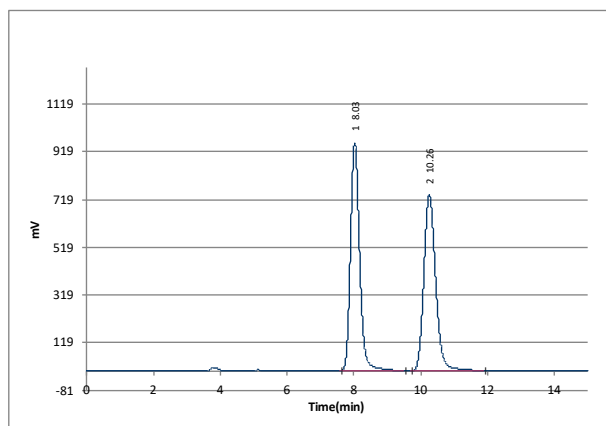
(2) Chromatogram of (*S*)-**35a** (>99% ee)



	Retention time (min)	Peak area (%)
1	32.1	0.23
2	36.3	99.77

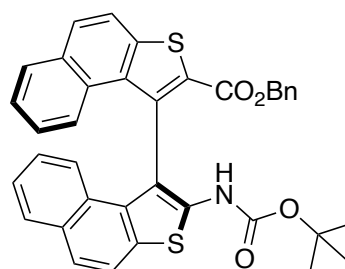
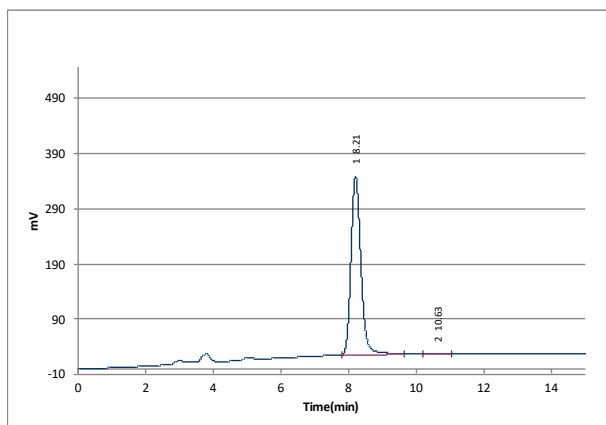
For δ -amino acid **35b**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHIRALPAK AD-H (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 0.5 mL/min, λ = 254 nm).

(1) Chromatogram of *rac*-**35b**



	Retention time (min)	Peak area (%)
1	8.0	50.07
2	10.3	49.93

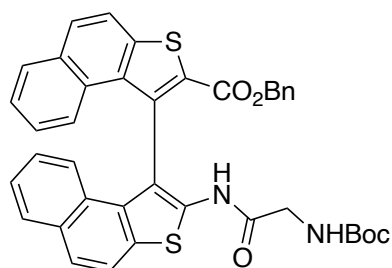
(2) Chromatogram of (*S*)-**35b** (>99% ee)



	Retention time (min)	Peak area (%)
1	8.2	99.62
2	10.6	0.38

Synthesis of Artificial Peptide *Rac-9* (Scheme 10)

Benzyl 2'-(2-((*tert*-butoxycarbonyl)amino)acetamido)-[1,1'-binaphtho[2,1-*b*]thiophene]-2-carboxylate (*rac-9*)



To a solution of *N*-(*tert*-butoxycarbonyl)glycine (*N*-Boc-glycine) (335 mg, 1.91 mmol, 5.00 equiv.) and DIPEA (333 μ L, 1.91 mmol, 5.00 equiv.) in THF (20 mL), a solution of ethyl chloroformate (182 μ L, 1.91 mmol, 5.00 equiv.) in THF (5.0 mL) was added at 0 $^{\circ}$ C. After being stirred at the same temperature for 30 min, *rac-8* (197 mg, 382 μ mol, 1.00 equiv.) in THF (20 mL) was added dropwise, and stirred at rt for

12 h, then refluxed for 4 h. The reaction was quenched with sat. aq. NH_4Cl , and extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO_2 , *n*-hexane:AcOEt = 5:1) to afford *rac-9* (144 mg, 56% yield).

Colorless prisms (CH_2Cl_2 /*n*-hexane); M.p. 222–224 $^{\circ}$ C; ^1H NMR (400 MHz, CDCl_3) δ 8.62 (br s, 1H), 7.97 (d, J = 8.7 Hz, 1H), 7.93–7.81 (m, 4H), 7.72 (d, J = 8.7 Hz, 1H), 7.49 (d, J = 8.7 Hz, 1H), 7.38–7.31 (m, 1H), 7.30–7.23 (m, 1H), 7.23–7.18 (m, 1H), 7.18–7.10 (m, 3H), 7.08–7.02 (m, 1H), 6.97–6.86 (m, 3H), 5.03 (d, J = 12.2 Hz, 1H), 4.93 (d, J = 12.2 Hz, 1H), 4.69 (br s, 1H), 3.69–3.57 (m, 2H), 1.17 (s, 9H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 166.6, 162.1, 156.1, 141.5, 136.9, 135.4, 135.0, 133.6, 132.8, 132.1, 132.0, 131.7, 130.8, 129.7, 129.3, 129.0, 128.9, 128.5, 128.2, 128.0, 126.2, 126.1, 124.9, 124.8, 122.8, 122.5, 120.7, 120.6, 116.4, 80.7, 67.4, 41.1, 28.1 (Two carbon signals were overlapped); IR (KBr) 3363, 3299, 1720, 1694, 1574, 1502, 1261, 1066, 802 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{39}\text{H}_{32}\text{N}_2\text{NaO}_5\text{S}_2$ 695.1645; Found 695.1648.

Crystallographic data for the single crystal of *rac-9* obtained by recrystallization from CH_2Cl_2 /*n*-hexane: $\text{C}_{39}\text{H}_{32}\text{N}_2\text{O}_5\text{S}_2$, M = 672.78, $0.18 \times 0.08 \times 0.05$ mm^3 , triclinic, $P\bar{1}$, a = 11.0505(2) \AA , b = 12.2836(3) \AA , c = 14.4309(3) \AA , α = 67.846(1) $^{\circ}$, β = 69.471(2) $^{\circ}$, γ = 79.494(2) $^{\circ}$, V = 1696.19(7) \AA^3 , Z = 2, ρ_{calcd} = 1.317 gcm^{-3} , T = 103(2) K, 33138 reflections measured, 6943 unique. The final R_1 and wR were 0.0623 and 0.1658 (all data). These data have been deposited with the Cambridge Crystallographic Data Center as CCDC 1914808.

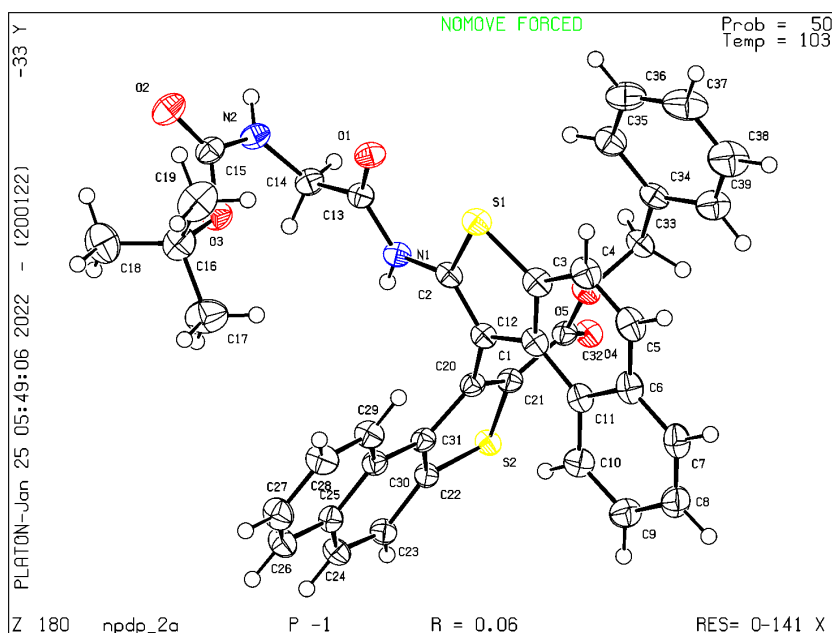


Figure S14. ORTEP Diagram of the Single Crystal of Racemic **9** (50% Probability).

NBO Analysis for Racemic **9** (Figure 17)

We performed NBO analysis for *rac*-**9** to investigate intramolecular orbital interactions at the ω B97XD/6-311G(d,p) level, based on the structure of (*S*)-**9** in the crystal structure of *rac*-**9** (CCDC 1914808), using the Gaussian 16 software package.⁴⁵

Second order perturbation theory analysis of Fock matrix in NBO basis

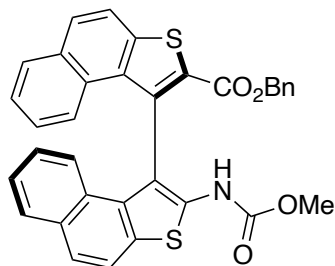
Donor NBO (i)	Acceptor NBO (j)	E(2) kcal/mol	E(j) – E(i) a.u.	F(i,j) a.u.
BD(1) N20–H21 (#30)	BD*(1) C2–S3 (#974)	4.77	1.15	0.066
LP(1) O23 (#163)	BD*(1) S3–C4 (#976)	1.05	1.11	0.031
LP(2) O23 (#164)	BD*(1) S3–C4 (#976)	3.06	0.67	0.041
LP(2) O65 (#175)	BD*(1) S47–C48 (#1029)	0.84	0.65	0.022
LP(1) O66 (#176)	BD*(1) C46–S47 (#1027)	0.67	0.96	0.023

Threshold for printing: 0.50 kcal/mol

第2章に関する実験

Preparation of Naphthothiophene-Type Rh(II) Carboxylate Complexes (*R*)-10a and 10b (Scheme 13A)

(*R*)-Benzyl 2'-((methoxycarbonyl)amino)-[1,1'-binaphtho[2,1-*b*]thiophene]-2-carboxylate ((*R*)-S10a)

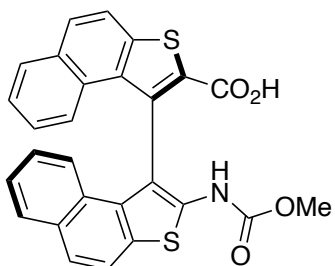


To a solution of (*R*)-**30** (403 mg, 0.740 mmol, 1.00 equiv.) in toluene (50 mL), DPPA (239 μ L, 1.11 mmol, 1.50 equiv.) and Et₃N (309 μ L, 2.22 mmol, 3.00 equiv.) were added at rt under an Ar atmosphere. After being stirred at 90 °C for 4.5 h, the reaction mixture was cooled to 50 °C, and MeOH (299 μ L, 7.40 mmol, 10.0 equiv.) was added. After being stirred at 50 °C for 3.5 h, the reaction mixture was quenched with sat. aq. NH₄Cl, and extracted with

AcOEt. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 4:1 to 3:1) to afford (*R*)-S10a (253 mg, 61% yield).

Pale yellow amorphous solid; $[\alpha]_D^{18} = +54.1$ (*c* 0.6, CHCl₃, for (*R*)-isomer); ¹H NMR (500 MHz, CDCl₃) δ 7.95 (d, *J* = 8.9 Hz, 1H), 7.90 (d, *J* = 8.9 Hz, 1H), 7.88–7.78 (m, 3H), 7.69 (d, *J* = 8.7 Hz, 1H), 7.59 (d, *J* = 8.6 Hz, 1H), 7.39–7.31 (m, 1H), 7.28–7.22 (m, 1H), 7.22–7.04 (m, 5H), 6.93 (ddd, *J* = 8.3, 6.8, 1.4 Hz, 1H), 6.86 (d, *J* = 7.5 Hz, 2H), 6.76 (br s, 1H), 4.98 (d, *J* = 3.0 Hz, 2H), 3.64 (s, 3H); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 162.1, 153.4, 141.5, 136.9, 136.6, 134.9, 133.5, 132.2, 132.0, 131.8, 131.5, 130.8, 129.8, 129.2, 129.1, 128.9, 128.4, 128.2, 128.0, 126.18, 126.15, 124.9, 124.5, 122.7, 122.4, 120.7, 120.6, 115.1, 67.4, 53.1 (Two carbon signals were overlapped); IR (neat) 3248, 1699, 1572, 1542, 1499, 1251, 1063, 800, 741, 698 cm⁻¹; HRMS (EI) *m/z*: [M]⁺ Calcd for C₃₄H₂₃NO₄S₂ 573.1069; Found 573.1071.

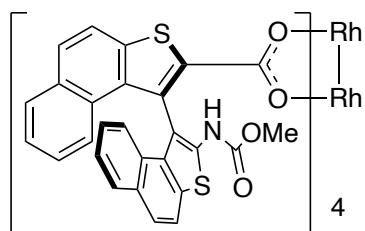
(*R*)-2'-((Methoxycarbonyl)amino)-[1,1'-binaphtho[2,1-*b*]thiophene]-2-carboxylic acid ((*R*)-39)



To a solution of (*R*)-S10a (608 mg, 1.06 mmol) in CHCl₃/MeOH (1:1, 20 mL), Pd/C (10 wt%) was added at rt. After being stirred at rt for 7.5 h under a H₂ atmosphere, the reaction mixture was filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 1:1) to afford (*R*)-39 (302 mg, 59% yield).

Yellow amorphous solid; $[\alpha]_D^{26} = +27.1$ (*c* 1, CHCl₃, for (*R*)-isomer); ¹H NMR (500 MHz, CDCl₃) δ 7.99–7.88 (m, 3H), 7.86 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.80 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.71 (d, *J* = 8.8 Hz, 1H), 7.52 (d, *J* = 8.6 Hz, 1H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.22 (ddd, *J* = 8.0, 6.8, 1.2 Hz, 1H), 7.12–7.02 (m, 2H), 6.90 (ddd, *J* = 8.5, 6.9, 1.3 Hz, 1H), 6.77 (br s, 1H), 3.63 (s, 3H); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 166.0, 153.6, 142.0, 138.3, 136.6, 133.6, 132.4, 132.1, 132.0, 131.3, 130.8, 130.6, 130.2, 129.2, 129.1, 128.9, 128.1, 126.3, 124.9, 124.6, 122.6, 122.5, 120.7, 120.6, 114.9, 53.1 (One carbon signal was overlapped); IR (neat) 3008, 1680, 1573, 1541, 1497, 1244, 1205, 1064, 801, 743 cm⁻¹; HRMS (EI) *m/z*: [M]⁺ Calcd for C₂₇H₁₇NO₄S₂ 483.0599; Found 483.0600.

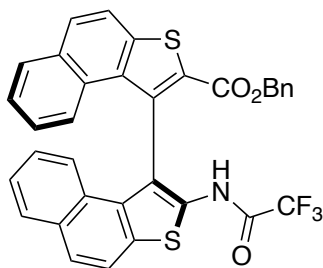
Complex (*R*)-**10a**



A solution of (*R*)-**39** (264 mg, 546 μ mol, 6.00 equiv.) and $\text{Rh}_2(\text{OAc})_4$ (40.2 mg, 91.0 μ mol, 1.00 equiv.) in chlorobenzene (15 mL) was stirred under reflux conditions. In the reaction time, chlorobenzene (10 mL) was added two times when there was little chlorobenzene in the flask. After being stirred for 8 h under reflux conditions, the reaction mixture was concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO_2 , *n*-hexane:AcOEt = 1:1) to afford complex (*R*)-**10a** (154 mg, 79% yield).

Green solid; M.p. >300 °C; $[\alpha]_{\text{D}}^{26} = +121$ (*c* 1, CHCl_3 , for (*R*)-isomer); ^1H NMR (300 MHz, CDCl_3) δ 8.25–7.61 (m, 24H), 7.38–7.27 (m, 4H), 7.25–7.10 (m, 8H), 7.01–6.79 (m, 8H), 6.71–6.57 (m, 4H), 2.32 (s, 12H); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3) δ 179.8, 153.2, 140.7, 135.8, 133.8, 133.0, 132.2, 132.0, 131.6, 130.6, 129.5, 128.8, 128.7, 127.4, 125.8, 125.6, 124.7, 122.7, 120.6, 52.3 (Seven carbon signals were overlapped); IR (neat) 1707, 1574, 1495, 1358, 1203, 1060, 799, 735, 525, 479 cm^{-1} ; HRMS (ESI) *m/z*: $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{108}\text{H}_{64}\text{N}_4\text{NaO}_{16}\text{Rh}_2\text{S}_8$ 2157.0085; Found 2157.0115.

(*S*)-Benzyl 2'-(2,2,2-trifluoroacetamido)-[1,1'-binaphtho[2,1-*b*]thiophene]-2-carboxylate ((*S*)-**S10b**)

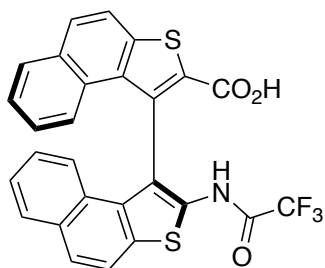


To a solution of (*S*)-**8** (886 mg, 1.72 mmol, 1.00 equiv.) in CH_2Cl_2 (20 mL), DIPEA (449 μ L, 2.58 mmol, 1.50 equiv.) and 2,2,2-trifluoroacetic anhydride (TFAA) (361 μ L, 2.58 mmol, 1.50 equiv.) were added at 0 °C under an Ar atmosphere. After being stirred at rt for 1 h, the reaction mixture was quenched with sat. aq. NH_4Cl , and extracted with CHCl_3 . The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO_2 , *n*-hexane:AcOEt = 5:1 to 4:1) to afford (*S*)-**S10b** (818 mg, 78% yield).

*(*R*)-**S10b** was also synthesized by following this procedure (89% yield).

Colorless oil; $[\alpha]_{\text{D}}^{20} = -2.2$ (*c* 1, CHCl_3 , for (*S*)-isomer); ^1H NMR (400 MHz, CDCl_3) δ 8.07 (br s, 1H), 8.01 (d, $J = 8.8$ Hz, 1H), 7.98–7.94 (m, 1H), 7.94–7.84 (m, 3H), 7.83–7.78 (m, 1H), 7.43–7.35 (m, 2H), 7.32 (ddd, $J = 8.1, 6.9, 1.2$ Hz, 1H), 7.28–7.22 (m, 1H), 7.22–7.13 (m, 3H), 7.08 (ddd, $J = 8.6, 7.2, 1.4$ Hz, 1H), 7.00 (ddd, $J = 8.4, 6.9, 1.4$ Hz, 1H), 6.96–6.88 (m, 2H), 5.08–4.94 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 161.9, 153.5 (q, $J = 39$ Hz), 141.6, 135.3, 134.7, 133.6, 133.2, 132.3, 132.2, 132.1, 131.7, 130.6, 130.4, 130.2, 129.4, 129.3, 129.1, 128.6, 128.5, 128.20, 128.15, 126.7, 126.4, 126.3, 125.4, 122.6, 122.1, 120.6, 120.5, 120.3, 115.3 (q, $J = 286$ Hz), 67.7; IR (neat) 3394, 3251, 3059, 1715, 1584, 1546, 1503, 1222, 1156, 736 cm^{-1} ; HRMS (ESI) *m/z*: $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{34}\text{H}_{20}\text{F}_3\text{NNaO}_3\text{S}_2$ 634.0729; Found 634.0728.

(*S*)-2'-(2,2,2-Trifluoroacetamido)-[1,1'-binaphtho[2,1-*b*]thiophene]-2-carboxylic acid ((*S*)-**40**)

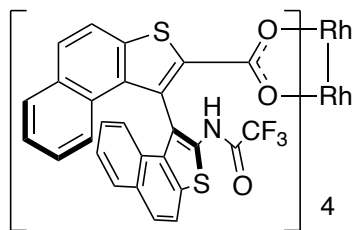


To a solution of (*S*)-**S10b** (818 mg, 1.34 mmol) in $\text{CHCl}_3/\text{MeOH}$ (1:1, 20 mL), Pd/C (10 wt%) was added at rt. After being stirred at rt for 15 h under a H_2 atmosphere, the reaction mixture was filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO_2 , *n*-hexane:AcOEt = 1:1) to afford (*S*)-**40** (637 mg, 91% yield).

*(*R*)-**40** was also synthesized by following this procedure (100% yield).

Yellow solid; M.p. 130–132 °C; $[\alpha]_{\text{D}}^{20} = -14.2$ (*c* 0.4, CHCl_3 , for (*S*)-isomer); ^1H NMR (600 MHz, CDCl_3) δ 9.83 (br s, 1H), 8.17 (br s, 1H), 7.99–7.88 (m, 3H), 7.88–7.81 (m, 2H), 7.78 (d, $J = 8.9$ Hz, 1H), 7.41–7.34 (m, 2H), 7.30–7.23 (m, 1H), 7.13–7.04 (m, 2H), 6.96 (ddd, $J = 8.4, 6.9, 1.4$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 166.9, 153.7 (q, $J = 39$ Hz), 142.2, 137.0, 133.7, 133.3, 132.3, 132.13, 132.06, 130.6, 130.5, 130.4, 130.2, 129.32, 129.26, 129.1, 128.2, 126.7, 126.5, 126.3, 125.4, 122.4, 122.1, 120.6, 120.5, 120.0, 115.3 (q, $J = 287$ Hz); IR (KBr) 3393, 3249, 3057, 1679, 1583, 1548, 1504, 1435, 1197, 908, 804, 735 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{27}\text{H}_{14}\text{F}_3\text{NNaO}_3\text{S}_2$ 544.0259; Found 544.0262.

Complex (*S*)-**10b**



A solution of (*S*)-**40** (257 mg, 493 μmol , 6.00 equiv.) and $\text{Rh}_2(\text{OAc})_4$ (36.3 mg, 82.1 μmol , 1.00 equiv.) in chlorobenzene (15 mL) was stirred under reflux conditions. In the reaction time, chlorobenzene (10 mL) was added two times when there was little chlorobenzene in the flask. After being stirred for 2 h under reflux conditions, the reaction mixture was concentrated *in vacuo* to

give a residue. The residue was purified by column chromatography (SiO_2 , *n*-hexane:AcOEt = 4:1 to 3:1) to afford complex (*S*)-**10b**. Purified complex (*S*)-**10b** was obtained by recrystallization from $\text{CHCl}_3/\text{hexane}$. Yield: 115 mg (61%).

*Complex (*R*)-**10b** was also synthesized by following this procedure (71% yield).

Green prisms; M.p. 280–282 °C; $[\alpha]_{\text{D}}^{20} = -68.8$ (*c* 0.3, CHCl_3 , for (*S*)-isomer); ^1H NMR (600 MHz, CDCl_3) δ 8.15 (d, $J = 8.9$ Hz, 4H), 8.02 (d, $J = 8.9$ Hz, 4H), 7.95 (d, $J = 7.8$ Hz, 4H), 7.81 (d, $J = 8.9$ Hz, 4H), 7.77 (d, $J = 7.7$ Hz, 4H), 7.71 (d, $J = 8.9$ Hz, 4H), 7.65 (br s, 4H), 7.28–7.23 (m, 4H), 7.03–6.96 (m, 8H), 6.92 (ddd, $J = 8.5, 7.0, 1.3$ Hz, 4H), 6.84 (d, $J = 8.7$ Hz, 4H), 6.37 (t, $J = 7.8$ Hz, 4H); $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 179.4, 153.3 (q, $J = 39$ Hz), 141.1, 133.1, 132.4, 132.3, 132.2, 132.01, 131.96, 131.8, 131.0, 130.2, 129.5, 129.1, 128.9, 127.6, 126.4, 126.0, 125.9, 125.4, 122.09, 122.05, 121.1, 120.8, 120.6, 115.0 (q, $J = 287$ Hz) (One carbon signal was overlapped); IR (KBr) 1724, 1581, 1546, 1498, 1404, 1362, 1152, 803, 773, 737 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{108}\text{H}_{75}\text{Cl}_{18}\text{F}_{12}\text{N}_4\text{NaO}_{16.50}\text{Rh}_2\text{S}_8$ 2308.9158; Found 2308.9124.

Crystallographic data for the single crystal of (*S*)-**10b**•2EtOH obtained by recrystallization from CHCl_3/n -hexane (CHCl_3 molecules are included in the crystal): $\text{C}_{118}\text{H}_{75}\text{Cl}_{18}\text{F}_{12}\text{N}_4\text{O}_{16.50}\text{Rh}_2\text{S}_8$, $M = 3141.22$, $0.40 \times 0.20 \times 0.060$ mm^3 , monoclinic, $C2$, $a = 30.9330(7)$ Å, $b = 17.5225(6)$ Å, $c = 24.1606(7)$ Å, $\alpha = 90^\circ$, $\beta = 92.0449(10)^\circ$, $\gamma = 90^\circ$, $V = 13087.3(7)$ Å³, $Z = 4$, $\rho_{\text{calcd}} = 1.594$ gcm^{-3} , $T = 113(2)$ K, 72940 reflections measured, 20019 unique. The

final R_1 and wR were 0.0897 and 0.1790 (all data). These data have been deposited with the Cambridge Crystallographic Data Center as CCDC 1837271.

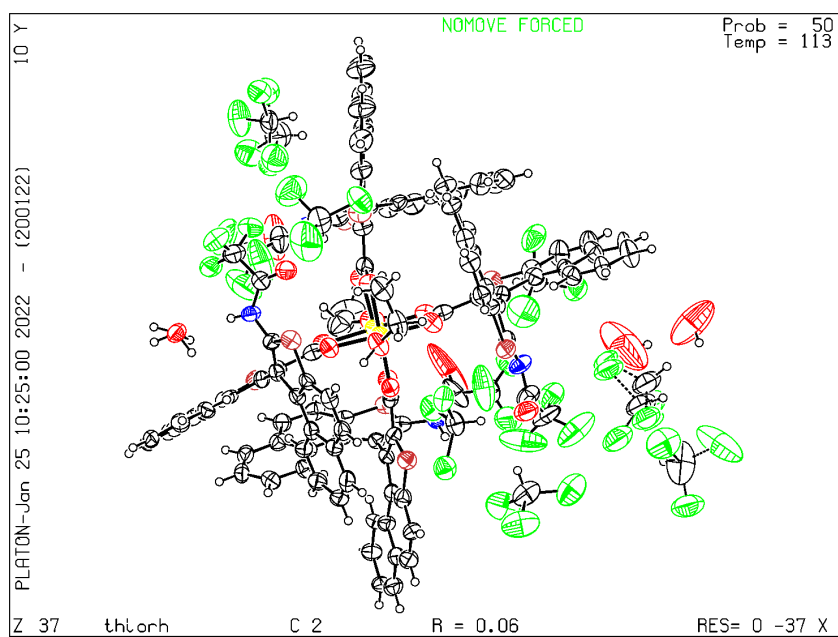
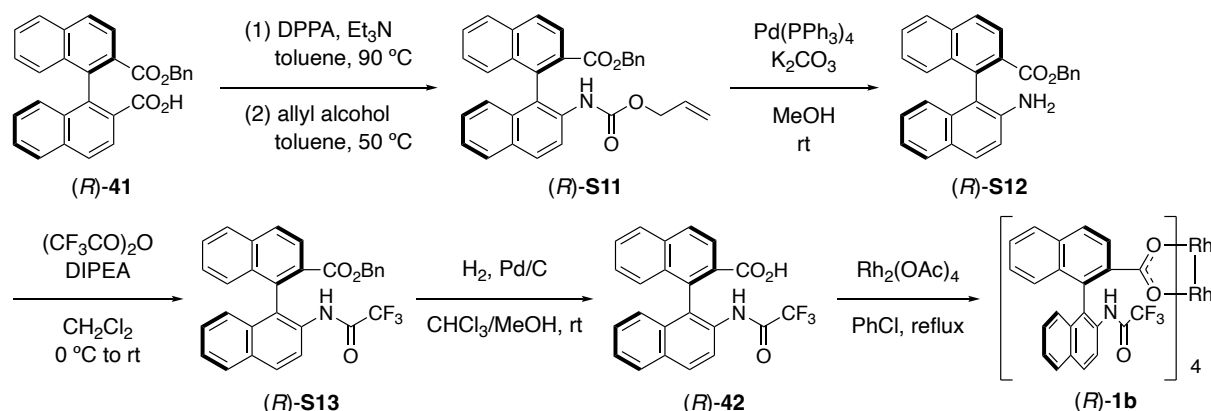


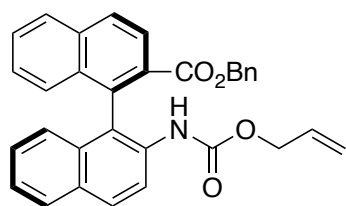
Figure S15. ORTEP Diagram of the Single Crystal of (*S*)-**10b**•2EtOH (50% Probability).

Preparation of Binaphthyl-Type Rh(II) Carboxylate Complex (*R*)-1b (Scheme 13B)



Scheme S12. Synthesis of Binaphthyl-Type Rh(II) Carboxylate Complex (*R*)-1b.

(*R*)-Benzyl 2'-(((allyloxy)carbonyl)amino)-[1,1'-binaphthalene]-2-carboxylate ((*R*)-S11)

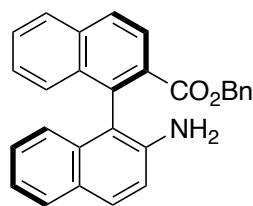


To a solution of (*R*)-**41**^{12b} (3.30 g, 7.36 mmol, 1.00 equiv.) in toluene (350 mL), Et₃N (3.19 mL, 22.9 mmol, 3.00 equiv.) and DPPA (2.46 mL, 11.4 mmol, 1.50 equiv.) were added at rt under an Ar atmosphere. After being stirred at 90 °C for 4 h, the reaction mixture was cooled to 50 °C, and allyl alcohol (5.19 mL, 76.3 mmol, 10.0 equiv.) was added. After being stirred at

50 °C for 5 h, the reaction mixture was quenched with sat. aq. NH₄Cl, and extracted with AcOEt. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 5:1) to afford (*R*)-**S11** (2.90 g, 78% yield).

Colorless oil; $[\alpha]_D^{20} = +16.5$ (*c* 0.5, CHCl₃, for (*R*)-isomer); ¹H NMR (400 MHz, CDCl₃) δ 8.28 (br s, 1H), 8.15 (d, *J* = 8.6 Hz, 1H), 8.08 (d, *J* = 8.7 Hz, 1H), 7.98 (d, *J* = 8.2 Hz, 1H), 7.92 (d, *J* = 9.0 Hz, 1H), 7.85 (d, *J* = 8.2 Hz, 1H), 7.58 (ddd, *J* = 8.1, 6.7, 1.2 Hz, 1H), 7.38–7.29 (m, 2H), 7.25–7.14 (m, 5H), 6.90–6.85 (m, 2H), 6.85–6.81 (m, 1H), 6.26 (br s, 1H), 5.80 (ddt, *J* = 17.3, 10.5, 5.7 Hz, 1H), 5.21–5.09 (m, 2H), 4.96–4.87 (m, 2H), 4.57–4.42 (m, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 167.4, 153.4, 135.4, 135.1, 134.8, 133.9, 133.0, 132.53, 132.46, 130.5, 130.2, 129.4, 129.0, 128.4, 128.33, 128.27, 128.12, 128.08, 127.7, 127.1, 126.7, 126.2, 125.3, 124.7, 123.6, 120.1, 118.2, 67.2, 65.9 (One carbon signal was overlapped); IR (neat) 3420, 3061, 1729, 1502, 1459, 1277, 1212, 1128, 971, 768 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₃₂H₂₅NNaO₄ 510.1676; Found 510.1680.

(*R*)-Benzyl 2'-amino-[1,1'-binaphthalene]-2-carboxylate ((*R*)-**S12**)

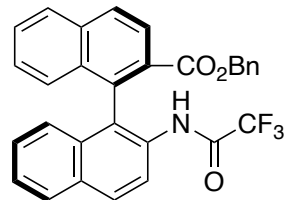


To a solution of (*R*)-**S11** (2.90 g, 5.95 mmol, 1.00 equiv.) in MeOH (80 mL), Pd(PPh₃)₄ (344 mg, 297 μmol, 5.00 mol%) and K₂CO₃ (2.47 g, 17.8 mmol, 3.00 equiv.) were added at rt under an Ar atmosphere. After being stirred at rt for 20 min, the reaction mixture was quenched with sat. aq. NH₄Cl, and extracted with AcOEt.

The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 5:1) to afford (*R*)-**S12** (1.80 g, 75% yield).

Yellow oil; $[\alpha]_D^{20} = +6.4$ (*c* 1.5, CHCl₃, for (*R*)-isomer); ¹H NMR (400 MHz, CDCl₃) δ 8.15 (d, *J* = 8.6 Hz, 1H), 8.04 (d, *J* = 8.8 Hz, 1H), 7.98 (d, *J* = 8.2 Hz, 1H), 7.77 (dd, *J* = 11.5, 8.8 Hz, 2H), 7.58 (ddd, *J* = 8.1, 6.7, 1.3 Hz, 1H), 7.42 (d, *J* = 8.5 Hz, 1H), 7.34 (ddd, *J* = 8.5, 6.7, 1.3 Hz, 1H), 7.28–7.17 (m, 4H), 7.15 (ddd, *J* = 8.3, 6.8, 1.4 Hz, 1H), 7.02 (d, *J* = 8.7 Hz, 1H), 6.91–6.84 (m, 3H), 4.96 (d, *J* = 1.5 Hz, 2H), 3.48 (br s, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 167.8, 141.7, 136.3, 135.5, 135.4, 134.2, 132.6, 130.3, 129.2, 128.6, 128.32, 128.26, 128.1, 128.04, 127.99, 127.9, 127.4, 127.3, 126.6, 126.4, 124.1, 122.2, 118.1, 116.0, 67.0 (One carbon signal was overlapped); IR (neat) 3472, 3379, 3058, 1712, 1621, 1380, 1276, 1123, 816, 769, 733 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₂₈H₂₁NNaO₂ 426.1464; Found 426.1463.

(*R*)-Benzyl 2'-(2,2,2-trifluoroacetamido)-[1,1'-binaphthalene]-2-carboxylate ((*R*)-**S13**)

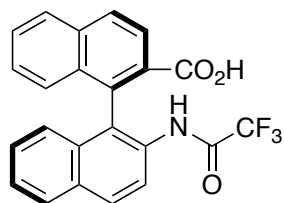


To a solution of (*R*)-**S12** (604 mg, 1.50 mmol, 1.00 equiv.) in CH₂Cl₂ (15 mL), DIPEA (391 μL, 2.25 mmol, 1.50 equiv.) and TFAA (314 μL, 2.25 mmol, 1.50 equiv.) were added at 0 °C under an Ar atmosphere. After being stirred at rt for 0.5 h, the reaction mixture was quenched with sat. aq. NH₄Cl, and extracted with CHCl₃. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and

concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 5:1) to afford (*R*)-**S13** (686 mg, 92% yield).

Colorless oil; $[\alpha]_D^{20} = -29.1$ (*c* 0.6, CHCl₃, for (*R*)-isomer); ¹H NMR (400 MHz, CDCl₃) δ 8.23 (d, *J* = 9.0 Hz, 1H), 8.19–8.11 (m, 2H), 8.05–7.97 (m, 2H), 7.94 (d, *J* = 8.3 Hz, 1H), 7.80 (br s, 1H), 7.59 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H), 7.48 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H), 7.36–7.15 (m, 6H), 7.03–6.92 (m, 3H), 4.99 (s, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 167.5, 154.9 (q, *J* = 37 Hz), 135.1, 134.8, 133.2, 132.8, 132.2, 131.8, 131.2, 130.1, 129.8, 129.4, 128.54, 128.49, 128.4, 128.34, 128.31, 128.25, 128.0, 127.18, 127.15, 126.6, 126.1, 125.7, 125.6, 120.8, 115.5 (q, *J* = 287 Hz), 67.5; IR (neat) 3402, 3296, 3063, 1731, 1601, 1531, 1329, 1277, 1162, 909, 734 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₃₀H₂₀F₃NNaO₃ 522.1287; Found 522.1295.

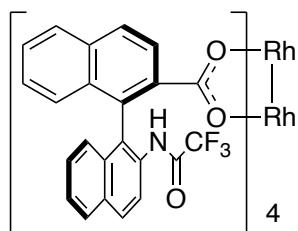
(*R*)-2'-(2,2,2-Trifluoroacetamido)-[1,1'-binaphthalene]-2-carboxylic acid ((*R*)-**42**)



To a solution of (*R*)-**S13** (510 mg, 1.02 mmol, 1.00 equiv.) in $\text{CHCl}_3/\text{MeOH}$ (1:1, 8.0 mL), Pd/C (10 wt%) was added at rt. After being stirred at rt for 3 h under a H_2 atmosphere, the reaction mixture was filtered, and concentrated *in vacuo* to give (*R*)-**42** (420 mg, quant.). This (*R*)-**42** was used for complexation without further purification.

White solid; M.p. 79–80 °C; $[\alpha]_{\text{D}}^{20} = -5.4$ (c 0.4, CHCl_3 , for (*R*)-isomer); ^1H NMR (600 MHz, CDCl_3) δ 9.55 (br s, 1H), 8.20 (d, $J = 9.0$ Hz, 1H), 8.10 (d, $J = 2.3$ Hz, 2H), 8.03 (d, $J = 9.0$ Hz, 1H), 7.98 (d, $J = 8.3$ Hz, 1H), 7.92 (d, $J = 8.2$ Hz, 1H), 7.67 (br s, 1H), 7.59 (ddd, $J = 8.1, 6.7, 1.1$ Hz, 1H), 7.43 (ddd, $J = 8.1, 6.7, 1.2$ Hz, 1H), 7.32 (ddd, $J = 8.3, 6.7, 1.3$ Hz, 1H), 7.20 (ddd, $J = 8.3, 6.8, 1.3$ Hz, 1H), 7.11 (d, $J = 8.6$ Hz, 1H), 6.86 (d, $J = 8.5$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 172.0, 155.2 (q, $J = 38$ Hz), 135.6, 134.7, 132.9, 132.3, 131.9, 131.1, 129.9, 129.5, 129.0, 128.51, 128.46, 128.3, 128.2, 127.4, 127.2, 126.9, 126.2, 125.9, 125.6, 121.0, 115.6 (q, $J = 288$ Hz); IR (KBr) 3401, 3063, 1721, 1600, 1510, 1253, 1165, 909, 770, 734 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{23}\text{H}_{14}\text{F}_3\text{NNaO}_3$ 432.0818; Found 432.0820.

Complex (*R*)-**1b**



A solution of (*R*)-**42** (250 mg, 611 μmol , 5.00 equiv.) and $\text{Rh}_2(\text{OAc})_4$ (54.0 mg, 122 μmol , 1.0 equiv.) in chlorobenzene (15 mL) was stirred under reflux conditions. In the reaction time, chlorobenzene (10 mL) was added two times when there was little chlorobenzene in the flask. After being stirred for 7.5 h under reflux conditions, the reaction mixture was quenched with sat. aq. NaHCO_3 , and

extracted with AcOEt . The organic layer was washed with sat. aq. NaHCO_3 and brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO_2 , n -hexane: $\text{AcOEt} = 7:3$) to afford complex (*R*)-**1b** (208 mg, 93% yield). Purified complex (*R*)-**1b** was obtained by recrystallization from CHCl_3/n -hexane.

Green prisms; M.p. >300 °C; $[\alpha]_{\text{D}}^{20} = -144.2$ (c 0.5, CHCl_3 , for (*R*)-isomer); ^1H NMR (400 MHz, CDCl_3) δ 8.14 (d, $J = 8.9$ Hz, 4H), 8.07 (d, $J = 8.9$ Hz, 4H), 7.89 (dd, $J = 12.6, 8.1$ Hz, 8H), 7.75 (d, $J = 8.7$ Hz, 4H), 7.52–7.43 (m, 8H), 7.24–7.14 (m, 8H), 6.99 (d, $J = 8.7$ Hz, 4H), 6.80 (d, $J = 8.6$ Hz, 4H), 6.71 (ddd, $J = 8.1, 6.7, 1.2$ Hz, 4H), 6.54 (d, $J = 8.5$ Hz, 4H); $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 184.9, 155.1 (q, $J = 38$ Hz), 134.7, 132.8, 131.8, 131.5, 131.2, 130.7, 130.5, 128.9, 128.81, 128.77, 128.2, 128.0, 127.6, 126.6, 126.5, 126.2, 126.1, 125.8, 121.0, 115.4 (q, $J = 287$ Hz) (One carbon signal was overlapped); IR (KBr) 3399, 1730, 1595, 1510, 1396, 1266, 1162, 909, 771, 735 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{92}\text{H}_{52}\text{F}_{12}\text{N}_4\text{NaO}_{12}\text{Rh}_2$ 1861.1392; Found 1861.1383.

Crystallographic data for the single crystal of (*R*)-**1b**•2EtOH obtained by recrystallization from CHCl_3/n -hexane (CHCl_3 molecules are included in the crystal): $\text{C}_{98}\text{H}_{66}\text{Cl}_6\text{F}_{12}\text{N}_4\text{O}_{14}\text{Rh}_2$, $M = 2170.06$, $0.10 \times 0.08 \times 0.02$ mm^3 , orthorhombic, $P2_12_12_1$, $a = 14.4646(3)$ Å, $b = 23.7613(5)$ Å, $c = 26.3686(6)$ Å, $\alpha = 90^\circ$, $\beta = 90^\circ$, $\gamma = 90^\circ$, $V = 9062.8(3)$ Å³, $Z = 4$, $\rho_{\text{calcd}} = 1.590$ gcm^{-3} , $T = 113(2)$ K, 123019 reflections measured, 15087 unique. The final R_1

and wR were 0.0988 and 0.1393 (all data). These data have been deposited with the Cambridge Crystallographic Data Center as CCDC 1839246.

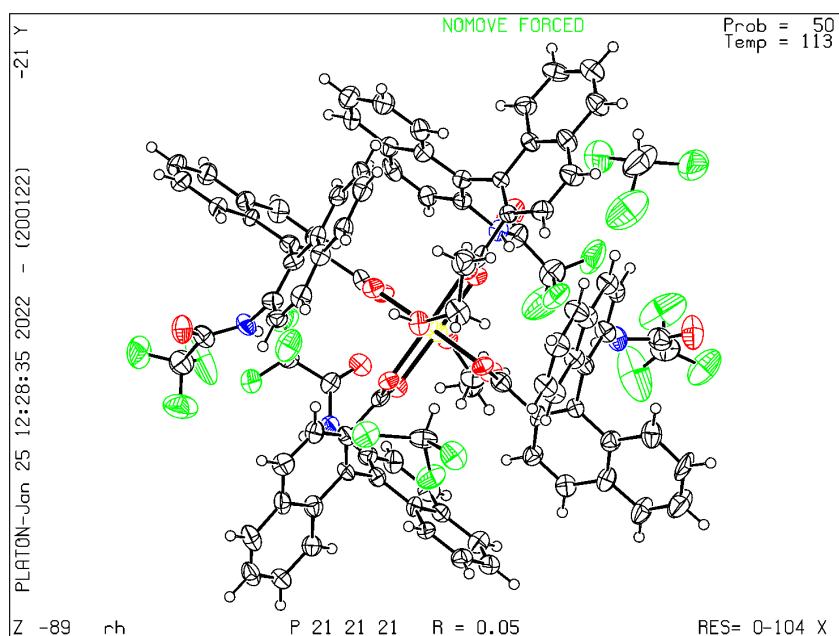
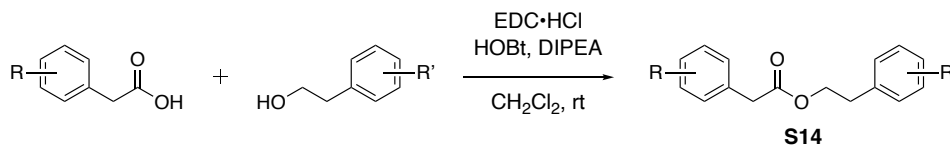


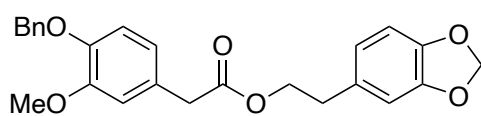
Figure S16. ORTEP Diagram of the Single Crystal of (*R*)-**1b**•2EtOH (50% Probability).

Preparation of Substrates



Scheme S13. Syntheses of 2-Arylethyl 2-Arylacetates **S14** (Method A).

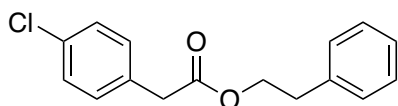
2-(Benzo[*d*][1,3]dioxol-5-yl)ethyl 2-(4-(benzyloxy)-3-methoxyphenyl)acetate (**S14a**)



To a solution of 2-(4-(benzyloxy)-3-methoxyphenyl)acetic acid (**43**) (2.65 g, 9.73 mmol, 1.00 equiv.) in CH_2Cl_2 (50 mL), EDC·HCl (2.33 g, 12.1 mmol, 1.25 equiv.) and anhydrous HOBT (1.64 g, 12.1 mmol, 1.25 equiv.) were added at rt. After being stirred at rt for 30 min, DIPEA (5.09 mL, 29.2 mmol, 3.00 equiv.) and 2-(benzo[*d*][1,3]dioxol-5-yl)ethan-1-ol (**44**) (2.02 g, 12.1 mmol, 1.25 equiv.) were added, and the reaction mixture was stirred at rt for 4.5 h. Then, the resulting mixture was quenched with sat. aq. NH_4Cl , and extracted with CHCl_3 . The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO_2 , *n*-hexane:AcOEt = 4:1 to 3:1) to afford **S14a** (3.23 g, 79% yield).

White solid; M.p. 76–77 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.46–7.41 (m, 2H), 7.39–7.33 (m, 2H), 7.32–7.27 (m, 1H), 6.83–6.78 (m, 2H), 6.73–6.68 (m, 2H), 6.63 (d, J = 1.7 Hz, 1H), 6.58 (dd, J = 7.9, 1.7 Hz, 1H), 5.92 (s, 2H), 5.15 (s, 2H), 4.25 (t, J = 6.9 Hz, 2H), 3.86 (s, 3H), 3.52 (s, 2H), 2.82 (t, J = 6.9 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 171.8, 149.7, 147.7, 147.4, 146.3, 137.3, 131.6, 128.7, 128.0, 127.4, 127.1, 121.9, 121.5, 114.0, 113.0, 109.4, 108.4, 101.0, 71.1, 65.6, 56.1, 41.1, 34.9; IR (KBr) 2952, 2360, 1731, 1511, 1446, 1249, 1144, 1036, 932, 808 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{25}\text{H}_{24}\text{NaO}_6$ 443.1465; Found 443.1476.

2-Phenylethyl 2-(4-chlorophenyl)acetate (**S14c**)

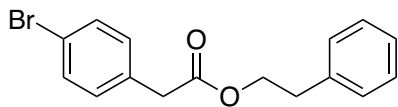


To a solution of 2-(4-chlorophenyl)acetic acid (1.00 g, 5.86 mmol, 1.00 equiv.) in CH_2Cl_2 (20 mL), EDC·HCl (1.41 g, 7.33 mmol, 1.25 equiv.) and anhydrous HOBT (991 mg, 7.33 mmol, 1.25 equiv.) were added at rt. After being stirred at rt for 1.5 h, DIPEA (3.07 mL, 17.6 mmol, 3.00 equiv.) and 2-phenylethanol (878 μL , 7.33 mmol, 1.25 equiv.) were added, and the reaction mixture was stirred at rt for 15 h. Then, the resulting mixture was quenched with sat. aq. NH_4Cl , and extracted with CHCl_3 . The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO_2 , *n*-hexane:AcOEt = 9:1) to afford **S14c** (1.06 g, 66% yield).

Colorless oil; ^1H NMR (300 MHz, CDCl_3) δ 7.29–7.14 (m, 5H), 7.14–7.04 (m, 4H), 4.28 (t, J = 6.9 Hz, 2H), 3.51 (s, 2H), 2.87 (t, J = 6.9 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3) δ 170.9, 137.7, 133.0, 132.5, 130.7, 128.9, 128.7, 128.5, 126.6, 65.4, 40.7, 35.0; IR (neat) 1736, 1493, 1250, 1156, 1091, 1013, 808, 748, 700, 498 cm^{-1} ;

HRMS (ESI) m/z : $[M+Na]^+$ Calcd for $C_{16}H_{15}ClNaO_2$ 297.0653; Found 297.0662.

2-Phenylethyl 2-(4-bromophenyl)acetate (**S14d**)

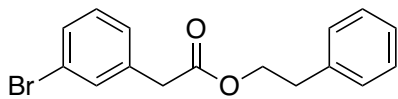


To a solution of 2-(4-bromophenyl)acetic acid (1.00 g, 4.65 mmol, 1.00 equiv.) in CH_2Cl_2 (15 mL), EDC·HCl (1.11 g, 5.81 mmol, 1.25 equiv.) and anhydrous HOBt (785 mg, 5.81 mmol, 1.25 equiv.) were added at rt.

After being stirred at rt for 30 min, DIPEA (2.43 mL, 13.9 mmol, 3.00 equiv.) and 2-phenylethanol (696 μ L, 5.81 mmol, 1.25 equiv.) were added, and the reaction mixture was stirred at rt for 15.5 h. Then, the resulting mixture was quenched with sat. aq. NH_4Cl , and extracted with $CHCl_3$. The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO_2 , *n*-hexane:AcOEt = 9:1) to afford **S14d** (886 mg, 60% yield).

Colorless oil; 1H NMR (300 MHz, $CDCl_3$) δ 7.44–7.34 (m, 2H), 7.31–7.15 (m, 3H), 7.15–7.02 (m, 4H), 4.29 (t, J = 6.9 Hz, 2H), 3.51 (s, 2H), 2.89 (t, J = 6.9 Hz, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 170.9, 137.7, 133.0, 131.7, 131.1, 129.0, 128.6, 126.7, 121.2, 65.5, 40.9, 35.1; IR (neat) 1736, 1490, 1250, 1157, 1071, 1011, 803, 749, 700, 491 cm^{-1} ; HRMS (ESI) m/z : $[M+Na]^+$ Calcd for $C_{16}H_{15}BrNaO_2$ 341.0148; Found 341.0163.

2-Phenylethyl 2-(3-bromophenyl)acetate (**S14e**)

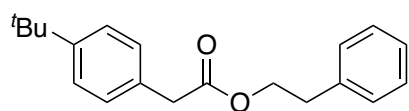


To a solution of 2-(3-bromophenyl)acetic acid (1.00 g, 4.65 mmol, 1.00 equiv.) in CH_2Cl_2 (15 mL), EDC·HCl (1.11 g, 5.81 mmol, 1.25 equiv.) and anhydrous HOBt (785 mg, 5.81 mmol, 1.25 equiv.) were added at rt.

After being stirred at rt for 30 min, DIPEA (2.43 mL, 13.9 mmol, 3.00 equiv.) and 2-phenylethanol (696 μ L, 5.81 mmol, 1.25 equiv.) were added, and the reaction mixture was stirred at rt for 11.5 h. Then, the resulting mixture was quenched with sat. aq. NH_4Cl , and extracted with $CHCl_3$. The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO_2 , *n*-hexane:AcOEt = 9:1) to afford **S14e** (931 mg, 63% yield).

Colorless oil; 1H NMR (500 MHz, $CDCl_3$) δ 7.43–7.34 (m, 2H), 7.30–7.24 (m, 2H), 7.23–7.19 (m, 1H), 7.18–7.09 (m, 4H), 4.30 (t, J = 6.9 Hz, 2H), 3.54 (s, 2H), 2.90 (t, J = 6.9 Hz, 2H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 170.9, 137.7, 136.2, 132.5, 130.3, 130.1, 129.0, 128.6, 128.1, 126.7, 122.6, 65.6, 41.0, 35.1; IR (neat) 1735, 1597, 1570, 1474, 1429, 1334, 1247, 1155, 1001, 749, 700 cm^{-1} ; HRMS (ESI) m/z : $[M+Na]^+$ Calcd for $C_{16}H_{15}BrNaO_2$ 341.0148; Found 341.0166.

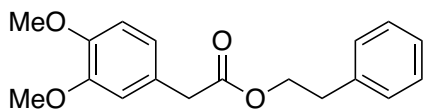
2-Phenylethyl 2-(4-*tert*-butylphenyl)acetate (**S14f**)



To a solution of 2-(4-*tert*-butylphenyl)acetic acid (1.50 g, 7.80 mmol, 1.00 equiv.) in CH_2Cl_2 (20 mL), EDC•HCl (1.87 g, 9.75 mmol, 1.25 equiv.) and anhydrous HOBt (1.32 g, 9.75 mmol, 1.25 equiv.) were added at rt. After being stirred at rt for 1.5 h, DIPEA (4.08 mL, 23.4 mmol, 3.00 equiv.) and 2-phenylethanol (1.17 mL, 9.75 mmol, 1.25 equiv.) were added, and the reaction mixture was stirred at rt for 57.5 h. Then, the resulting mixture was quenched with sat. aq. NH_4Cl , and extracted with CHCl_3 . The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO_2 , *n*-hexane:AcOEt = 9:1) to afford **S14f** (1.90 g, 82% yield).

Colorless oil; ^1H NMR (500 MHz, CDCl_3) δ 7.34–7.28 (m, 2H), 7.26–7.05 (m, 7H), 4.27 (t, J = 7.0 Hz, 2H), 3.53 (s, 2H), 2.87 (t, J = 7.0 Hz, 2H), 1.30 (s, 9H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 171.6, 149.8, 137.8, 131.0, 129.0, 128.9, 128.5, 126.5, 125.5, 65.3, 40.9, 35.1, 34.5, 31.4; IR (neat) 2961, 1737, 1515, 1457, 1252, 1149, 1004, 816, 748, 700 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{20}\text{H}_{24}\text{NaO}_2$ 319.1669; Found 319.1677.

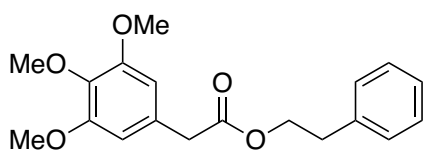
2-Phenylethyl 2-(3,4-dimethoxyphenyl)acetate (**S14g**)



To a solution of 2-(3,4-dimethoxyphenyl)acetic acid (1.50 g, 7.65 mmol, 1.00 equiv.) in CH_2Cl_2 (20 mL), EDC•HCl (1.83 g, 9.56 mmol, 1.25 equiv.) and anhydrous HOBt (1.29 g, 9.56 mmol, 1.25 equiv.) were added at rt. After being stirred at rt for 1.5 h, DIPEA (3.99 mL, 22.9 mmol, 3.00 equiv.) and 2-phenylethanol (1.45 mL, 9.56 mmol, 1.25 equiv.) were added, and the reaction mixture was stirred at rt for 57 h. Then, the resulting mixture was quenched with sat. aq. NH_4Cl , and extracted with CHCl_3 . The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO_2 , *n*-hexane:AcOEt = 4:1) to afford **S14g** (1.91 g, 83% yield).

Colorless oil; ^1H NMR (500 MHz, CDCl_3) δ 7.29–7.15 (m, 3H), 7.15–7.07 (m, 2H), 6.82–6.71 (m, 3H), 4.29 (t, J = 6.9 Hz, 2H), 3.83 (s, 3H), 3.80 (s, 3H), 3.51 (s, 2H), 2.89 (t, J = 7.0 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 171.6, 148.8, 148.1, 137.7, 128.8, 128.4, 126.42, 126.41, 121.4, 112.4, 111.2, 65.2, 55.8, 55.7, 40.9, 34.9; IR (neat) 2955, 1734, 1592, 1515, 1460, 1265, 1150, 1029, 751, 702 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{18}\text{H}_{20}\text{NaO}_4$ 323.1254; Found 323.1270.

2-Phenylethyl 2-(3,4,5-trimethoxyphenyl)acetate (**S14h**)

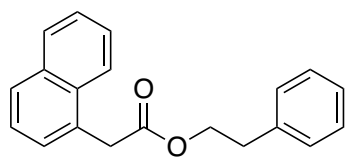


To a solution of 2-(3,4,5-trimethoxyphenyl)acetic acid (1.50 g, 6.63 mmol, 1.00 equiv.) in CH_2Cl_2 (20 mL), EDC•HCl (1.59 g, 8.29 mmol, 1.25 equiv.) and anhydrous HOBt (1.12 g, 8.29 mmol, 1.25 equiv.) were added at rt. After being stirred at rt for 1.5 h, DIPEA (3.46 mL, 19.9 mmol, 3.00 equiv.) and 2-phenylethanol (993 μL , 8.29 mmol, 1.25 equiv.) were added, and the reaction mixture was stirred at rt for 58 h. Then, the resulting mixture was quenched with sat. aq. NH_4Cl , and extracted with CHCl_3 . The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to

give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 7:3) to afford **S14h** (2.35 g, quant.).

Colorless oil; ¹H NMR (500 MHz, CDCl₃) δ 7.29–7.23 (m, 2H), 7.23–7.17 (m, 1H), 7.16–7.10 (m, 2H), 6.46 (s, 2H), 4.32 (t, *J* = 6.9 Hz, 2H), 3.83 (s, 3H), 3.80 (s, 6H), 3.52 (s, 2H), 2.92 (t, *J* = 6.9 Hz, 2H); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 171.4, 153.2, 137.7, 137.1, 129.5, 128.9, 128.4, 126.5, 106.3, 65.3, 60.8, 56.1, 41.7, 35.0; IR (neat) 2940, 1734, 1591, 1506, 1459, 1424, 1317, 1241, 1127, 1008, 750, 701 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₁₉H₂₂NaO₅ 353.1359; Found 353.1378.

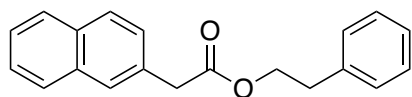
2-Phenylethyl 2-(1-naphthyl)acetate (**S14i**)



To a solution of 2-(1-naphthyl)acetic acid (1.00 g, 5.37 mmol, 1.00 equiv.) in CH₂Cl₂ (20 mL), EDC•HCl (1.29 g, 6.71 mmol, 1.25 equiv.) and anhydrous HOBT (907 mg, 6.71 mmol, 1.25 equiv.) were added at rt. After being stirred at rt for 1.5 h, DIPEA (2.80 mL, 16.1 mmol, 3.00 equiv.) and 2-phenylethanol (804 μL, 6.71 mmol, 1.25 equiv.) were added, and the reaction mixture was stirred at rt for 18 h. Then, the resulting mixture was quenched with sat. aq. NH₄Cl, and extracted with CHCl₃. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 9:1) to afford **S14i** (1.11 g, 71% yield).

Colorless oil; ¹H NMR (500 MHz, CDCl₃) δ 7.95–7.87 (m, 1H), 7.86–7.79 (m, 1H), 7.76 (d, *J* = 8.3 Hz, 1H), 7.51–7.41 (m, 2H), 7.41–7.30 (m, 2H), 7.22–7.13 (m, 3H), 7.06–6.97 (m, 2H), 4.27 (t, *J* = 6.9 Hz, 2H), 4.01 (s, 2H), 2.82 (t, *J* = 6.9 Hz, 2H); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 171.5, 137.8, 133.9, 132.2, 130.6, 128.9, 128.8, 128.5, 128.1, 126.5, 126.4, 125.8, 125.6, 123.9, 65.5, 39.3, 35.1 (One carbon signal was overlapped); IR (neat) 1733, 1453, 1329, 1253, 1149, 1050, 1001, 783, 748, 700 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₂₀H₁₈NaO₂ 313.1199; Found 313.1205.

2-Phenylethyl 2-(2-naphthyl)acetate (**S14j**)

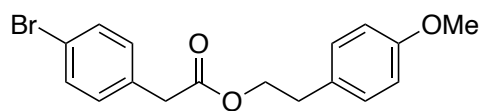


To a solution of 2-(2-naphthyl)acetic acid (1.00 g, 5.37 mmol, 1.00 equiv.) in CH₂Cl₂ (15 mL), EDC•HCl (1.29 g, 6.71 mmol, 1.25 equiv.) and anhydrous HOBT (907 mg, 6.71 mmol, 1.25 equiv.) were added at rt. After being stirred at rt for 30 min, DIPEA (2.80 mL, 16.1 mmol, 3.00 equiv.) and 2-phenylethanol (804 μL, 6.71 mmol, 1.25 equiv.) were added, and the reaction mixture was stirred at rt for 16 h. Then, the resulting mixture was quenched with sat. aq. NH₄Cl, and extracted with CHCl₃. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 9:1) to afford **S14j** (1.12 g, 72% yield).

White solid; M.p. 60–61 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.81–7.66 (m, 3H), 7.62 (s, 1H), 7.46–7.26 (m, 3H), 7.21–6.98 (m, 5H), 4.27 (t, *J* = 6.9 Hz, 2H), 3.68 (s, 2H), 2.83 (t, *J* = 6.9 Hz, 2H); ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 171.4, 137.7, 133.5, 132.5, 131.5, 128.9, 128.4, 128.2, 128.0, 127.70, 127.65, 127.4, 126.5, 126.1, 125.8, 65.3, 41.6, 35.0; IR (KBr) 2956, 1734, 1454, 1260, 1158, 1006, 816, 746, 700, 477 cm⁻¹; HRMS (ESI)

m/z : $[M+Na]^+$ Calcd for $C_{20}H_{18}NaO_2$ 313.1199; Found 313.1202.

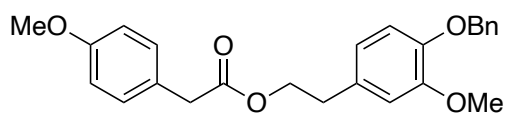
2-(4-Methoxyphenyl)ethyl 2-(4-bromophenyl)acetate (**S14t**)



To a solution of 2-(4-bromophenyl)acetic acid (1.50 g, 6.97 mmol, 1.00 equiv.) in CH_2Cl_2 (30 mL), EDC·HCl (1.67 g, 8.72 mmol, 1.25 equiv.) and anhydrous HOBt (1.18 g, 8.72 mmol, 1.25 equiv.) were added at rt. After being stirred at rt for 30 min, DIPEA (3.64 mL, 20.9 mmol, 3.00 equiv.) and 2-(4-methoxyphenyl)ethanol (1.33 g, 8.72 mmol, 1.25 equiv.) were added, and the reaction mixture was stirred at rt for 29 h. Then, the resulting mixture was quenched with sat. aq. NH_4Cl , and extracted with $CHCl_3$. The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO_2 , n -hexane:AcOEt = 9:1) to afford **S14t** (1.95 g, 80% yield).

Colorless oil; 1H NMR (500 MHz, $CDCl_3$) δ 7.47–7.40 (m, 2H), 7.14–7.08 (m, 2H), 7.08–7.02 (m, 2H), 6.85–6.79 (m, 2H), 4.28 (t, J = 6.9 Hz, 2H), 3.80 (s, 3H), 3.55 (s, 2H), 2.86 (t, J = 6.9 Hz, 2H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 171.0, 158.4, 133.1, 131.7, 131.1, 129.9, 129.7, 121.2, 114.0, 65.8, 55.3, 40.9, 34.2; IR (neat) 1735, 1612, 1513, 1489, 1248, 1158, 1071, 1035, 1011, 805 cm^{-1} ; HRMS (ESI) m/z : $[M+Na]^+$ Calcd for $C_{17}H_{17}BrNaO_3$ 371.0253; Found 371.0268.

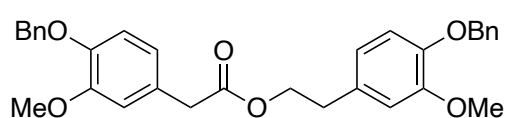
2-(4-Benzyloxy-3-methoxyphenyl)ethyl 2-(4-methoxyphenyl)acetate (**S14u**)



To a solution of 2-(4-methoxyphenyl)acetic acid (638 mg, 3.84 mmol, 1.00 equiv.) in CH_2Cl_2 (20 mL), EDC·HCl (920 mg, 4.80 mmol, 1.25 equiv.) and anhydrous HOBt (649 mg, 4.80 mmol, 1.25 equiv.) were added at rt. After being stirred at rt for 30 min, DIPEA (2.00 mL, 11.5 mmol, 3.00 equiv.) and 2-(4-benzyloxy-3-methoxyphenyl)ethanol (**50**) (1.24 g, 4.80 mmol, 1.25 equiv.) were added, and the reaction mixture was stirred at rt for 23 h. Then, the resulting mixture was quenched with sat. aq. NH_4Cl , and extracted with $CHCl_3$. The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO_2 , n -hexane:AcOEt = 4:1) to afford **S14u** (1.45 g, 93% yield).

Colorless oil; 1H NMR (500 MHz, $CDCl_3$) δ 7.49–7.42 (m, 2H), 7.42–7.34 (m, 2H), 7.34–7.27 (m, 1H), 7.20–7.12 (m, 2H), 6.88–6.83 (m, 2H), 6.80 (d, J = 8.1 Hz, 1H), 6.74 (d, J = 2.0 Hz, 1H), 6.64 (dd, J = 8.1, 2.0 Hz, 1H), 5.15 (s, 2H), 4.29 (t, J = 7.1 Hz, 2H), 3.86 (s, 3H), 3.80 (s, 3H), 3.55 (s, 2H), 2.87 (t, J = 7.1 Hz, 2H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 171.9, 158.8, 149.7, 147.0, 137.4, 131.0, 130.3, 128.6, 127.9, 127.3, 126.1, 121.0, 114.3, 114.0, 112.8, 71.2, 65.4, 56.0, 55.3, 40.6, 34.7; IR (neat) 1730, 1511, 1454, 1418, 1246, 1140, 1032, 820, 737, 697 cm^{-1} ; HRMS (EI) m/z : $[M]^+$ Calcd for $C_{25}H_{26}O_5$ 406.1780; Found 406.1777.

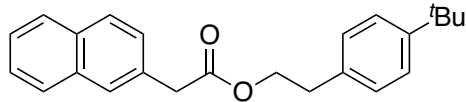
2-(4-Benzyloxy-3-methoxyphenyl)ethyl 2-(4-benzyloxy-3-methoxyphenyl)acetate (**S14v**)



To a solution of 2-(4-benzyloxy-3-methoxyphenyl)acetic acid (**43**) (927 mg, 3.40 mmol, 1.00 equiv.) in CH₂Cl₂ (15 mL), EDC•HCl (816 mg, 4.25 mmol, 1.25 equiv.) and anhydrous HOBt (575 mg, 4.25 mmol, 1.25 equiv.) were added at rt. After being stirred at rt for 30 min, DIPEA (1.78 mL, 10.2 mmol, 3.00 equiv.) and 2-(4-benzyloxy-3-methoxyphenyl)ethanol (**50**) (1.10 g, 4.25 mmol, 1.25 equiv.) were added, and the reaction mixture was stirred at rt for 47.5 h. Then, the resulting mixture was quenched with sat. aq. NH₄Cl, and extracted with CHCl₃. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 4:1 to 7:3) to afford **S14v** (1.56 g, 89% yield).

White solid; M.p. 68–69 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.48–7.40 (m, 4H), 7.40–7.26 (m, 6H), 6.85–6.75 (m, 3H), 6.75–6.67 (m, 2H), 6.62 (dd, *J* = 8.2, 2.0 Hz, 1H), 5.14 (s, 2H), 5.13 (s, 2H), 4.28 (t, *J* = 7.1 Hz, 2H), 3.86 (s, 3H), 3.85 (s, 3H), 3.53 (s, 2H), 2.86 (t, *J* = 7.1 Hz, 2H); ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 171.8, 149.7, 147.4, 147.0, 137.4, 137.3, 130.9, 128.64, 128.63, 127.92, 127.90, 127.4, 127.3, 127.1, 121.5, 121.0, 114.2, 114.1, 113.0, 112.7, 71.2, 71.1, 65.5, 56.1, 41.1, 34.8 (Two carbon signals were overlapped); IR (neat) 1729, 1511, 1453, 1259, 1224, 1011, 852, 795, 736, 696 cm⁻¹; HRMS (EI) *m/z*: [M]⁺ Calcd for C₃₂H₃₂O₆ 512.2199; Found 512.2202.

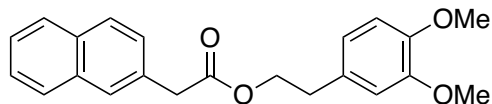
2-(4-*tert*-Butylphenyl)ethyl 2-(2-naphthyl)acetate (**S14w**)



To a solution of 2-(2-naphthyl)acetic acid (1.52 g, 8.16 mmol, 1.00 equiv.) in CH₂Cl₂ (20 mL), EDC•HCl (1.96 g, 10.2 mmol, 1.25 equiv.) and anhydrous HOBt (1.38 g, 10.2 mmol, 1.25 equiv.) were added at rt. After being stirred at rt for 30 min, DIPEA (4.27 mL, 24.5 mmol, 3.00 equiv.) and 2-(4-*tert*-butylphenyl)ethanol (1.82 g, 10.2 mmol, 1.25 equiv.) were added, and the reaction mixture was stirred at rt for 42 h. Then, the resulting mixture was quenched with sat. aq. NH₄Cl, and extracted with CHCl₃. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 19:1) to afford **S14w** (2.01 g, 71% yield).

White solid; M.p. 69–70 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.82–7.72 (m, 3H), 7.68 (s, 1H), 7.48–7.39 (m, 2H), 7.36 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.21–7.16 (m, 2H), 7.05–6.96 (m, 2H), 4.29 (t, *J* = 7.0 Hz, 2H), 3.74 (s, 2H), 2.85 (t, *J* = 7.0 Hz, 2H), 1.27 (s, 9H); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 171.5, 149.4, 134.7, 133.6, 132.6, 131.6, 128.7, 128.3, 128.1, 127.8, 127.7, 127.5, 126.2, 125.9, 125.4, 65.6, 41.8, 34.6, 34.5, 31.4; IR (KBr) 2959, 1725, 1300, 1261, 1136, 985, 810, 739, 564, 477 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₂₄H₂₆NaO₂ 369.1825; Found 369.1840.

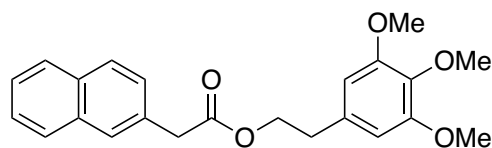
2-(3,4-Dimethoxyphenyl)ethyl 2-(2-naphthyl)acetate (**S14x**)



To a solution of 2-(2-naphthyl)acetic acid (1.09 g, 5.88 mmol, 1.00 equiv.) in CH_2Cl_2 (20 mL), EDC•HCl (1.41 g, 7.35 mmol, 1.25 equiv.) and anhydrous HOBt (993 mg, 7.35 mmol, 1.25 equiv.) were added at rt. After being stirred at rt for 30 min, DIPEA (3.07 mL, 17.6 mmol, 3.00 equiv.) and 2-(3,4-dimethoxyphenyl)ethanol (1.34 g, 7.35 mmol, 1.25 equiv.) were added, and the reaction mixture was stirred at rt for 43 h. Then, the resulting mixture was quenched with sat. aq. NH_4Cl , and extracted with CHCl_3 . The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO_2 , *n*-hexane:AcOEt = 7:3) to afford **S14x** (2.07 g, quant.).

Colorless oil; ^1H NMR (500 MHz, CDCl_3) δ 7.86–7.76 (m, 3H), 7.70 (s, 1H), 7.52–7.42 (m, 2H), 7.38 (dd, J = 8.4, 1.8 Hz, 1H), 6.71–6.60 (m, 3H), 4.32 (t, J = 7.0 Hz, 2H), 3.82 (s, 3H), 3.79 (s, 3H), 3.78 (s, 2H), 2.87 (t, J = 7.0 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 171.6, 148.9, 147.8, 133.5, 132.5, 131.6, 130.2, 128.3, 128.0, 127.8, 127.7, 127.4, 126.2, 125.9, 121.0, 112.1, 111.3, 65.6, 55.9, 55.8, 41.7, 34.7; IR (neat) 2955, 1732, 1515, 1463, 1263, 1238, 1158, 1028, 807, 764 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{22}\text{H}_{22}\text{NaO}_4$ 373.1410; Found 373.1428.

2-(3,4,5-Trimethoxyphenyl)ethyl 2-(2-naphthyl)acetate (**S14y**)



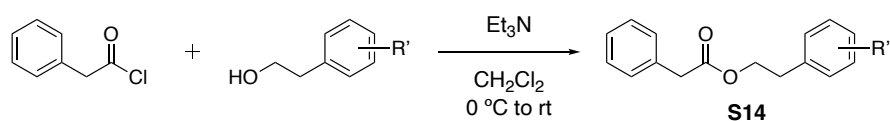
To a solution of 2-(2-naphthyl)acetic acid (1.49 g, 7.99 mmol, 1.00 equiv.) in CH_2Cl_2 (20 mL), EDC•HCl (1.91 g, 9.99 mmol, 1.25 equiv.) and anhydrous HOBt (1.35 g, 9.99 mmol, 1.25 equiv.) were added at rt. After being stirred at rt for 30 min, DIPEA (4.18 mL, 24.0 mmol, 3.00 equiv.) and 2-(3,4,5-trimethoxyphenyl)ethanol (2.12 g, 9.99 mmol, 1.25 equiv.) were added, and the reaction mixture was stirred at rt for 43 h. Then, the resulting mixture was quenched with sat. aq. NH_4Cl , and extracted with CHCl_3 . The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO_2 , *n*-hexane:AcOEt = 7:3) to afford **S14y** (2.56 g, 84% yield).

Colorless oil; ^1H NMR (500 MHz, CDCl_3) δ 7.85–7.75 (m, 3H), 7.71 (s, 1H), 7.51–7.42 (m, 2H), 7.38 (dd, J = 8.4, 1.8 Hz, 1H), 6.40 (s, 2H), 4.35 (t, J = 7.0 Hz, 2H), 3.85 (s, 3H), 3.79 (s, 2H), 3.76 (s, 6H), 2.89 (t, J = 7.0 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 171.4, 153.1, 136.6, 133.4, 133.3, 132.4, 131.4, 128.1, 127.8, 127.6, 127.2, 126.1, 125.8, 105.7, 65.3, 60.8, 55.9, 41.5, 35.3 (One carbon signal was overlapped); IR (neat) 2939, 1733, 1591, 1508, 1461, 1423, 1239, 1128, 1008, 822, 736 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{23}\text{H}_{24}\text{NaO}_5$ 403.1516; Found 403.1534.

2-(4-(Benzyloxy)-3-methoxyphenyl)ethyl 2-(4-(benzyloxy)phenyl)acetate (**S14z**)

To a solution of 2-(4-(benzyloxy)phenyl)acetic acid (**49**) (375 mg, 1.55 mmol, 1.00 equiv.) in CH₂Cl₂ (10 mL), EDC•HCl (371 mg, 1.94 mmol, 1.25 equiv.) and anhydrous HOBt (262 mg, 1.94 mmol, 1.25 equiv.) were added at rt. After being stirred at rt for 30 min, DIPEA (810 μL, 4.65 mmol, 3.00 equiv.) and 2-(4-(benzyloxy)-3-methoxyphenyl)ethanol (**50**) (500 mg, 1.94 mmol, 1.25 equiv.) were added, and the reaction mixture was stirred at rt for 14 h. Then, the resulting mixture was quenched with sat. aq. NH₄Cl, and extracted with CHCl₃. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 4:1) to afford **S14z** (440 mg, 59% yield).

White solid; M.p. 64–65 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.47–7.29 (m, 10H), 7.19–7.15 (m, 2H), 6.96–6.91 (m, 2H), 6.81 (d, *J* = 8.1 Hz, 1H), 6.74 (d, *J* = 2.0 Hz, 1H), 6.65 (dd, *J* = 8.1, 2.0 Hz, 1H), 5.15 (s, 2H), 5.06 (s, 2H), 4.30 (t, *J* = 7.1 Hz, 2H), 3.87 (s, 3H), 3.56 (s, 2H), 2.87 (t, *J* = 7.1 Hz, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 171.9, 158.0, 149.6, 146.9, 137.3, 137.1, 130.9, 130.4, 128.7, 128.6, 128.1, 127.9, 127.6, 127.3, 126.4, 121.0, 115.0, 114.2, 112.7, 71.1, 70.1, 65.5, 56.0, 40.6, 34.7; IR (KBr) 1733, 1610, 1513, 1457, 1382, 1230, 1144, 1019, 736, 698 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₃₁H₃₀NaO₅ 505.1985; Found 505.1996.



Scheme S14. Preparation of 2-Arylethyl 2-Phenylacetates **S14** (**Method B**).

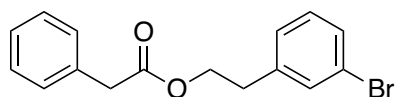
We assumed that 2-arylethyl 2-phenylacetates **S14** also could be prepared through the condensation reactions (**Method A**). However, as 2-phenylacetic acid, which is used as a starting material, is used in the manufacture of stimulants such as amphetamine, its distribution is regulated. Therefore, we prepared 2-arylethyl 2-phenylacetates **S14** through the nucleophilic addition and substitution reactions between 2-phenylacetyl chloride and 2-arylethanol (**Method B**).

2-(4-Bromophenyl)ethyl 2-phenylacetate (**S14l**)

To a solution of 2-(4-bromophenyl)ethanol (573 mg, 2.85 mmol, 1.00 equiv.) and Et₃N (1.19 mL, 8.55 mmol, 3.00 equiv.) in CH₂Cl₂ (10 mL), 2-phenylacetyl chloride (564 μL, 4.27 mmol, 1.50 equiv.) was added dropwise at 0 °C under a N₂ atmosphere. After being stirred at rt for 2 h, the reaction mixture was quenched with H₂O, and extracted with CHCl₃. The organic layer was washed with sat. aq. NaHCO₃ and brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 9:1) to afford **S14l** (552 mg, 61% yield).

Colorless oil; ^1H NMR (300 MHz, CDCl_3) δ 7.39–7.12 (m, 7H), 6.99–6.88 (m, 2H), 4.24 (t, J = 6.7 Hz, 2H), 3.55 (s, 2H), 2.81 (t, J = 6.7 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3) δ 171.3, 136.8, 133.9, 131.5, 130.7, 129.3, 128.6, 127.1, 120.4, 64.8, 41.4, 34.4; IR (neat) 1736, 1491, 1454, 1338, 1249, 1154, 1072, 1011, 821, 701, 528 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{16}\text{H}_{15}\text{BrNaO}_2$ 341.0148; Found 341.0159.

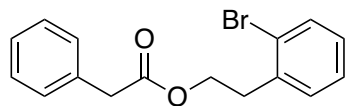
2-(3-Bromophenyl)ethyl 2-phenylacetate (**S14m**)



To a solution of 2-(3-bromophenyl)ethanol (1.49 g, 7.41 mmol, 1.00 equiv.) and Et_3N (2.07 mL, 14.8 mmol, 2.00 equiv.) in CH_2Cl_2 (20 mL), 2-phenylacetyl chloride (1.47 mL, 11.1 mmol, 1.50 equiv.) was added dropwise at 0 °C under an Ar atmosphere. After being stirred at rt for 2 h, the reaction mixture was quenched with sat. aq. NaHCO_3 , and extracted with CHCl_3 . The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO_2 , n -hexane:AcOEt = 9:1) to afford **S14m** (1.68 g, 71% yield).

Colorless oil; ^1H NMR (300 MHz, CDCl_3) δ 7.40–7.13 (m, 7H), 7.11–6.96 (m, 2H), 4.24 (t, J = 6.8 Hz, 2H), 3.55 (s, 2H), 2.82 (t, J = 6.7 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3) δ 171.3, 140.2, 133.9, 132.0, 130.0, 129.7, 129.2, 128.6, 127.5, 127.1, 122.5, 64.8, 41.4, 34.6; IR (neat) 1736, 1567, 1473, 1428, 1338, 1249, 1153, 1072, 1011, 780, 695 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{16}\text{H}_{15}\text{BrNaO}_2$ 341.0148; Found 341.0160.

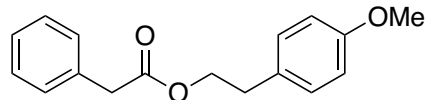
2-(2-Bromophenyl)ethyl 2-phenylacetate (**S14n**)



To a solution of 2-(2-bromophenyl)ethanol (1.49 g, 7.41 mmol, 1.00 equiv.) and Et_3N (2.07 mL, 14.8 mmol, 2.00 equiv.) in CH_2Cl_2 (20 mL), 2-phenylacetyl chloride (1.47 mL, 11.1 mmol, 1.50 equiv.) was added dropwise at 0 °C under an Ar atmosphere. After being stirred at rt for 6 h, the reaction mixture was quenched with sat. aq. NaHCO_3 , and extracted with CHCl_3 . The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO_2 , n -hexane:AcOEt = 9:1) to afford **S14n** (1.65 g, 70% yield).

Colorless oil; ^1H NMR (500 MHz, CDCl_3) δ 7.48 (dd, J = 8.1, 1.3 Hz, 1H), 7.31–7.16 (m, 5H), 7.12 (td, J = 7.4, 1.3 Hz, 1H), 7.07–6.98 (m, 2H), 4.29 (t, J = 6.9 Hz, 2H), 3.55 (s, 2H), 3.02 (t, J = 6.9 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 171.3, 137.0, 133.9, 132.8, 131.1, 129.3, 128.5, 128.3, 127.4, 127.0, 124.6, 63.6, 41.3, 35.2; IR (neat) 1737, 1496, 1471, 1439, 1338, 1249, 1152, 1025, 752, 723, 700 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{16}\text{H}_{15}\text{BrNaO}_2$ 341.0148; Found 341.0166.

2-(4-Methoxyphenyl)ethyl 2-phenylacetate (**S14o**)

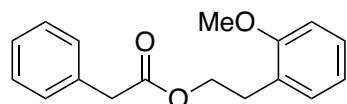


To a solution of 2-(4-methoxyphenyl)ethanol (1.68 g, 11.0 mmol, 1.00 equiv.) and Et₃N (3.08 mL, 22.1 mmol, 2.00 equiv.) in CH₂Cl₂ (20 mL), 2-phenylacetyl chloride (2.19 mL, 16.6 mmol, 1.50 equiv.)

was added dropwise at 0 °C under an Ar atmosphere. After being stirred at rt for 6 h, the reaction mixture was quenched with sat. aq. NaHCO₃, and extracted with CHCl₃. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 9:1) to afford **S14o** (2.26 g, 76% yield).

Colorless oil; ¹H NMR (500 MHz, CDCl₃) δ 7.34–7.18 (m, 5H), 7.08–7.00 (m, 2H), 6.83–6.76 (m, 2H), 4.25 (t, *J* = 7.0 Hz, 2H), 3.77 (s, 3H), 3.59 (s, 2H), 2.84 (t, *J* = 7.0 Hz, 2H); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 171.6, 158.4, 134.1, 130.0, 129.8, 129.4, 128.6, 127.1, 114.0, 65.7, 55.3, 41.5, 34.2; IR (neat) 2955, 1735, 1611, 1513, 1458, 1248, 1155, 1035, 828, 701 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₁₇H₁₈NaO₃ 293.1148; Found 293.1163.

2-(2-Methoxyphenyl)ethyl 2-phenylacetate (**S14p**)

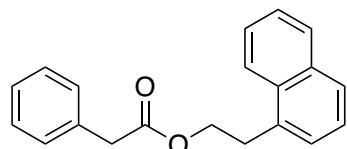


To a solution of 2-(2-methoxyphenyl)ethanol (1.65 g, 10.8 mmol, 1.00 equiv.) and Et₃N (3.02 mL, 21.7 mmol, 2.00 equiv.) in CH₂Cl₂ (20 mL), 2-phenylacetyl chloride (2.15 mL, 16.3 mmol, 1.50 equiv.) was added

dropwise at 0 °C under an Ar atmosphere. After being stirred at rt for 2 h, the reaction mixture was quenched with sat. aq. NaHCO₃, and extracted with CHCl₃. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 9:1) to afford **S14p** (2.11 g, 72% yield).

Colorless oil; ¹H NMR (500 MHz, CDCl₃) δ 7.33–7.14 (m, 6H), 7.04 (dd, *J* = 7.3, 1.8 Hz, 1H), 6.87–6.78 (m, 2H), 4.28 (t, *J* = 7.0 Hz, 2H), 3.76 (s, 3H), 3.56 (s, 2H), 2.92 (t, *J* = 7.0 Hz, 2H); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 171.6, 157.7, 134.2, 130.8, 129.4, 128.6, 127.9, 127.0, 126.0, 120.4, 110.3, 64.3, 55.2, 41.5, 29.9; IR (neat) 1735, 1601, 1496, 1460, 1245, 1155, 1031, 1005, 755, 701 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₁₇H₁₈NaO₃ 293.1148; Found 293.1163.

2-(1-Naphthyl)ethyl 2-phenylacetate (**S14q**)

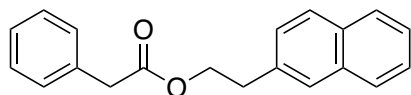


To a solution of 2-(1-naphthyl)ethanol (1.75 g, 10.2 mmol, 1.00 equiv.) and Et₃N (2.83 mL, 20.3 mmol, 2.00 equiv.) in CH₂Cl₂ (20 mL), 2-phenylacetyl chloride (2.01 mL, 15.2 mmol, 1.50 equiv.) was added dropwise at 0 °C under an Ar atmosphere. After being stirred at rt for 2 h, the reaction mixture

was quenched with sat. aq. NaHCO₃, and extracted with CHCl₃. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 9:1) to afford **S14q** (1.71 g, 58% yield).

White solid; M.p. 41–42 °C; ^1H NMR (300 MHz, CDCl_3) δ 8.03 (d, J = 8.6 Hz, 1H), 7.85–7.76 (m, 1H), 7.70 (d, J = 8.1 Hz, 1H), 7.54–7.38 (m, 2H), 7.37–7.15 (m, 7H), 4.40 (t, J = 7.3 Hz, 2H), 3.56 (s, 2H), 3.34 (t, J = 7.3 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3) δ 171.6, 134.1, 133.9, 133.7, 132.1, 129.4, 128.9, 128.6, 127.5, 127.2, 127.1, 126.2, 125.7, 125.5, 123.6, 64.9, 41.5, 32.2; IR (KBr) 1734, 1496, 1454, 1335, 1251, 1152, 1001, 779, 726, 700 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{20}\text{H}_{18}\text{NaO}_2$ 313.1199; Found 313.1205.

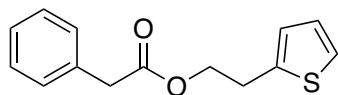
2-(2-Naphthyl)ethyl 2-phenylacetate (**S14r**)



To a solution of 2-(2-naphthyl)ethanol (1.74 g, 10.1 mmol, 1.00 equiv.) and Et_3N (2.82 mL, 20.2 mmol, 2.00 equiv.) in CH_2Cl_2 (20 mL), 2-phenylacetyl chloride (2.01 mL, 15.2 mmol, 1.50 equiv.) was added dropwise at 0 °C under an Ar atmosphere. After being stirred at rt for 2 h, the reaction mixture was quenched with sat. aq. NaHCO_3 , and extracted with CHCl_3 . The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO_2 , n -hexane:AcOEt = 9:1) to afford **S14r** (1.91 g, 65% yield).

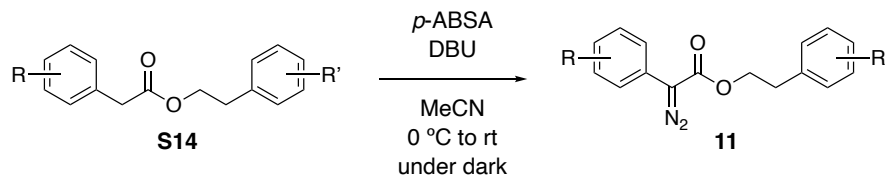
White solid; M.p. 63–64 °C; ^1H NMR (300 MHz, CDCl_3) δ 7.81–7.63 (m, 3H), 7.54 (s, 1H), 7.47–7.34 (m, 2H), 7.28–7.10 (m, 6H), 4.36 (t, J = 6.9 Hz, 2H), 3.55 (s, 2H), 3.02 (t, J = 6.9 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3) δ 171.5, 135.3, 134.0, 133.6, 132.4, 129.3, 128.6, 128.1, 127.7, 127.6, 127.4, 127.3, 127.1, 126.1, 125.6, 65.2, 41.5, 35.2; IR (KBr) 1727, 1500, 1454, 1222, 1164, 999, 857, 821, 705, 474 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{20}\text{H}_{18}\text{NaO}_2$ 313.1199; Found 313.1213.

2-(Thiophen-2-yl)ethyl 2-phenylacetate (**S14s**)



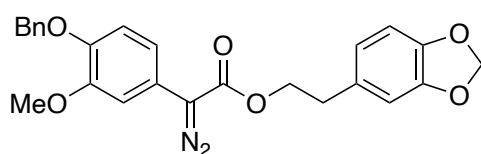
To a solution of 2-(thiophen-2-yl)ethanol (1.67 g, 13.0 mmol, 1.00 equiv.) and Et_3N (3.63 mL, 26.1 mmol, 2.00 equiv.) in CH_2Cl_2 (20 mL), 2-phenylacetyl chloride (2.58 mL, 19.5 mmol, 1.50 equiv.) was added dropwise at 0 °C under an Ar atmosphere. After being stirred at rt for 2 h, the reaction mixture was quenched with sat. aq. NaHCO_3 , and extracted with CHCl_3 . The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO_2 , n -hexane:AcOEt = 9:1) to afford **S14s** (1.18 g, 37% yield).

Colorless oil; ^1H NMR (300 MHz, CDCl_3) δ 7.34–7.18 (m, 5H), 7.09 (dd, J = 5.1, 1.2 Hz, 1H), 6.87 (dd, J = 5.1, 3.4 Hz, 1H), 6.74 (dq, J = 3.4, 1.0 Hz, 1H), 4.28 (t, J = 6.7 Hz, 2H), 3.59 (s, 2H), 3.09 (td, J = 6.7, 0.9 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3) δ 171.3, 139.8, 134.0, 129.3, 128.6, 127.1, 126.9, 125.6, 124.0, 65.0, 41.4, 29.2; IR (neat) 1736, 1496, 1454, 1384, 1335, 1249, 1151, 1007, 849, 699 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{14}\text{H}_{14}\text{NaO}_2\text{S}$ 269.0607; Found 269.0614.



Scheme S15. Preparations of Diazo Substrates **11**.

2-(Benzo[*d*][1,3]dioxol-5-yl)ethyl 2-(4-(benzyloxy)-3-methoxyphenyl)-2-diazoacetate (**11a**)

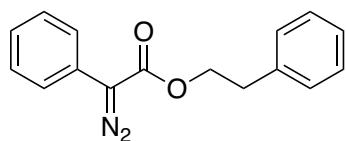


To a solution of **S14a** (710 mg, 1.69 mmol, 1.00 equiv.) in MeCN (15 mL), *p*-ABSA (1.01 g, 4.22 mmol, 2.50 equiv.) and DBU (630 μ L, 4.22 mmol, 2.50 equiv.) were added at 0 °C under an Ar atmosphere. After being stirred at rt under dark for 18 h,

the reaction mixture was quenched with 1 M aq. NaOH, and extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 7:1) to afford **11a** (595 mg, 79% yield).

Orange solid; M.p. 91–92 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.45–7.40 (m, 2H), 7.39–7.33 (m, 2H), 7.33–7.27 (m, 1H), 7.18 (d, *J* = 2.2 Hz, 1H), 6.88 (d, *J* = 8.5 Hz, 1H), 6.80–6.73 (m, 2H), 6.71 (d, *J* = 1.6 Hz, 1H), 6.67 (dd, *J* = 7.9, 1.7 Hz, 1H), 5.94 (s, 2H), 5.15 (s, 2H), 4.40 (t, *J* = 6.9 Hz, 2H), 3.89 (s, 3H), 2.91 (t, *J* = 6.8 Hz, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 165.6, 150.3, 147.8, 146.5, 146.4, 137.1, 131.4, 128.7, 128.0, 127.4, 122.0, 118.0, 116.4, 114.6, 109.4, 108.8, 108.4, 101.0, 71.2, 65.6, 62.9, 56.1, 35.1; IR (KBr) 2083, 1697, 1514, 1447, 1251, 1140, 1035, 933, 806, 738 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₂₅H₂₂N₂NaO₆ 469.1370; Found 469.1392.

2-Phenylethyl 2-diazo-2-phenylacetate (**11b**)

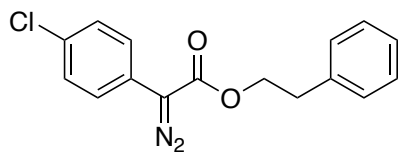


To a solution of 2-phenylethyl 2-phenylacetate (**S14b**)⁴⁷ (1.78 g, 7.41 mmol, 1.00 equiv.) in MeCN (15 mL), *p*-ABSA (2.67 g, 11.1 mmol, 1.50 equiv.) and DBU (2.22 mL, 14.8 mmol, 2.00 equiv.) were added at 0 °C under an Ar atmosphere. After being stirred at rt for 17 h under dark, the reaction mixture

was quenched with 1 M aq. NaOH, and extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:Et₂O = 24:1) to afford **11b** (1.61 g, 82% yield).

Orange liquid; ¹H NMR (400 MHz, CDCl₃) δ 7.48–7.40 (m, 2H), 7.38–7.28 (m, 4H), 7.26–7.14 (m, 4H), 4.46 (t, *J* = 6.9 Hz, 2H), 3.00 (t, *J* = 6.9 Hz, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 165.2, 137.8, 129.1, 129.0, 128.7, 126.8, 125.9, 125.6, 124.1, 65.6, 63.5, 35.4; IR (neat) 2088, 1703, 1497, 1387, 1344, 1247, 1156, 1053, 1020, 753, 695 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₁₆H₁₄N₂NaO₂ 289.0947; Found 289.0953.

2-Phenylethyl 2-(4-chlorophenyl)-2-diazoacetate (**11c**)

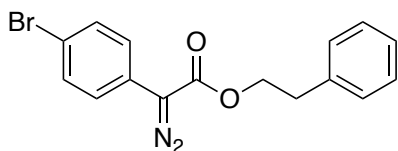


To a solution of **S14c** (692 mg, 2.52 mmol, 1.00 equiv.) in MeCN (10 mL), *p*-ABSA (908 mg, 3.78 mmol, 1.50 equiv.) and DBU (752 μ L, 5.04 mmol, 2.00 equiv.) were added at 0 °C under an Ar atmosphere.

After being stirred at rt for 8 h under dark, the reaction mixture was quenched with 1 M aq. NaOH, and extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:Et₂O = 19:1) to afford **11c** (659 mg, 87% yield).

Yellow solid; M.p. 48–49 °C; ¹H NMR (600 MHz, CDCl₃) δ 7.41–7.28 (m, 6H), 7.28–7.19 (m, 3H), 4.47 (t, *J* = 6.9 Hz, 2H), 3.00 (t, *J* = 6.9 Hz, 2H); ¹³C{¹H} NMR (151 MHz, CDCl₃) δ 164.9, 137.7, 131.6, 129.2, 129.1, 128.7, 126.8, 125.2, 124.3, 65.7, 63.3, 35.4; IR (KBr) 2089, 1704, 1494, 1341, 1279, 1243, 1158, 1095, 826, 699 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₁₆H₁₃ClN₂NaO₂ 323.0558; Found 323.0562.

2-Phenylethyl 2-(4-bromophenyl)-2-diazoacetate (**11d**)

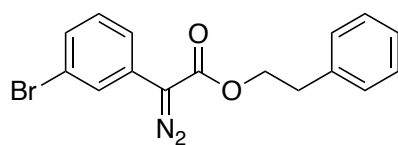


To a solution of **S14d** (641 mg, 2.01 mmol, 1.00 equiv.) in MeCN (10 mL), *p*-ABSA (724 mg, 3.01 mmol, 1.50 equiv.) and DBU (599 μ L, 4.02 mmol, 2.00 equiv.) were added at 0 °C under an Ar atmosphere.

After being stirred at rt for 5 h under dark, the reaction mixture was quenched with 1 M aq. NaOH, and extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:Et₂O = 19:1) to afford **11d** (605 mg, 87% yield).

Yellow solid; M.p. 62–63 °C; ¹H NMR (600 MHz, CDCl₃) δ 7.49–7.44 (m, 2H), 7.34–7.28 (m, 4H), 7.27–7.20 (m, 3H), 4.47 (t, *J* = 6.9 Hz, 2H), 3.00 (t, *J* = 6.9 Hz, 2H); ¹³C{¹H} NMR (151 MHz, CDCl₃) δ 164.9, 137.7, 132.1, 129.1, 128.7, 126.9, 125.5, 124.8, 119.5, 65.7, 63.4, 35.4; IR (KBr) 2089, 1703, 1491, 1341, 1243, 1157, 1077, 1028, 1005, 771, 699 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₁₆H₁₃BrN₂NaO₂ 367.0053; Found 367.0051.

2-Phenylethyl 2-(3-bromophenyl)-2-diazoacetate (**11e**)



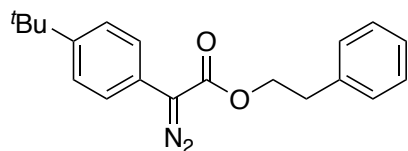
To a solution of **S14e** (720 mg, 2.26 mmol, 1.00 equiv.) in MeCN (10 mL), *p*-ABSA (813 mg, 3.38 mmol, 1.50 equiv.) and DBU (673 μ L, 4.51 mmol, 2.00 equiv.) were added at 0 °C under an Ar atmosphere.

After being stirred at rt for 12 h under dark, the reaction mixture was quenched with 1 M aq. NaOH, and extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:Et₂O = 19:1) to afford **11e** (580 mg, 74% yield).

Orange solid; M.p. 47–48 °C; ¹H NMR (600 MHz, CDCl₃) δ 7.65 (t, *J* = 1.9 Hz, 1H), 7.36–7.18 (m, 8H), 4.47 (t, *J* = 6.9 Hz, 2H), 3.01 (t, *J* = 6.9 Hz, 2H); ¹³C{¹H} NMR (151 MHz, CDCl₃) δ 164.6, 137.7, 130.4, 129.1, 128.8,

128.7, 128.1, 126.9, 126.7, 123.3, 122.3, 65.8, 63.3, 35.4; IR (KBr) 2090, 1704, 1591, 1478, 1344, 1280, 1244, 1158, 1032, 776, 700 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{16}\text{H}_{13}\text{BrN}_2\text{NaO}_2$ 367.0053; Found 367.0056.

2-Phenylethyl 2-(4-*tert*-butylphenyl)-2-diazoacetate (**11f**)

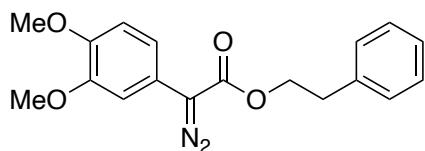


To a solution of **S14f** (1.41 g, 4.76 mmol, 1.00 equiv.) in MeCN (20 mL), *p*-ABSA (1.71 g, 7.14 mmol, 1.50 equiv.) and DBU (1.42 mL, 9.51 mmol, 2.00 equiv.) were added at 0 °C under an Ar atmosphere.

After being stirred at rt for 18 h under dark, the reaction mixture was quenched with 1 M aq. NaOH, and extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:Et₂O = 49:1) to afford **11f** (876 mg, 57% yield).

Orange solid; M.p. 39–40 °C; ¹H NMR (600 MHz, CDCl₃) δ 7.42–7.28 (m, 6H), 7.27–7.20 (m, 3H), 4.47 (t, J = 7.0 Hz, 2H), 3.01 (t, J = 6.9 Hz, 2H), 1.31 (s, 9H); ¹³C{¹H} NMR (151 MHz, CDCl₃) δ 165.5, 149.2, 137.8, 129.1, 128.7, 126.8, 126.1, 124.2, 122.3, 65.5, 63.1, 35.5, 34.6, 31.4; IR (KBr) 2961, 2085, 1704, 1515, 1342, 1247, 1159, 1111, 772, 699 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{20}\text{H}_{22}\text{N}_2\text{NaO}_2$ 345.1573; Found 345.1588.

2-Phenylethyl 2-diazo-2-(3,4-dimethoxyphenyl)acetate (**11g**)

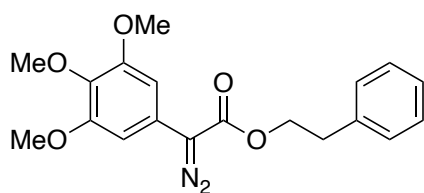


To a solution of **S14g** (1.22 g, 4.06 mmol, 1.00 equiv.) in MeCN (20 mL), *p*-ABSA (1.46 g, 6.09 mmol, 1.50 equiv.) and DBU (1.21 mL, 8.12 mmol, 2.00 equiv.) were added at 0 °C under an Ar atmosphere.

After being stirred at rt for 13 h under dark, the reaction mixture was quenched with 1 M aq. NaOH, and extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:Et₂O = 4:1) to afford **11g** (798 mg, 60% yield).

Orange solid; M.p. 57–58 °C; ¹H NMR (600 MHz, CDCl₃) δ 7.35–7.29 (m, 2H), 7.28–7.20 (m, 3H), 7.14 (s, 1H), 6.90–6.82 (m, 2H), 4.47 (t, J = 6.9 Hz, 2H), 3.90–3.85 (m, 6H), 3.01 (t, J = 6.9 Hz, 2H); ¹³C{¹H} NMR (151 MHz, CDCl₃) δ 165.7, 149.6, 147.5, 137.8, 129.1, 128.7, 126.8, 117.5, 116.6, 111.8, 108.5, 65.6, 62.9, 56.1, 56.0, 35.5; IR (KBr) 2083, 1699, 1583, 1517, 1461, 1256, 1142, 1061, 1027, 765 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{18}\text{H}_{18}\text{N}_2\text{NaO}_4$ 349.1159; Found 349.1169.

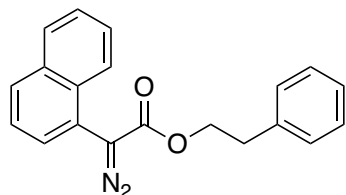
2-Phenylethyl 2-diazo-2-(3,4,5-trimethoxyphenyl)acetate (**11h**)



To a solution of **S14h** (1.82 g, 5.51 mmol, 1.00 equiv.) in MeCN (20 mL), *p*-ABSA (1.99 g, 8.26 mmol, 1.50 equiv.) and DBU (2.06 mL, 13.8 mmol, 2.00 equiv.) were added at 0 °C under an Ar atmosphere. After being stirred at rt for 86 h under dark, the reaction mixture was

quenched with 1 M aq. NaOH, and extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:Et₂O = 7:3) to afford **11h** (928 mg, 47% yield). Orange solid; M.p. 76–77 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.36–7.29 (m, 2H), 7.29–7.19 (m, 3H), 6.69 (s, 2H), 4.47 (t, *J* = 6.9 Hz, 2H), 3.88–3.80 (m, 9H), 3.02 (t, *J* = 6.9 Hz, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 165.4, 153.8, 137.7, 136.3, 129.1, 128.7, 126.8, 120.8, 101.6, 65.5, 63.5, 61.1, 56.3, 35.4; IR (KBr) 2085, 1698, 1580, 1509, 1453, 1278, 1127, 1076, 1005, 698 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₁₉H₂₀N₂NaO₅ 379.1264; Found 379.1270.

2-Phenylethyl 2-diazo-2-(1-naphthyl)acetate (**11i**)

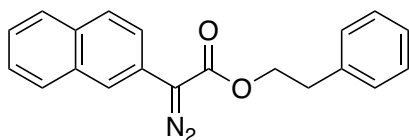


To a solution of **S14i** (1.08 g, 3.72 mmol, 1.00 equiv.) in MeCN (15 mL), *p*-ABSA (1.34 g, 5.58 mmol, 1.50 equiv.) and DBU (1.11 mL, 7.44 mmol, 2.00 equiv.) were added at 0 °C under an Ar atmosphere. After being stirred at rt for 13 h under dark, the reaction mixture was quenched with 1 M aq. NaOH, and extracted with Et₂O. The organic layer was washed with brine,

dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 9:1) to afford **11i** (763 mg, 65% yield).

Yellow solid; M.p. 75–76 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.96–7.86 (m, 2H), 7.86–7.79 (m, 1H), 7.64–7.47 (m, 4H), 7.36–7.11 (m, 5H), 4.48 (t, *J* = 6.9 Hz, 2H), 2.99 (t, *J* = 6.9 Hz, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 166.5, 137.9, 134.2, 131.7, 129.9, 129.8, 129.2, 129.0, 128.6, 127.0, 126.7, 126.4, 125.7, 124.5, 122.1, 65.8, 59.8, 35.5; IR (KBr) 2089, 1700, 1329, 1271, 1214, 1159, 1103, 798, 774, 742, 699 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₂₀H₁₆N₂NaO₂ 339.1104; Found 339.1110.

2-Phenylethyl 2-diazo-2-(2-naphthyl)acetate (**11j**)

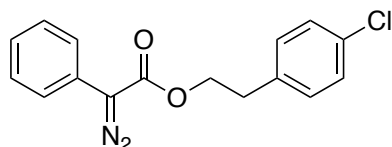


To a solution of **S14j** (660 mg, 2.27 mmol, 1.00 equiv.) in MeCN (10 mL), *p*-ABSA (819 mg, 3.41 mmol, 1.50 equiv.) and DBU (679 μL, 4.55 mmol, 2.00 equiv.) were added at 0 °C under an Ar atmosphere.

After being stirred at rt for 18 h under dark, the reaction mixture was quenched with 1 M aq. NaOH, and extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:Et₂O = 19:1) to afford **11j** (515 mg, 72% yield).

Orange solid; M.p. 68–69 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.97 (d, J = 1.9 Hz, 1H), 7.83 (d, J = 8.7 Hz, 1H), 7.80–7.73 (m, 2H), 7.52–7.39 (m, 3H), 7.38–7.29 (m, 2H), 7.29–7.21 (m, 3H), 4.51 (t, J = 6.9 Hz, 2H), 3.04 (t, J = 6.9 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 165.4, 137.8, 133.7, 131.6, 129.1, 128.8, 128.7, 127.8, 127.7, 126.8, 126.7, 125.9, 122.8, 122.7, 122.0, 65.7, 64.0, 35.5; IR (KBr) 2085, 1701, 1325, 1251, 1152, 1124, 1052, 1033, 810, 735, 699 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{20}\text{H}_{16}\text{N}_2\text{NaO}_2$ 339.1104; Found 339.1107.

2-(4-Chlorophenyl)ethyl 2-diazo-2-phenylacetate (**11k**)

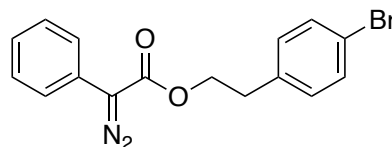


To a solution of 2-(4-chlorophenyl)ethyl 2-phenylacetate (**S14k**)⁴⁸ (1.06 g, 3.86 mmol, 1.00 equiv.) in MeCN (10 mL), *p*-ABSA (1.39 g, 5.79 mmol, 1.50 equiv.) and DBU (1.15 mL, 7.72 mmol, 2.00 equiv.) were added at 0 °C under an Ar atmosphere. After being stirred at rt for 11 h

under dark, the reaction mixture was quenched with 1 M aq. NaOH, and extracted with Et_2O . The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO_2 , *n*-hexane: Et_2O = 19:1) to afford **11k** (663 mg, 57% yield).

Yellow solid; M.p. 66–67 °C; ^1H NMR (600 MHz, CDCl_3) δ 7.46–7.41 (m, 2H), 7.39–7.35 (m, 2H), 7.32–7.27 (m, 2H), 7.21–7.14 (m, 3H), 4.45 (t, J = 6.8 Hz, 2H), 2.99 (t, J = 6.8 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 165.2, 136.3, 132.7, 130.4, 129.1, 128.8, 126.1, 125.5, 124.2, 65.2, 63.5, 34.8; IR (KBr) 2087, 1703, 1496, 1387, 1344, 1246, 1155, 1049, 1018, 755 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{16}\text{H}_{13}\text{ClN}_2\text{NaO}_2$ 323.0558; Found 323.0565.

2-(4-Bromophenyl)ethyl 2-diazo-2-phenylacetate (**11l**)

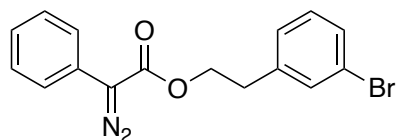


To a solution of **S14l** (1.00 g, 3.13 mmol, 1.00 equiv.) in MeCN (10 mL), *p*-ABSA (1.13 g, 4.70 mmol, 1.50 equiv.) and DBU (935 μL , 6.27 mmol, 2.00 equiv.) were added at 0 °C under an Ar atmosphere. After being stirred at rt for 11.5 h under dark, the reaction mixture was

quenched with 1 M aq. NaOH, and extracted with Et_2O . The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO_2 , *n*-hexane: Et_2O = 19:1) to afford **11l** (786 mg, 73% yield).

Orange solid; M.p. 90–91 °C; ^1H NMR (600 MHz, CDCl_3) δ 7.48–7.40 (m, 4H), 7.40–7.33 (m, 2H), 7.22–7.15 (m, 1H), 7.14–7.07 (m, 2H), 4.45 (t, J = 6.8 Hz, 2H), 2.97 (t, J = 6.8 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 165.2, 136.8, 131.8, 130.8, 129.1, 126.1, 125.5, 124.2, 120.7, 65.2, 63.5, 34.9; IR (KBr) 2087, 1702, 1494, 1386, 1343, 1246, 1155, 1067, 1015, 755, 691 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{16}\text{H}_{13}\text{BrN}_2\text{NaO}_2$ 367.0053; Found 367.0059.

2-(3-Bromophenyl)ethyl 2-diazo-2-phenylacetate (**11m**)

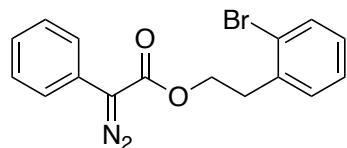


To a solution of **S14m** (839 mg, 2.63 mmol, 1.00 equiv.) in MeCN (10 mL), *p*-ABSA (947 mg, 3.94 mmol, 1.50 equiv.) and DBU (785 μ L, 5.26 mmol, 2.00 equiv.) were added at 0 °C under an Ar atmosphere.

After being stirred at rt for 16.5 h under dark, the reaction mixture was quenched with 1 M aq. NaOH, and extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:Et₂O = 19:1) to afford **11m** (426 mg, 47% yield).

Yellow solid; M.p. 54–55 °C; ¹H NMR (600 MHz, CDCl₃) δ 7.48–7.41 (m, 2H), 7.41–7.34 (m, 4H), 7.23–7.12 (m, 3H), 4.46 (t, *J* = 6.8 Hz, 2H), 2.98 (t, *J* = 6.8 Hz, 2H); ¹³C{¹H} NMR (151 MHz, CDCl₃) δ 165.1, 140.2, 132.2, 130.3, 130.0, 129.1, 127.7, 126.1, 125.5, 124.2, 122.7, 65.1, 63.5, 35.1; IR (KBr) 2088, 1702, 1498, 1386, 1344, 1246, 1156, 1021, 755, 691 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₁₆H₁₃BrN₂NaO₂ 367.0053; Found 367.0059.

2-(2-Bromophenyl)ethyl 2-diazo-2-phenylacetate (**11n**)

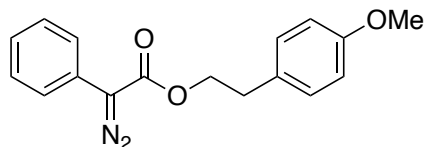


To a solution of **S14n** (859 mg, 2.69 mmol, 1.00 equiv.) in MeCN (10 mL), *p*-ABSA (970 mg, 4.04 mmol, 1.50 equiv.) and DBU (803 μ L, 5.38 mmol, 2.00 equiv.) were added at 0 °C under an Ar atmosphere. After being stirred at rt for 35 h under dark, the reaction mixture was quenched with 1 M aq.

NaOH, and extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:Et₂O = 19:1) to give **11n** (504 mg, 54% yield).

Orange solid; M.p. 65–67 °C; ¹H NMR (600 MHz, CDCl₃) δ 7.56 (d, *J* = 8.0 Hz, 1H), 7.48–7.41 (m, 2H), 7.39–7.33 (m, 2H), 7.29–7.23 (m, 2H), 7.20–7.14 (m, 1H), 7.14–7.08 (m, 1H), 4.51 (t, *J* = 6.8 Hz, 2H), 3.17 (t, *J* = 6.8 Hz, 2H); ¹³C{¹H} NMR (151 MHz, CDCl₃) δ 165.2, 137.2, 133.1, 131.4, 129.1, 128.6, 127.7, 126.0, 125.6, 124.8, 124.1, 64.0, 63.5, 35.6; IR (KBr) 2087, 1702, 1498, 1471, 1343, 1246, 1157, 1023, 752, 690 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₁₆H₁₃BrN₂NaO₂ 367.0053; Found 367.0056.

2-(4-Methoxyphenyl)ethyl 2-diazo-2-phenylacetate (**11o**)

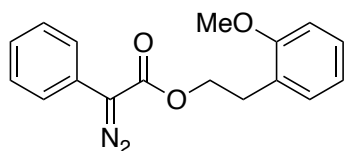


To a solution of **S14o** (970 mg, 3.59 mmol, 1.00 equiv.) in MeCN (10 mL), *p*-ABSA (1.29 g, 5.38 mmol, 1.50 equiv.) and DBU (1.07 mL, 7.18 mmol, 2.00 equiv.) were added at 0 °C under an Ar atmosphere.

After being stirred at rt for 35 h under dark, the reaction mixture was quenched with 1 M aq. NaOH, and extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:Et₂O = 19:1) to afford **11o** (613 mg, 58% yield).

Orange solid; M.p. 55–56 °C; ^1H NMR (600 MHz, CDCl_3) δ 7.48–7.42 (m, 2H), 7.41–7.35 (m, 2H), 7.21–7.12 (m, 3H), 6.90–6.84 (m, 2H), 4.44 (t, J = 6.9 Hz, 2H), 3.81 (s, 3H), 2.96 (t, J = 7.0 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 165.3, 158.5, 130.1, 129.8, 129.0, 125.9, 125.6, 124.1, 114.1, 65.8, 63.5, 55.4, 34.6; IR (KBr) 2088, 1702, 1512, 1343, 1287, 1246, 1156, 1021, 756, 691 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{17}\text{H}_{16}\text{N}_2\text{NaO}_3$ 319.1053; Found 319.1053.

2-(2-Methoxyphenyl)ethyl 2-diazo-2-phenylacetate (**11p**)

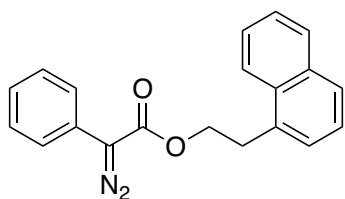


To a solution of **S14p** (875 mg, 3.24 mmol, 1.00 equiv.) in MeCN (10 mL), *p*-ABSA (1.17 g, 4.86 mmol, 1.50 equiv.) and DBU (966 μL , 6.47 mmol, 2.00 equiv.) were added at 0 °C under an Ar atmosphere. After being stirred at rt for 17 h under dark, the reaction mixture was quenched with 1 M aq.

NaOH, and extracted with Et_2O . The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO_2 , *n*-hexane: Et_2O = 19:1) to afford **11p** (675 mg, 70% yield).

Yellow solid; M.p. 38–39 °C; ^1H NMR (600 MHz, CDCl_3) δ 7.47–7.39 (m, 2H), 7.38–7.32 (m, 2H), 7.25–7.20 (m, 1H), 7.18–7.12 (m, 2H), 6.90 (td, J = 7.4, 1.1 Hz, 1H), 6.86 (d, J = 8.2 Hz, 1H), 4.46 (t, J = 6.9 Hz, 2H), 3.82 (s, 3H), 3.02 (t, J = 6.9 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 165.3, 157.8, 131.0, 129.0, 128.1, 126.0, 125.83, 125.79, 124.1, 120.6, 110.4, 64.6, 63.5, 55.3, 30.2; IR (KBr) 2087, 1703, 1496, 1463, 1344, 1287, 1246, 1157, 1048, 1020, 754 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{17}\text{H}_{16}\text{N}_2\text{NaO}_3$ 319.1053; Found 319.1059.

2-(1-Naphthyl)ethyl 2-diazo-2-phenylacetate (**11q**)

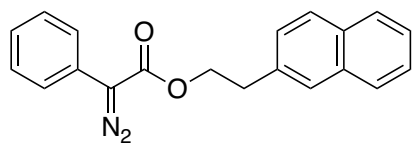


To a solution of **S14q** (861 mg, 2.97 mmol, 1.00 equiv.) in MeCN (10 mL), *p*-ABSA (1.07 g, 4.45 mmol, 1.50 equiv.) and DBU (885 μL , 5.93 mmol, 2.00 equiv.) were added at 0 °C under an Ar atmosphere. After being stirred at rt for 16 h under dark, the reaction mixture was quenched with 1 M aq.

NaOH, and extracted with Et_2O . The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO_2 , *n*-hexane: Et_2O = 19:1) to afford **11q** (481 mg, 51% yield).

Yellow solid; M.p. 82–83 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.14 (d, J = 8.5 Hz, 1H), 7.94–7.85 (m, 1H), 7.79 (d, J = 7.9 Hz, 1H), 7.62–7.32 (m, 8H), 7.24–7.15 (m, 1H), 4.63 (t, J = 7.2 Hz, 2H), 3.51 (t, J = 7.2 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 165.3, 134.0, 133.7, 132.2, 129.1, 129.0, 127.7, 127.3, 126.4, 126.0, 125.8, 125.62, 125.60, 124.2, 123.7, 65.1, 63.5, 32.6; IR (KBr) 2087, 1700, 1498, 1343, 1246, 1154, 1048, 1019, 777, 755 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{20}\text{H}_{16}\text{N}_2\text{NaO}_2$ 339.1104; Found 339.1111.

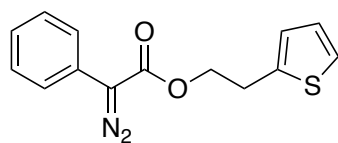
2-(2-Naphthyl)ethyl 2-diazo-2-phenylacetate (**11r**)



To a solution of **S14r** (968 mg, 3.33 mmol, 1.00 equiv.) in MeCN (10 mL), *p*-ABSA (1.20 g, 5.00 mmol, 1.50 equiv.) and DBU (995 μ L, 6.67 mmol, 2.00 equiv.) were added at 0 °C under an Ar atmosphere. After being stirred at rt for 17 h under dark, the reaction mixture was quenched with 1 M aq. NaOH, and extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:Et₂O = 19:1) to afford **11r** (660 mg, 63% yield).

Yellow solid; M.p. 68–69 °C; ¹H NMR (600 MHz, CDCl₃) δ 7.88–7.77 (m, 3H), 7.70 (s, 1H), 7.53–7.41 (m, 4H), 7.40–7.32 (m, 3H), 7.21–7.14 (m, 1H), 4.58 (t, *J* = 6.9 Hz, 2H), 3.19 (t, *J* = 6.9 Hz, 2H); ¹³C{¹H} NMR (151 MHz, CDCl₃) δ 165.3, 135.3, 133.7, 132.5, 129.0, 128.3, 127.8, 127.7, 127.6, 127.4, 126.3, 126.0, 125.7, 125.6, 124.2, 65.5, 63.5, 35.6; IR (KBr) 2088, 1701, 1500, 1342, 1246, 1157, 1021, 817, 753, 691, 477 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₂₀H₁₆N₂NaO₂ 339.1104; Found 339.1109.

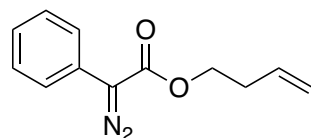
2-(Thiophen-2-yl)ethyl 2-diazo-2-phenylacetate (**11s**)



To a solution of **S14s** (769 mg, 3.12 mmol, 1.00 equiv.) in MeCN (10 mL), *p*-ABSA (1.13 g, 4.68 mmol, 1.50 equiv.) and DBU (931 μ L, 6.24 mmol, 2.00 equiv.) were added at 0 °C under an Ar atmosphere. After being stirred at rt for 35 h under dark, the reaction mixture was quenched with 1 M aq. NaOH, and extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:Et₂O = 19:1) to afford **11s** (549 mg, 65% yield).

Orange liquid; ¹H NMR (600 MHz, CDCl₃) δ 7.50–7.45 (m, 2H), 7.42–7.35 (m, 2H), 7.22–7.16 (m, 2H), 6.97 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.92–6.86 (m, 1H), 4.50 (t, *J* = 6.6 Hz, 2H), 3.25 (t, *J* = 6.6 Hz, 2H); ¹³C{¹H} NMR (151 MHz, CDCl₃) δ 165.1, 139.9, 129.1, 127.0, 126.0, 125.8, 125.6, 124.3, 124.1, 65.2, 63.5, 29.7; IR (neat) 2088, 1703, 1498, 1387, 1343, 1245, 1155, 1046, 1020, 756, 693 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₁₄H₁₂N₂NaO₂S 295.0512; Found 295.0518.

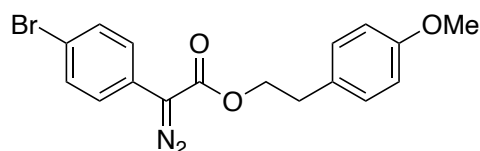
3-Butenyl 2-diazo-2-phenylacetate (**2**)



To a solution of 3-butenyl 2-phenylacetate⁴⁹ (842 mg, 4.43 mmol, 1.00 equiv.) in MeCN (10 mL), *p*-ABSA (1.59 g, 6.64 mmol, 1.50 equiv.) and DBU (1.32 mL, 8.85 mmol, 2.00 equiv.) were added at 0 °C under an Ar atmosphere. After being stirred at rt for 58 h under dark, the reaction mixture was quenched with 1 M aq. NaOH, and extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:Et₂O = 19:1) to afford **2** (735 mg, 77% yield).

Orange liquid; ^1H NMR (600 MHz, CDCl_3) δ 7.51–7.45 (m, 2H), 7.40–7.36 (m, 2H), 7.21–7.15 (m, 1H), 5.82 (ddt, J = 17.1, 10.2, 6.8 Hz, 1H), 5.20–5.06 (m, 2H), 4.33 (t, J = 6.7 Hz, 2H), 2.47 (qt, J = 6.7, 1.4 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 165.3, 133.9, 129.1, 125.9, 125.7, 124.1, 117.6, 64.1, 63.5, 33.4; IR (neat) 2087, 1705, 1498, 1387, 1344, 1286, 1247, 1158, 1050, 1022, 755 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{12}\text{H}_{12}\text{N}_2\text{NaO}_2$ 239.0791; Found 239.0798.

2-(4-Methoxyphenyl)ethyl 2-(4-bromophenyl)-2-diazoacetate (**11t**)

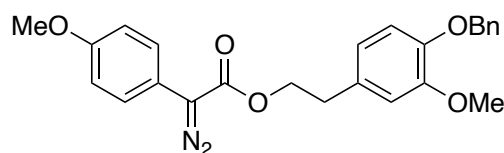


To a solution of **S14t** (1.80 g, 5.15 mmol, 1.00 equiv.) in MeCN (20 mL), *p*-ABSA (1.86 g, 7.73 mmol, 1.50 equiv.) and DBU (1.54 mL, 10.3 mmol, 2.00 equiv.) were added at 0 °C under an Ar atmosphere. After being stirred at rt for 16 h under dark, the

reaction mixture was quenched with 1 M aq. NaOH, and extracted with Et_2O . The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO_2 , *n*-hexane: Et_2O = 19:1) to afford **11t** (1.80 g, 93% yield).

Orange solid; M.p. 74–75 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.52–7.44 (m, 2H), 7.35–7.28 (m, 2H), 7.18–7.09 (m, 2H), 6.90–6.80 (m, 2H), 4.43 (t, J = 6.9 Hz, 2H), 3.80 (s, 3H), 2.95 (t, J = 6.9 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 164.9, 158.6, 132.1, 130.1, 129.7, 125.5, 124.9, 119.5, 114.1, 66.0, 55.4, 34.5 (One carbon signal was overlapped); IR (KBr) 2089, 1702, 1513, 1491, 1341, 1245, 1157, 1076, 1031, 822 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{17}\text{H}_{15}\text{BrN}_2\text{NaO}_3$ 397.0158; Found 397.0169.

2-(4-Benzyloxy-3-methoxyphenyl)ethyl 2-diazo-2-(4-methoxyphenyl)acetate (**11u**)

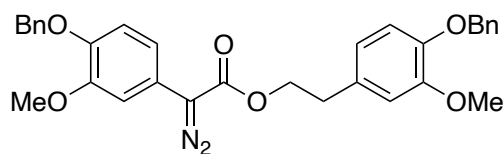


To a solution of **S14u** (1.37 g, 3.37 mmol, 1.00 equiv.) in MeCN (20 mL), *p*-ABSA (2.43 g, 10.1 mmol, 3.00 equiv.) and DBU (1.52 mL, 10.1 mmol, 3.00 equiv.) were added at 0 °C under a N_2 atmosphere. After being stirred at rt for 35 h

under dark, the reaction mixture was quenched with 2 M aq. NaOH, and extracted with CPME. The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO_2 , *n*-hexane: AcOEt = 3:1) to afford **11u** (1.21 g, 83% yield).

Orange solid; M.p. 85–86 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.44 (d, J = 7.2 Hz, 2H), 7.40–7.32 (m, 4H), 7.32–7.27 (m, 1H), 6.95–6.91 (m, 2H), 6.83 (d, J = 8.2 Hz, 1H), 6.77 (d, J = 2.0 Hz, 1H), 6.70 (dd, J = 8.2, 2.0 Hz, 1H), 5.14 (s, 2H), 4.43 (t, J = 6.9 Hz, 2H), 3.88 (s, 3H), 3.81 (s, 3H), 2.94 (t, J = 6.9 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 165.8, 158.2, 149.8, 147.0, 137.4, 131.0, 128.6, 127.9, 127.4, 126.1, 121.0, 116.9, 114.7, 114.4, 112.9, 71.3, 65.7, 62.6, 56.1, 55.5, 35.1; IR (neat) 2076, 1694, 1511, 1236, 1222, 1163, 1135, 1026, 999, 834, 804, 746, 737, 696 cm^{-1} ; HRMS (EI) m/z : $[\text{M}]^+$ Calcd for $\text{C}_{25}\text{H}_{24}\text{N}_2\text{O}_5$ 432.1685; Found 432.1687.

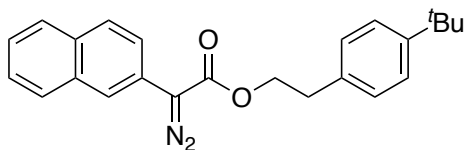
2-(4-Benzyloxy-3-methoxyphenyl)ethyl 2-(4-benzyloxy-3-methoxyphenyl)-2-diazoacetate (**11v**)



To a solution of **S14v** (2.92 g, 5.70 mmol, 1.00 equiv.) in MeCN (40 mL), *p*-ABSA (4.11 g, 17.1 mmol, 3.00 equiv.) and DBU (2.58 mL, 17.1 mmol, 3.00 equiv.) were added at 0 °C under a N₂ atmosphere. After being stirred at rt for 37 h under dark, the reaction mixture was quenched with 2 M aq. NaOH, and extracted with CPME. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 3:1) to afford **11v** (2.40 g, 78% yield).

Orange solid; M.p. 81–82 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.48–7.24 (m, 10H), 7.18 (d, *J* = 2.2 Hz, 1H), 6.88 (d, *J* = 8.5 Hz, 1H), 6.83 (d, *J* = 8.2 Hz, 1H), 6.79–6.74 (m, 2H), 6.70 (dd, *J* = 8.1, 2.0 Hz, 1H), 5.15 (s, 2H), 5.13 (s, 2H), 4.43 (t, *J* = 6.9 Hz, 2H), 3.88 (s, 3H), 3.87 (s, 3H), 2.94 (t, *J* = 6.9 Hz, 2H); ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 165.7, 150.3, 149.8, 147.1, 146.5, 137.4, 137.1, 131.0, 128.70, 128.65, 128.0, 127.9, 127.4, 121.0, 118.1, 116.5, 114.7, 114.4, 112.8, 108.9, 71.3, 65.7, 62.9, 56.2, 56.1, 35.1 (Two carbon signals were overlapped); IR (neat) 2071, 1692, 1512, 1251, 1220, 1136, 1025, 1002, 744, 697 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₃₂H₃₀N₂NaO₆ 561.1996; Found 561.2004.

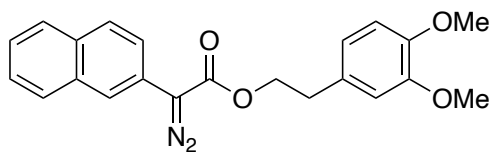
2-(4-*tert*-Butylphenyl)ethyl 2-diazo-2-(2-naphthyl)acetate (**11w**)



To a solution of **S14w** (1.93 g, 5.57 mmol, 1.00 equiv.) in MeCN (20 mL), *p*-ABSA (2.01 g, 8.36 mmol, 1.50 equiv.) and DBU (1.67 mL, 11.1 mmol, 2.00 equiv.) were added at 0 °C under an Ar atmosphere. After being stirred at rt for 140 h under dark, the reaction mixture was quenched with 1 M aq. NaOH, and extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:Et₂O = 19:1) to afford **11w** (1.39 g, 67% yield).

Orange solid; M.p. 101–102 °C; ¹H NMR (600 MHz, CDCl₃) δ 7.99 (d, *J* = 2.0 Hz, 1H), 7.84 (d, *J* = 8.7 Hz, 1H), 7.81–7.75 (m, 2H), 7.52–7.41 (m, 3H), 7.39–7.34 (m, 2H), 7.23–7.18 (m, 2H), 4.51 (t, *J* = 7.0 Hz, 2H), 3.02 (t, *J* = 7.0 Hz, 2H), 1.33 (s, 9H); ¹³C{¹H} NMR (151 MHz, CDCl₃) δ 165.4, 149.7, 134.7, 133.8, 131.6, 128.82, 128.79, 127.80, 127.75, 126.7, 125.9, 125.6, 122.8, 122.7, 122.1, 65.8, 64.1, 34.9, 34.6, 31.5; IR (KBr) 2960, 2083, 1701, 1325, 1253, 1153, 1124, 1034, 810, 736 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₂₄H₂₄N₂NaO₂ 395.1730; Found 395.1738.

2-(3,4-Dimethoxyphenyl)ethyl 2-diazo-2-(2-naphthyl)acetate (**11x**)

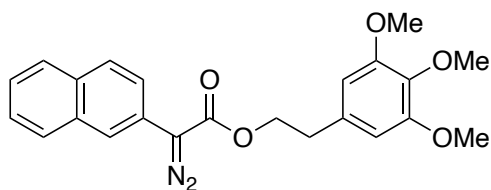


To a solution of **S14x** (1.56 g, 4.45 mmol, 1.00 equiv.) in MeCN (20 mL), *p*-ABSA (1.60 g, 6.68 mmol, 1.50 equiv.) and DBU (1.33 mL, 8.90 mmol, 2.00 equiv.) were added at 0 °C under an Ar atmosphere. After being stirred at rt for 14 h

under dark, the reaction mixture was quenched with 1 M aq. NaOH, and extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:Et₂O = 7:3) to afford **11x** (1.07 g, 64% yield).

Orange solid; M.p. 80–81 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.99 (d, *J* = 2.2 Hz, 1H), 7.88–7.74 (m, 3H), 7.55–7.39 (m, 3H), 6.87–6.74 (m, 3H), 4.50 (t, *J* = 6.9 Hz, 2H), 3.87 (s, 6H), 2.99 (t, *J* = 6.9 Hz, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 165.4, 149.0, 147.9, 133.7, 131.6, 130.3, 128.8, 127.74, 127.72, 126.7, 125.9, 122.71, 122.68, 122.0, 121.0, 112.2, 111.4, 65.9, 64.0, 56.0, 55.9, 35.1; IR (KBr) 2085, 1701, 1515, 1465, 1326, 1261, 1155, 1126, 1031, 810, 734 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₂₂H₂₀N₂NaO₄ 399.1315; Found 399.1323.

2-(3,4,5-Trimethoxyphenyl)ethyl 2-diazo-2-(2-naphthyl)acetate (**11y**)

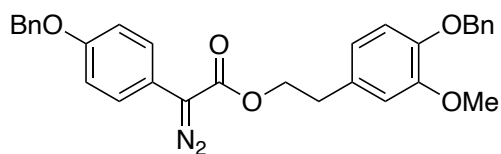


To a solution of **S14y** (1.91 g, 5.02 mmol, 1.00 equiv.) in MeCN (20 mL), *p*-ABSA (1.81 g, 7.53 mmol, 1.50 equiv.) and DBU (1.50 mL, 10.0 mmol, 2.00 equiv.) were added at 0 °C under an Ar atmosphere. After being stirred at rt for 16.5 h under dark, the reaction mixture was quenched with 1 M aq.

NaOH, and extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:Et₂O = 7:3) to afford **11y** (1.10 g, 54% yield).

Orange solid; M.p. 85–86 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.02–7.95 (m, 1H), 7.89–7.72 (m, 3H), 7.55–7.37 (m, 3H), 6.47 (s, 2H), 4.51 (t, *J* = 6.8 Hz, 2H), 3.91–3.78 (m, 9H), 2.99 (t, *J* = 6.8 Hz, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 165.3, 153.3, 136.7, 133.7, 133.5, 131.5, 128.8, 127.7, 126.7, 125.9, 122.7, 122.6, 121.9, 105.9, 65.7, 64.0, 60.9, 56.1, 35.8 (One carbon signal was overlapped); IR (KBr) 2086, 1702, 1592, 1507, 1462, 1324, 1241, 1128, 1038, 734 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₂₃H₂₂N₂NaO₅ 429.1421; Found 429.1427.

2-(4-(Benzyloxy)-3-methoxyphenyl)ethyl 2-(4-(benzyloxy)phenyl)-2-diazoacetate (**11z**)

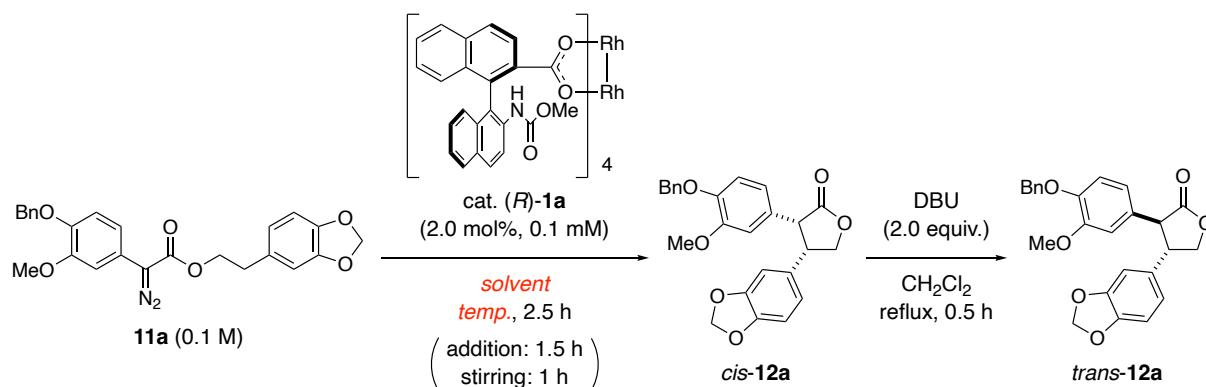


To a solution of **S14z** (642 mg, 1.33 mmol, 1.00 equiv.) in MeCN (15 mL), *p*-ABSA (799 mg, 3.33 mmol, 2.50 equiv.) and DBU (496 μ L, 3.33 mmol, 2.50 equiv.) were added at 0 °C under an Ar atmosphere. After being stirred at rt for 24 h under dark, the reaction mixture was quenched with 1 M aq. NaOH, and extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 6:1 to 4:1) to afford **11z** (392 mg, 58% yield).

Orange solid; M.p. 78–79 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.49–7.30 (m, 12H), 7.07–6.99 (m, 2H), 6.87 (d, *J* = 8.1 Hz, 1H), 6.83 (s, 1H), 6.73 (d, *J* = 8.1 Hz, 1H), 5.17 (s, 2H), 5.08 (s, 2H), 4.46 (t, *J* = 6.8 Hz, 2H), 3.90 (s, 3H), 2.96 (t, *J* = 6.8 Hz, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 165.7, 157.2, 149.6, 146.9, 137.3, 136.8, 130.9, 128.7, 128.6, 128.1, 127.8, 127.5, 127.3, 126.0, 120.9, 117.1, 115.6, 114.2, 112.7, 71.1, 70.1, 65.7, 62.6, 56.0, 35.0; IR (KBr) 2084, 1698, 1513, 1457, 1384, 1255, 1158, 1025, 827, 737, 698 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₃₁H₂₈N₂NaO₅ 531.1890; Found 531.1906.

Optimization of Reaction Conditions for Rh(II)-Catalyzed Intramolecular C–H Insertion of 11a

Table S1. Optimization of Reaction Conditions for Rh(II)-Catalyzed Intramolecular C–H Insertion of 11a in the Presence of Complex (R)-1a.^a

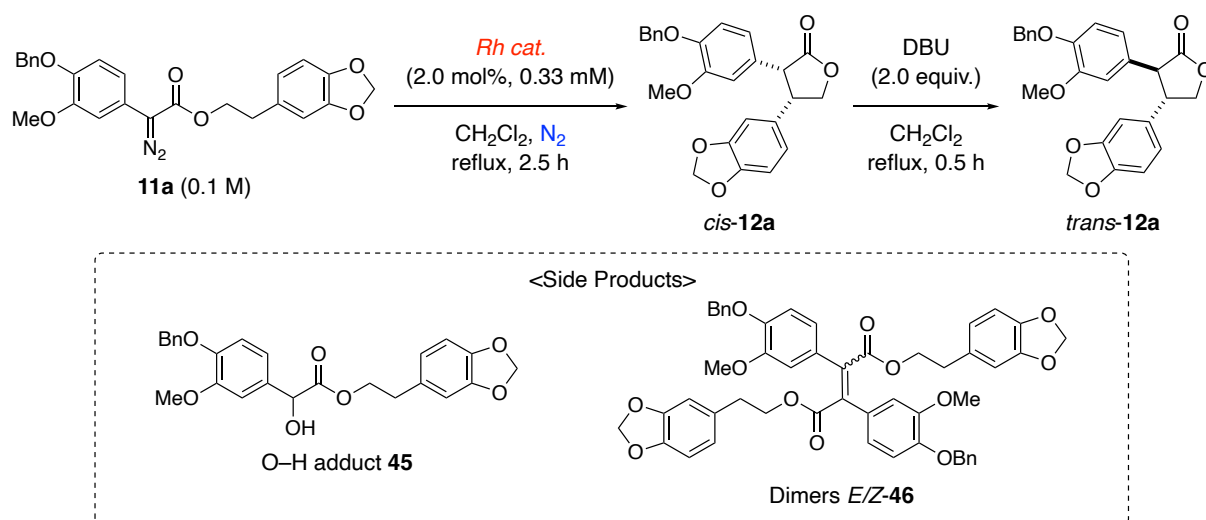


Entry	Solvent	Temperature	Yield of <i>Cis</i> -12a (%) ^b	Ee of <i>Trans</i> -12a (% ee) ^c
1	CH ₂ Cl ₂	rt	trace	ND
2	CH ₂ Cl ₂	reflux	45	50
3 ^d	CH ₂ Cl ₂	reflux	40	58
4	CHCl ₃	50 °C	16	50
5	CHCl ₃	reflux	39	46
6	1,2-dichloroethane	50 °C	11	51
7	1,2-dichloroethane	reflux	10	59
8	benzene	rt	0	-
9	benzene	50 °C	0	-
10	benzene	reflux	9	35
11	PhCF ₃	50 °C	0	-

^aEach reaction was conducted with an Ar balloon. ^bDetermined by integrating the ¹H NMR signals in the presence of 1,3,5-trimethoxybenzene as an internal standard. ^cDetermined by chiral HPLC analysis. ^dThe concentration of cat. (R)-1a was 0.33 mM.

Judging from the investigation of the reaction conditions, the conditions in CH₂Cl₂ under reflux (entry 3) were employed for the C–H insertion in the manuscript.

Table S2. Survey of Catalysts for Stereoselective Intramolecular C–H Insertion of 11a Including the Chemical Yields of O–H Adduct 45 and Dimers *E/Z*-46.



Entry	Rh(II) Catalyst	Yield (%) ^a of <i>Trans</i> - 12a (<i>Cis</i> - 12a)	Ee (% ee) ^b of <i>Trans</i> - 12a	Yield (%) ^a of 45	Combined Yield (%) ^a of 46 (diastomeric ratio) ^c
1	$\text{Rh}_2(\text{S-DOSP})_4$	68 (71)	27	trace	28 (1.6:1)
2	$\text{Rh}_2(\text{S-PTTL})_4$	64 (64)	–41	trace	34 (2.1:1)
3	$\text{Rh}_2(\text{S-TCPTTL})_4$	80 (80)	–37	trace	19 (1.9:1)
4	$\text{Rh}_2(\text{S-PTAD})_4$	60 (61)	–39	trace	38 (2.7:1)
5	$\text{Rh}_2(\text{S-NTTL})_4$	68 (69)	–54	trace	27 (2.4:1)
6	$\text{Rh}_2(\text{R-BTPCP})_4$	96 (97)	40	trace	trace
7	$\text{Rh}_2(\text{5R-MEPY})_4^d$	20 (41)	47	trace	47 (3.4:1)
8	(<i>R</i>)- 47	83 (85)	29	trace	13 (2.9:1)
9	(<i>R</i>)- 1a	60 (65)	55	trace	24 (2.5:1)
10	(<i>R</i>)- 1b	84 (84)	67	trace	15 (2.4:1)
11 ^e	(<i>R</i>)- 10a	81 (81)	70	16	trace
12	(<i>R</i>)- 10b	95 ^f (96)	95	trace	trace
13	(<i>R</i>)- 10b	(95 ^f , 95% ee ^g)	–	trace	trace

^aDetermined by integrating the ^1H NMR signals in the presence of 1,3,5-trimethoxybenzene as an internal standard. ^bDetermined by chiral HPLC analysis. ^cThe stereochemistries of these *E/Z*-isomers have yet to be determined. ^d5 mol% of $\text{Rh}_2(\text{5R-MEPY})_4$ was used. ^eThe reaction was conducted with an Ar balloon instead of under a N_2 atmosphere. ^fIsolated yield. ^gEe (%) of *cis*-**12a**.

As shown in **Table S2**, it was important to conduct this reaction under a N_2 atmosphere instead of an Ar balloon to prevent the generation of O–H adduct **45**.

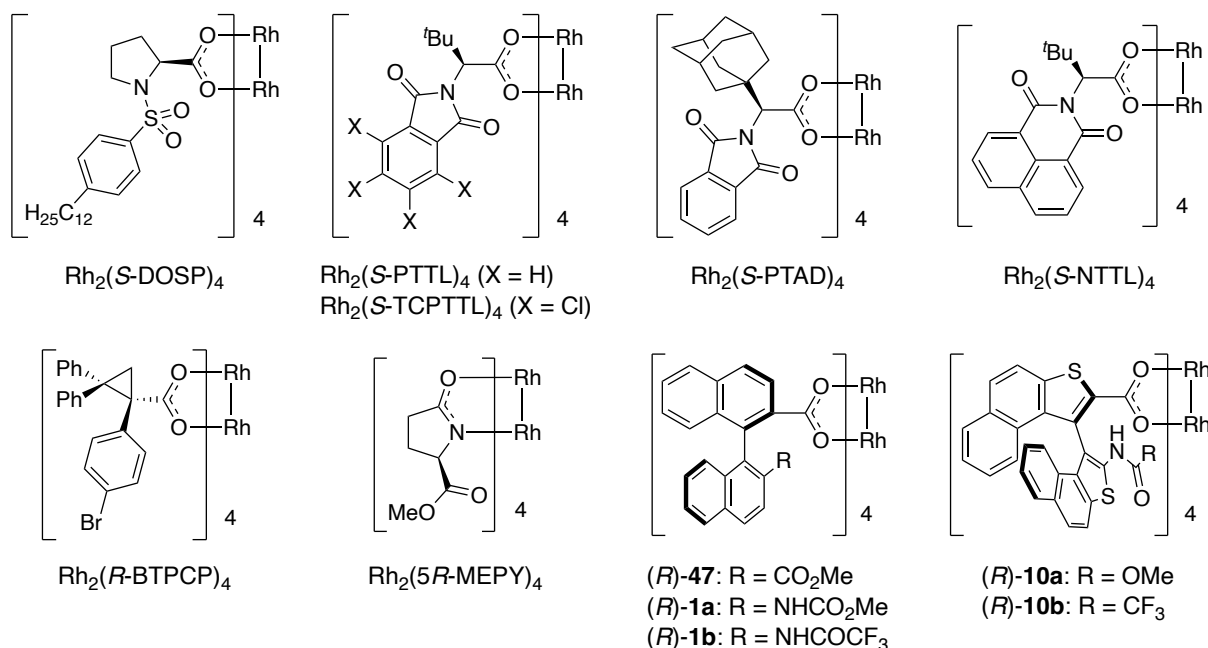
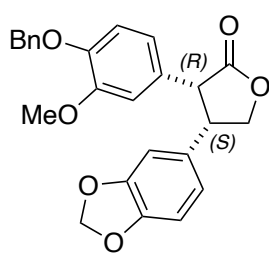


Figure S17. Structures of Rh(II) Catalysts Employed in **Table S2**.

Cis-4-(Benzo[*d*][1,3]dioxol-5-yl)-3-(4-(benzyloxy)-3-methoxyphenyl)dihydrofuran-2(3*H*)-one (*cis*-**12a**)

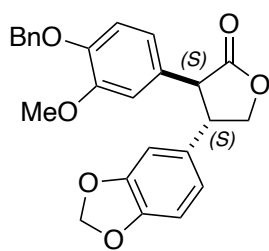


(Reaction conditions: **Table S2**, entry 13)

To a refluxing solution of cat. (*R*)-**10b** (3.43 mg, 1.50 μmol, 2.00 mol%) in CH₂Cl₂ (4.5 mL), a solution of **11a** (33.5 mg, 75.0 μmol, 1.00 equiv.) in CH₂Cl₂ (0.75 mL) was added dropwise over 1.5 h via a syringe pump under a N₂ atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12a**:*trans*-**12a** were determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard (96% yield, *cis*-**12a** only). The residue was purified by prep. TLC (SiO₂, CHCl₃:MeOH = 49:1) to afford *cis*-**12a** (29.7 mg, 95% yield, 95% ee for (3*R*,4*S*)). The enantiomeric excess of *cis*-**12a** was determined by HPLC analysis; HPLC (CHIRALPAK IC (4.6 mm × 250 mm), *n*-hexane/IPA = 3/2, flow rate = 1.0 mL/min, λ = 254 nm) *t*_R = 36.1 min (for *cis*-(3*S*,4*R*)-**12a**), 53.8 min (for *cis*-(3*R*,4*S*)-**12a**). The absolute configuration of the major enantiomer was determined to be (3*R*,4*S*) by the asymmetric synthesis of cinnamomumolide (*trans*-(3*S*,4*S*)-**13**) as shown in **Scheme 15**.

White solid; M.p. 166–167 °C; [α]_D²⁰ = +120.0 (*c* 0.8, CH₂Cl₂, 95% ee for (3*R*,4*S*)); ¹H NMR (400 MHz, CDCl₃) δ 7.41–7.31 (m, 4H), 7.31–7.24 (m, 1H), 6.72–6.68 (m, 1H), 6.62–6.57 (m, 1H), 6.47 (dd, *J* = 8.2, 2.1 Hz, 1H), 6.39–6.34 (m, 2H), 6.19 (d, *J* = 2.1 Hz, 1H), 5.87 (s, 2H), 5.08 (s, 2H), 4.70–4.59 (m, 2H), 4.15 (d, *J* = 8.5 Hz, 1H), 3.86 (ddd, *J* = 8.4, 6.2, 3.7 Hz, 1H), 3.61 (s, 3H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 176.8, 149.3, 147.9, 147.5, 146.9, 137.1, 131.0, 128.7, 128.0, 127.4, 126.1, 122.0, 121.3, 113.7, 113.2, 108.5, 108.4, 101.2, 71.6, 71.0, 55.9, 51.9, 47.8; IR (KBr) 2905, 1770, 1512, 1448, 1259, 1143, 1034, 932, 735, 699 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₂₅H₂₂NaO₆ 441.1309; Found 441.1317.

Trans-4-(Benzo[*d*][1,3]dioxol-5-yl)-3-(4-(benzyloxy)-3-methoxyphenyl)dihydrofuran-2(3*H*)-one (*trans*-**12a**)



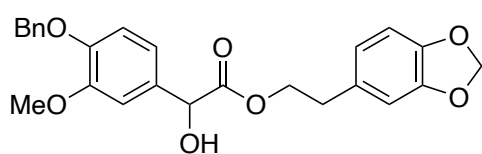
(Reaction conditions: **Table S2, entry 12**)

To a refluxing solution of cat. (*R*)-**10b** (3.43 mg, 1.50 μ mol, 2.00 mol%) in CH_2Cl_2 (4.5 mL), a solution of **11a** (33.5 mg, 75.0 μ mol, 1.00 equiv.) in CH_2Cl_2 (0.75 mL) was added dropwise over 1.5 h via a syringe pump under a N_2 atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12a**:*trans*-**12a** were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (96% yield, *cis*-**12a** only).

To a solution of the residue in CH_2Cl_2 (1.0 mL), DBU (22.4 μ L, 0.150 mmol, 2.00 equiv.) was added at rt under an Ar atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The residue was purified by prep. TLC (SiO_2 , CHCl_3 :MeOH = 49:1) to afford *trans*-**12a** (29.9 mg, 95% yield in 2 steps from **11a**, 95% ee for (3*S*,4*S*)). The enantiomeric excess of *trans*-**12a** was determined by HPLC analysis; HPLC (CHIRALPAK IC (4.6 mm \times 250 mm), *n*-hexane/IPA = 3/2, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 60.0 min (for *trans*-(3*S*,4*S*)-**12a**), 78.0 min (for *trans*-(3*R*,4*R*)-**12a**). The absolute configuration of the major enantiomer was determined to be (3*S*,4*S*) by the asymmetric synthesis of cinnamomumolide (*trans*-(3*S*,4*S*)-**13**) as shown in **Scheme 15**.

White solid; M.p. 128–129 $^\circ\text{C}$; $[\alpha]_D^{20}$ = +194.0 (c 0.3, CH_2Cl_2 , 95% ee for (3*S*,4*S*)); ^1H NMR (400 MHz, CDCl_3) δ 7.44–7.38 (m, 2H), 7.38–7.32 (m, 2H), 7.32–7.26 (m, 1H), 6.81 (d, J = 8.3 Hz, 1H), 6.75 (d, J = 8.0 Hz, 1H), 6.70 (t, J = 2.1 Hz, 2H), 6.64 (dt, J = 7.9, 1.7 Hz, 2H), 5.95 (s, 2H), 5.12 (s, 2H), 4.65 (dd, J = 9.1, 7.4 Hz, 1H), 4.24 (t, J = 9.5 Hz, 1H), 3.83 (s, 3H), 3.80–3.67 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 176.5, 149.9, 148.4, 148.0, 147.4, 137.1, 130.8, 128.7, 128.1, 128.0, 127.3, 120.9, 120.7, 114.1, 112.0, 108.8, 107.4, 101.4, 71.8, 71.1, 56.2, 53.0, 50.4; IR (KBr) 1771, 1513, 1448, 1251, 1144, 1034, 931, 795, 734, 699 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{25}\text{H}_{22}\text{NaO}_6$ 441.1309; Found 441.1313.

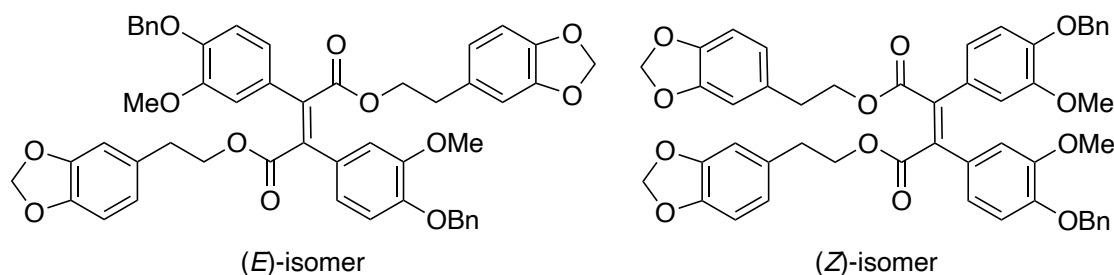
2-(Benzo[*d*][1,3]dioxol-5-yl)ethyl 2-(4-(benzyloxy)-3-methoxyphenyl)-2-hydroxyacetate (**45**)



Colorless oil; ^1H NMR (400 MHz, CDCl_3) δ 7.48–7.40 (m, 2H), 7.40–7.33 (m, 2H), 7.33–7.27 (m, 1H), 6.89 (s, 1H), 6.84 (s, 2H), 6.64 (d, J = 7.9 Hz, 1H), 6.51 (d, J = 1.7 Hz, 1H), 6.46 (dd, J = 7.9, 1.7 Hz, 1H), 5.91 (s, 2H), 5.16 (s, 2H), 5.06 (d, J = 5.4 Hz, 1H), 4.37 (dt, J = 10.8, 6.7 Hz, 1H), 4.27 (dt, J = 10.8, 6.7 Hz, 1H), 3.86 (s, 3H), 3.37 (d, J = 5.5 Hz, 1H), 2.86–2.69 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 173.8, 149.8, 148.4, 147.7, 146.4, 137.1, 131.3, 130.9, 128.7, 128.0, 127.4, 121.9, 119.3, 113.7, 109.9, 109.3, 108.3, 101.1, 72.8, 71.0, 66.7, 56.1, 34.7; IR (neat) 3496, 1735, 1509, 1446, 1251, 1140, 1036, 931, 772, 740 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{25}\text{H}_{24}\text{NaO}_7$ 459.1414; Found 459.1427.

Bis(2-(benzo[*d*][1,3]dioxol-5-yl)ethyl) 2,3-bis(4-(benzyloxy)-3-methoxyphenyl)fumarate (*E*-**46**)

Bis(2-(benzo[*d*][1,3]dioxol-5-yl)ethyl) 2,3-bis(4-(benzyloxy)-3-methoxyphenyl)maleate (*Z*-**46**)



(E)- and *(Z)*-isomers of **46** were separated by recycled prep. HPLC and characterized individually, although stereochemistries of these isomers have yet to be determined.

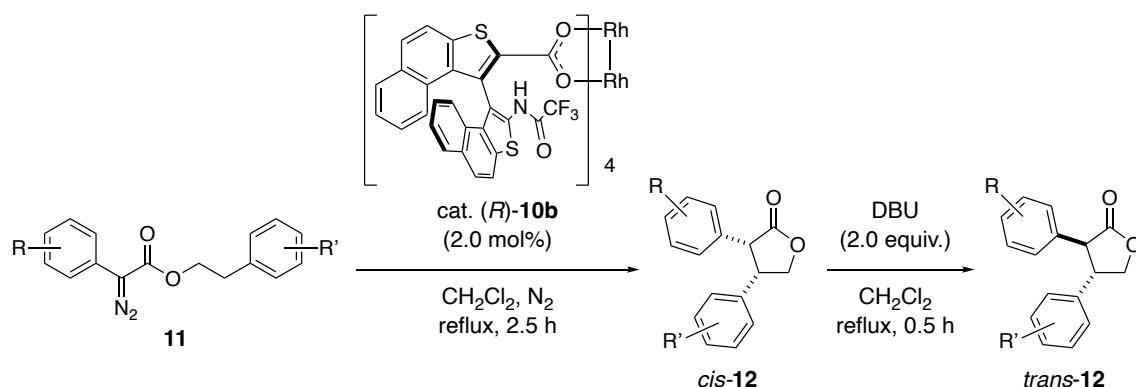
46-isomer 1

Colorless oil; ^1H NMR (400 MHz, CDCl_3) δ 7.42 (d, $J = 7.3$ Hz, 4H), 7.34 (t, $J = 7.4$ Hz, 4H), 7.29 (d, $J = 7.4$ Hz, 2H), 6.90 (s, 2H), 6.86–6.77 (m, 4H), 6.64 (d, $J = 7.9$ Hz, 2H), 6.46 (s, 2H), 6.43 (dd, $J = 7.8, 1.7$ Hz, 2H), 5.90 (s, 4H), 5.15 (s, 4H), 4.12 (t, $J = 6.9$ Hz, 4H), 3.83 (s, 6H), 2.55 (t, $J = 6.9$ Hz, 4H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 168.6, 149.4, 148.8, 147.7, 146.3, 136.9, 136.3, 131.2, 128.7, 128.4, 128.1, 127.3, 121.8, 121.0, 113.3, 111.5, 109.3, 108.3, 101.0, 70.9, 66.1, 56.0, 34.5; IR (neat) 1721, 1510, 1446, 1246, 1196, 1170, 1143, 1036, 1011, 734 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{50}\text{H}_{44}\text{NaO}_{12}$ 859.2725; Found 859.2732.

46-isomer 2

Colorless oil; ^1H NMR (400 MHz, CDCl_3) δ 7.43–7.39 (m, 4H), 7.39–7.33 (m, 4H), 7.33–7.27 (m, 2H), 6.71 (d, $J = 8.4$ Hz, 2H), 6.65 (d, $J = 7.9$ Hz, 2H), 6.63–6.57 (m, 4H), 6.55 (dd, $J = 7.9, 1.7$ Hz, 2H), 6.50 (d, $J = 2.0$ Hz, 2H), 5.89 (s, 4H), 5.12 (s, 4H), 4.36 (t, $J = 6.9$ Hz, 4H), 3.51 (s, 6H), 2.85 (t, $J = 6.9$ Hz, 4H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 168.2, 149.1, 148.3, 147.7, 146.3, 137.6, 136.9, 131.5, 128.7, 128.1, 127.5, 127.3, 122.6, 122.0, 113.6, 113.1, 109.6, 108.3, 101.0, 70.8, 66.4, 55.8, 34.6; IR (neat) 1716, 1509, 1446, 1246, 1142, 1036, 1008, 911, 809, 733 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{50}\text{H}_{44}\text{NaO}_{12}$ 859.2725; Found 859.2732.

Substrate Scope for Stereoselective Intramolecular C–H Insertion Catalyzed by Complex **10b** (Table 2)



Scheme S16. Asymmetric Intramolecular C–H Insertion Catalyzed by Complex **10b** and Successive Epimerization of *Cis*-Product.

In each reaction, the absolute configuration of the major enantiomer was assigned in analogy; that is, we estimated that the reaction catalyzed by complex (*R*)-**10b** could produce *cis*-(3*R*,4*S*)-**12** as a major enantiomer.

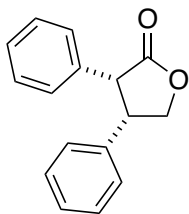
Intramolecular C–H Insertion of **11b**

To a refluxing solution of cat. (*R*)-**10b** (3.43 mg, 1.50 μ mol, 2.00 mol%) in CH_2Cl_2 (4.5 mL), a solution of **11b** (20.0 mg, 75.0 μ mol, 1.00 equiv.) in CH_2Cl_2 (0.75 mL) was added dropwise over 1.5 h via a syringe pump under a N_2 atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12b**:*trans*-**12b** were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (66% yield, *cis*-**12b** only).

To a solution of the residue in CH_2Cl_2 (1.0 mL), DBU (22.4 μ L, 0.150 mmol, 2.00 equiv.) was added at rt under an Ar atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The yield of *trans*-**12b** was determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (65% yield). The residue was purified by recycled prep. HPLC to afford pure *trans*-**12b**; HPLC (COSMOSIL 5SL-II (20 mm \times 250 mm), *n*-hexane/AcOEt = 4/1, flow rate = 20 mL/min, λ = 254 nm). The enantiomeric excess of *trans*-**12b** was determined to be 90% ee by HPLC analysis; HPLC (CHIRAL 5C (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 15.9 min (for *trans*-(3*R*,4*R*)-**12b**), 19.9 min (for *trans*-(3*S*,4*S*)-**12b**). The absolute configuration of the major enantiomer was determined to be (3*S*,4*S*) by comparison of its optical rotation to literature data for *trans*-(3*R*,4*R*)-**12b**; $[\alpha]_D^{23}$ = -196.7 (c 0.231, CHCl_3).⁵⁰

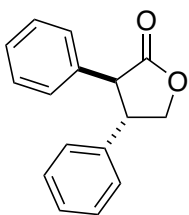
For physical data collection, *cis*-**12b** and *trans*-**12b** were synthesized alternatively by $\text{Rh}_2(\text{TPA})_4$ -catalyzed intramolecular C–H insertion of **11b** and successive epimerization (for *trans*-**12b**). Each diastereomer was separated by recycled prep. HPLC under the same conditions as mentioned above.

Cis-3,4-Diphenyldihydrofuran-2(3*H*)-one (*cis*-**12b**)



The spectral data was identical to the literature data.⁵¹

Trans-3,4-Diphenyldihydrofuran-2(3*H*)-one (*trans*-**12b**)



White solid; M.p. 93–94 °C; $[\alpha]_D^{20} = +186.3$ (*c* 0.5, CH₂Cl₂, 90% ee for (3*S*,4*S*)); ¹H NMR (500 MHz, CDCl₃) δ 7.37–7.24 (m, 6H), 7.23–7.14 (m, 4H), 4.72 (t, *J* = 8.5 Hz, 1H), 4.34 (t, *J* = 9.6 Hz, 1H), 3.95 (d, *J* = 11.5 Hz, 1H), 3.86 (td, *J* = 10.8, 8.0 Hz, 1H); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 176.4, 137.2, 135.4, 129.3, 129.0, 128.5, 128.1, 128.0, 127.4, 71.9, 53.3, 50.6; IR (KBr) 1773, 1497, 1453, 1351, 1144, 1053, 1019, 755, 698, 628, 581 cm⁻¹;

HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₁₆H₁₄NaO₂ 261.0886; Found 261.0893.

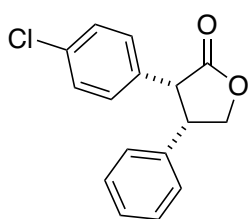
Intramolecular C–H Insertion of **11c**

To a refluxing solution of cat. (*R*)-**10b** (3.43 mg, 1.50 μ mol, 2.00 mol%) in CH₂Cl₂ (4.5 mL), a solution of **11c** (22.6 mg, 75.0 μ mol, 1.00 equiv.) in CH₂Cl₂ (0.75 mL) was added dropwise over 1.5 h via a syringe pump under a N₂ atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12c**:*trans*-**12c** were determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard (81% yield, *cis*-**12c** only).

To a solution of the residue in CH₂Cl₂ (1.0 mL), DBU (22.4 μ L, 0.150 mmol, 2.00 equiv.) was added at rt under an Ar atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The yield of *trans*-**12c** was determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard (73% yield). The residue was purified by recycled prep. HPLC to afford pure *trans*-**12c**; HPLC (COSMOSIL SSL-II (20 mm \times 250 mm), *n*-hexane/AcOEt = 4/1, flow rate = 20 mL/min, λ = 254 nm). The enantiomeric excess of *trans*-**12c** was determined to be 94% ee by HPLC analysis; HPLC (CHIRALPAK IC (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, λ = 254 nm) *t*_R = 14.1 min (for *trans*-(3*R*,4*R*)-**12c**), 17.0 min (for *trans*-(3*S*,4*S*)-**12c**).

For physical data collection, *cis*-**12c** and *trans*-**12c** were synthesized alternatively by Rh₂(TPA)₄-catalyzed intramolecular C–H insertion of **11c** and successive epimerization (for *trans*-**12c**). Each diastereomer was separated by recycled prep. HPLC under the same conditions as mentioned above.

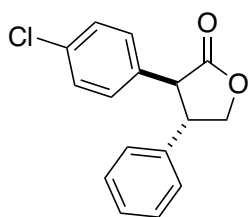
Cis-3-(4-Chlorophenyl)-4-phenyldihydrofuran-2(3*H*)-one (*cis*-**12c**)



White solid; M.p. 90–91 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.20–7.13 (m, 3H), 7.11–7.05 (m, 2H), 6.91–6.83 (m, 2H), 6.78–6.71 (m, 2H), 4.77–4.68 (m, 2H), 4.25 (d, J = 8.5 Hz, 1H), 3.98 (ddd, J = 8.5, 6.0, 3.5 Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 176.1, 136.8, 133.5, 131.7, 130.9, 128.8, 128.4, 127.9, 127.7, 71.5, 51.5, 47.7; IR (KBr) 1771, 1494, 1371, 1210, 1146, 1091, 1019, 911, 730, 701 cm^{-1} ; HRMS (ESI) m/z :

$[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{16}\text{H}_{13}\text{ClNaO}_2$ 295.0496; Found 295.0499.

Trans-3-(4-Chlorophenyl)-4-phenyldihydrofuran-2(3*H*)-one (*trans*-**12c**)



Colorless oil; $[\alpha]_{\text{D}}^{20}$ = +221.2 (c 0.9, CH_2Cl_2 , 94% ee for (3*S*,4*S*)); ^1H NMR (500 MHz, CDCl_3) δ 7.38–7.27 (m, 5H), 7.22–7.17 (m, 2H), 7.14–7.08 (m, 2H), 4.70 (dd, J = 9.2, 7.9 Hz, 1H), 4.33 (dd, J = 10.4, 9.2 Hz, 1H), 3.93 (d, J = 11.9 Hz, 1H), 3.80 (ddd, J = 11.9, 10.4, 7.9 Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 175.9, 136.6, 133.9, 133.8, 129.9, 129.3, 129.2, 128.3, 127.4, 71.8, 52.7, 50.7; IR (neat) 1773, 1494, 1146,

1091, 1018, 810, 758, 699, 583, 505 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{16}\text{H}_{13}\text{ClNaO}_2$ 295.0496; Found 295.0497.

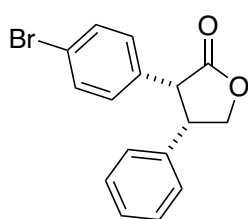
Intramolecular C–H Insertion of **11d**

To a refluxing solution of cat. (*R*)-**10b** (3.43 mg, 1.50 μmol , 2.00 mol%) in CH_2Cl_2 (4.5 mL), a solution of **11d** (25.9 mg, 75.0 μmol , 1.00 equiv.) in CH_2Cl_2 (0.75 mL) was added dropwise over 1.5 h via a syringe pump under a N_2 atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12d**:*trans*-**12d** were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (87% yield, *cis*-**12d** only).

To a solution of the residue in CH_2Cl_2 (1.0 mL), DBU (22.4 μL , 0.150 mmol, 2.00 equiv.) was added at rt under an Ar atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The yield of *trans*-**12d** was determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (86% yield). The residue was purified by recycled prep. HPLC to afford pure *trans*-**12d**; HPLC (COSMOSIL SSL-II (20 mm \times 250 mm), *n*-hexane/AcOEt = 4/1, flow rate = 20 mL/min, λ = 254 nm). The enantiomeric excess of *trans*-**12d** was determined to be 95% ee by HPLC analysis; HPLC (CHIRALPAK IC (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, λ = 254 nm) t_{R} = 15.5 min (for *trans*-(3*R*,4*R*)-**12d**), 18.4 min (for *trans*-(3*S*,4*S*)-**12d**).

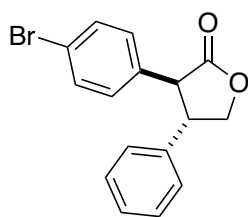
For physical data collection, *cis*-**12d** and *trans*-**12d** were synthesized alternatively by $\text{Rh}_2(\text{TPA})_4$ -catalyzed intramolecular C–H insertion of **11d** and successive epimerization (for *trans*-**12d**). Each diastereomer was separated by recycled prep. HPLC under the same conditions as mentioned above.

Cis-3-(4-Bromophenyl)-4-phenyldihydrofuran-2(3*H*)-one (*cis*-**12d**)



Pale yellow solid; M.p. 127–128 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.28–7.21 (m, 2H), 7.20–7.13 (m, 3H), 6.91–6.83 (m, 2H), 6.72–6.66 (m, 2H), 4.77–4.68 (m, 2H), 4.23 (d, J = 8.4 Hz, 1H), 3.99 (ddd, J = 8.4, 6.1, 3.6 Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 176.0, 136.8, 132.2, 131.4, 131.2, 128.8, 127.9, 127.8, 121.7, 71.6, 51.6, 47.7; IR (KBr) 1771, 1490, 1370, 1210, 1145, 1074, 1015, 912, 717, 701 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{16}\text{H}_{13}\text{BrNaO}_2$ 338.9991; Found 338.9992.

Trans-3-(4-Bromophenyl)-4-phenyldihydrofuran-2(3*H*)-one (*trans*-**12d**)



Colorless oil; $[\alpha]_{\text{D}}^{20}$ = +184.3 (c 0.7, CH_2Cl_2 , 95% ee for (3*S*,4*S*)); ^1H NMR (500 MHz, CDCl_3) δ 7.48–7.41 (m, 2H), 7.39–7.28 (m, 3H), 7.23–7.16 (m, 2H), 7.08–7.01 (m, 2H), 4.71 (dd, J = 9.2, 7.9 Hz, 1H), 4.34 (dd, J = 10.4, 9.2 Hz, 1H), 3.91 (d, J = 11.9 Hz, 1H), 3.80 (ddd, J = 11.9, 10.3, 7.9 Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 175.8, 136.6, 134.3, 132.2, 130.2, 129.4, 128.3, 127.4, 122.1, 71.8, 52.8, 50.7; IR (neat) 1772, 1490, 1349, 1146, 1072, 1015, 911, 806, 760, 699, 582 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{16}\text{H}_{13}\text{BrNaO}_2$ 338.9991; Found 338.9990.

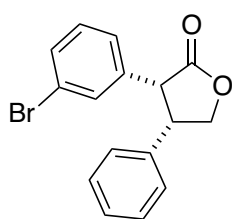
Intramolecular C–H Insertion of **11e**

To a refluxing solution of cat. (*R*)-**10b** (3.43 mg, 1.50 μmol , 2.00 mol%) in CH_2Cl_2 (4.5 mL), a solution of **11e** (25.9 mg, 75.0 μmol , 1.00 equiv.) in CH_2Cl_2 (0.75 mL) was added dropwise over 1.5 h via a syringe pump under a N_2 atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12e**:*trans*-**12e** were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (73% yield, *cis*-**12e** only).

To a solution of the residue in CH_2Cl_2 (1.0 mL), DBU (22.4 μL , 0.150 mmol, 2.00 equiv.) was added at rt under an Ar atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The yield of *trans*-**12e** was determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (70% yield). The residue was purified by recycled prep. HPLC to afford pure *trans*-**12e**; HPLC (COSMOSIL 5SL-II (20 mm \times 250 mm), *n*-hexane/AcOEt = 4/1, flow rate = 20 mL/min, λ = 254 nm). The enantiomeric excess of *trans*-**12e** was determined to be 91% ee by HPLC analysis; HPLC (CHIRAL 5A (4.6 mm \times 250 mm), *n*-hexane/IPA = 9/1, flow rate = 1.0 mL/min, λ = 254 nm) t_{R} = 15.4 min (for *trans*-(3*R*,4*R*)-**12e**), 18.8 min (for *trans*-(3*S*,4*S*)-**12e**).

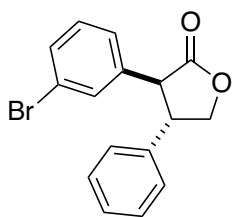
For physical data collection, *cis*-**12e** and *trans*-**12e** were synthesized alternatively by $\text{Rh}_2(\text{TPA})_4$ -catalyzed intramolecular C–H insertion of **11e** and successive epimerization (for *trans*-**12e**). Each diastereomer was separated by recycled prep. HPLC under the same conditions as mentioned above.

Cis-3-(3-Bromophenyl)-4-phenyldihydrofuran-2(3*H*)-one (*cis*-**12e**)



White solid; M.p. 119–120 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.29–7.22 (m, 1H), 7.21–7.13 (m, 3H), 7.02–6.93 (m, 2H), 6.91–6.84 (m, 2H), 6.71 (d, J = 7.8 Hz, 1H), 4.77–4.68 (m, 2H), 4.23 (d, J = 8.5 Hz, 1H), 3.99 (ddd, J = 8.5, 6.0, 3.7 Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 175.8, 136.7, 135.4, 132.6, 130.6, 129.7, 128.8, 128.2, 127.9, 127.8, 122.2, 71.5, 51.7, 47.8; IR (KBr) 1772, 1566, 1476, 1370, 1209, 1145, 1021, 775, 732, 698 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{16}\text{H}_{13}\text{BrNaO}_2$ 338.9991; Found 338.9995.

Trans-3-(3-Bromophenyl)-4-phenyldihydrofuran-2(3*H*)-one (*trans*-**12e**)



Colorless oil; $[\alpha]_{\text{D}}^{20}$ = +148.7 (c 1, CH_2Cl_2 , 91% ee for (3*S*,4*S*)); ^1H NMR (500 MHz, CDCl_3) δ 7.42 (ddd, J = 8.0, 2.1, 1.1 Hz, 1H), 7.39–7.28 (m, 4H), 7.24–7.14 (m, 3H), 7.10 (dt, J = 7.7, 1.4 Hz, 1H), 4.71 (dd, J = 9.2, 7.8 Hz, 1H), 4.33 (dd, J = 10.1, 9.2 Hz, 1H), 3.92 (d, J = 11.7 Hz, 1H), 3.84 (ddd, J = 11.7, 10.0, 7.8 Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 175.7, 137.5, 136.6, 131.5, 131.2, 130.5, 129.4, 128.3, 127.31, 127.26, 123.0, 71.9, 52.8, 50.5; IR (neat) 1774, 1597, 1568, 1476, 1350, 1146, 1019, 780, 758, 693 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{16}\text{H}_{13}\text{BrNaO}_2$ 338.9991; Found 338.9993.

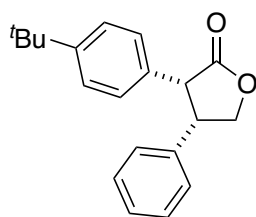
Intramolecular C–H Insertion of **11f**

To a refluxing solution of cat. (*R*)-**10b** (3.43 mg, 1.50 μmol , 2.00 mol%) in CH_2Cl_2 (4.5 mL), a solution of **11f** (24.2 mg, 75.0 μmol , 1.00 equiv.) in CH_2Cl_2 (0.75 mL) was added dropwise over 1.5 h via a syringe pump under a N_2 atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12f**:*trans*-**12f** were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (80% yield, *cis*-**12f** only).

To a solution of the residue in CH_2Cl_2 (1.0 mL), DBU (22.4 μL , 0.150 mmol, 2.00 equiv.) was added at rt under an Ar atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The yield of *trans*-**12f** was determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (78% yield). The residue was purified by recycled prep. HPLC to afford pure *trans*-**12f**; HPLC (COSMOSIL SSL-II (20 mm \times 250 mm), *n*-hexane/AcOEt = 5/1, flow rate = 20 mL/min, λ = 254 nm). The enantiomeric excess of *trans*-**12f** was determined to be 81% ee by HPLC analysis; HPLC (CHIRAL 5A (4.6 mm \times 250 mm), *n*-hexane/IPA = 9/1, flow rate = 1.0 mL/min, λ = 254 nm) t_{R} = 9.8 min (for *trans*-(3*R*,4*R*)-**12f**), 11.3 min (for *trans*-(3*S*,4*S*)-**12f**).

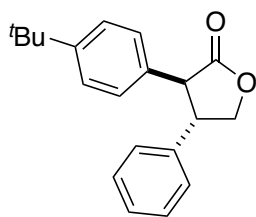
For physical data collection, *cis*-**12f** and *trans*-**12f** were synthesized alternatively by $\text{Rh}_2(\text{TPA})_4$ -catalyzed intramolecular C–H insertion of **11f** and successive epimerization (for *trans*-**12f**). Each diastereomer was separated by recycled prep. HPLC under the same conditions as mentioned above.

Cis-3-(4-*tert*-Butylphenyl)-4-phenyldihydrofuran-2(3*H*)-one (*cis*-**12f**)



White solid; M.p. 113–114 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.17–7.09 (m, 5H), 6.84 (dt, J = 6.5, 1.6 Hz, 2H), 6.75–6.70 (m, 2H), 4.73–4.65 (m, 2H), 4.22 (d, J = 8.4 Hz, 1H), 3.98 (ddd, J = 8.5, 6.3, 4.7 Hz, 1H), 1.22 (s, 9H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 176.9, 150.4, 136.9, 130.0, 129.1, 128.4, 128.1, 127.5, 125.2, 71.4, 51.7, 47.9, 34.5, 31.3; IR (KBr) 2962, 1772, 1516, 1458, 1367, 1209, 1143, 1022, 912, 731, 700 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{20}\text{H}_{22}\text{NaO}_2$ 317.1512; Found 317.1518.

Trans-3-(4-*tert*-Butylphenyl)-4-phenyldihydrofuran-2(3*H*)-one (*trans*-**12f**)



White solid; M.p. 138–139 °C; $[\alpha]_{\text{D}}^{20}$ = +164.9 (c 0.4, CH_2Cl_2 , 81% ee for (3*S*,4*S*)); ^1H NMR (500 MHz, CDCl_3) δ 7.37–7.31 (m, 4H), 7.31–7.26 (m, 1H), 7.26–7.20 (m, 2H), 7.15–7.09 (m, 2H), 4.70 (dd, J = 9.1, 7.8 Hz, 1H), 4.29 (t, J = 9.7 Hz, 1H), 3.94 (d, J = 11.3 Hz, 1H), 3.91–3.82 (m, 1H), 1.28 (s, 9H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 176.7, 150.7, 137.5, 132.2, 129.2, 128.04, 128.01, 127.4, 126.0, 72.0, 52.6, 50.2, 34.6, 31.4; IR (KBr) 2963, 1782, 1458, 1354, 1146, 1012, 817, 760, 701, 594 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{20}\text{H}_{22}\text{NaO}_2$ 317.1512; Found 317.1512.

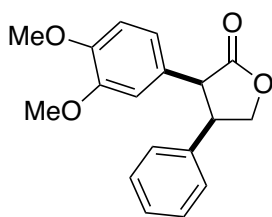
Intramolecular C–H Insertion of **11g**

To a refluxing solution of cat. (*S*)-**10b** (3.43 mg, 1.50 μmol , 2.00 mol%) in CH_2Cl_2 (4.5 mL), a solution of **12g** (24.5 mg, 75.0 μmol , 1.00 equiv.) in CH_2Cl_2 (0.75 mL) was added dropwise over 1.5 h via a syringe pump under a N_2 atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12g**:*trans*-**12g** were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (36% yield, *cis*-**12g** only).

To a solution of the residue in CH_2Cl_2 (1.0 mL), DBU (22.4 μL , 0.150 mmol, 2.00 equiv.) was added at rt under an Ar atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The yield of *trans*-**12g** was determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (34% yield). The residue was purified by recycled prep. HPLC to afford pure *trans*-**12g**; HPLC (COSMOSIL SSL-II (20 mm \times 250 mm), *n*-hexane/AcOEt = 3/2, flow rate = 20 mL/min, λ = 254 nm). The enantiomeric excess of *trans*-**12g** was determined to be 93% ee by HPLC analysis; HPLC (CHIRAL 5B (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, λ = 230 nm) t_{R} = 46.0 min (for *trans*-(3*S*,4*S*)-**12g**), 50.8 min (for *trans*-(3*R*,4*R*)-**12g**).

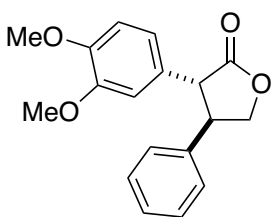
For physical data collection, *cis*-**12g** and *trans*-**12g** were synthesized alternatively by $\text{Rh}_2(\text{TPA})_4$ -catalyzed intramolecular C–H insertion of **11g** and successive epimerization (for *trans*-**12g**). Each diastereomer was separated by recycled prep. HPLC under the same conditions as mentioned above.

Cis-3-(3,4-Dimethoxyphenyl)-4-phenyldihydrofuran-2(3*H*)-one (*cis*-**12g**)



Pale yellow solid; M.p. 137–138 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.20–7.13 (m, 3H), 6.93–6.87 (m, 2H), 6.68 (d, J = 8.2 Hz, 1H), 6.54 (dd, J = 8.2, 2.1 Hz, 1H), 6.01 (d, J = 2.1 Hz, 1H), 4.72 (d, J = 5.0 Hz, 2H), 4.21 (d, J = 8.3 Hz, 1H), 3.96 (dt, J = 8.3, 4.9 Hz, 1H), 3.79 (s, 3H), 3.49 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 176.8, 148.6, 148.4, 137.3, 128.7, 128.1, 127.6, 125.5, 122.0, 112.7, 110.8, 71.4, 55.9, 55.7, 52.0, 48.0; IR (KBr) 1771, 1591, 1517, 1461, 1264, 1142, 1025, 964, 762, 703 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{18}\text{H}_{18}\text{NaO}_4$ 321.1097; Found 321.1100.

Trans-3-(3,4-Dimethoxyphenyl)-4-phenyldihydrofuran-2(3*H*)-one (*trans*-**12g**)



Colorless oil; $[\alpha]_{\text{D}}^{20}$ = -301.1 (c 0.1, CH_2Cl_2 , 93% ee for (3*R*,4*R*)); ^1H NMR (500 MHz, CDCl_3) δ 7.37–7.32 (m, 2H), 7.32–7.27 (m, 1H), 7.24–7.18 (m, 2H), 6.80 (d, J = 8.3 Hz, 1H), 6.72 (dd, J = 8.2, 2.1 Hz, 1H), 6.66 (d, J = 2.1 Hz, 1H), 4.71 (dd, J = 9.2, 7.7 Hz, 1H), 4.34 (dd, J = 10.0, 9.1 Hz, 1H), 3.91–3.76 (m, 8H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 176.5, 149.3, 148.8, 137.3, 129.3, 128.1, 127.7, 127.4, 120.7, 111.5, 71.7, 56.0, 53.0, 50.7 (Two carbon signals were overlapped); IR (neat) 1771, 1592, 1518, 1462, 1258, 1233, 1142, 1023, 807, 760, 700 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{18}\text{H}_{18}\text{NaO}_4$ 321.1097; Found 321.1095.

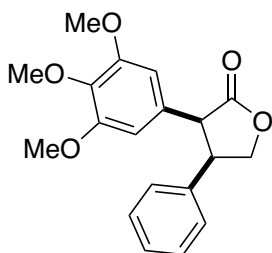
Intramolecular C–H Insertion of **11h**

To a refluxing solution of cat. (*S*)-**10b** (3.43 mg, 1.50 μmol , 2.00 mol%) in CH_2Cl_2 (4.5 mL), a solution of **11h** (26.7 mg, 75.0 μmol , 1.00 equiv.) in CH_2Cl_2 (0.75 mL) was added dropwise over 1.5 h via a syringe pump under a N_2 atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12h**:*trans*-**12h** were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (100% yield, *cis*-**12h** only).

To a solution of the residue in CH_2Cl_2 (1.0 mL), DBU (22.4 μL , 0.150 mmol, 2.00 equiv.) was added at rt under an Ar atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The yield of *trans*-**12h** was determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (96% yield). The residue was purified by recycled prep. HPLC to afford pure *trans*-**12h**; HPLC (COSMOSIL SSL-II (20 mm \times 250 mm), *n*-hexane/AcOEt = 1/1, flow rate = 20 mL/min, λ = 254 nm). The enantiomeric excess of *trans*-**12h** was determined to be 94% ee by HPLC analysis; HPLC (CHIRALPAK IC (4.6 mm \times 250 mm), *n*-hexane/IPA = 3/2, flow rate = 1.0 mL/min, λ = 230 nm) t_{R} = 20.9 min (for *trans*-(3*R*,4*R*)-**12h**), 27.5 min (for *trans*-(3*S*,4*S*)-**12h**).

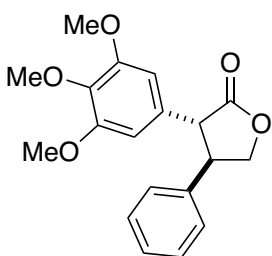
For physical data collection, *cis*-**12h** and *trans*-**12h** were synthesized alternatively by $\text{Rh}_2(\text{TPA})_4$ -catalyzed intramolecular C–H insertion of **11h** and successive epimerization (for *trans*-**12h**). Each diastereomer was separated by recycled prep. HPLC under the same conditions as mentioned above.

Cis-4-Phenyl-3-(3,4,5-trimethoxyphenyl)dihydrofuran-2(3*H*)-one (*cis*-**12h**)



White solid; M.p. 165–166 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.20–7.14 (m, 3H), 6.93–6.87 (m, 2H), 5.94 (s, 2H), 4.76–4.69 (m, 2H), 4.19 (d, $J = 8.3$ Hz, 1H), 3.97 (ddd, $J = 8.3, 5.3, 4.3$ Hz, 1H), 3.74 (s, 3H), 3.58 (s, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 176.4, 152.9, 137.5, 137.2, 128.7, 128.4, 128.1, 127.6, 107.0, 71.5, 60.9, 56.1, 52.5, 48.0; IR (KBr) 1761, 1588, 1456, 1425, 1245, 1127, 1018, 1003, 961, 759, 703 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{19}\text{H}_{20}\text{NaO}_5$ 351.1203; Found 351.1189.

Trans-4-Phenyl-3-(3,4,5-trimethoxyphenyl)dihydrofuran-2(3*H*)-one (*trans*-**12h**)



White solid; M.p. 146–147 °C; $[\alpha]_{\text{D}}^{20} = -159.9$ (c 0.9, CH_2Cl_2 , 94% ee for (3*R*,4*R*)); ^1H NMR (500 MHz, CDCl_3) δ 7.39–7.33 (m, 2H), 7.33–7.28 (m, 1H), 7.25–7.17 (m, 2H), 6.35 (s, 2H), 4.72 (dd, $J = 9.2, 7.6$ Hz, 1H), 4.35 (t, $J = 9.4$ Hz, 1H), 3.90–3.70 (m, 11H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 176.3, 153.6, 137.7, 137.3, 130.9, 129.3, 128.2, 127.4, 105.5, 71.7, 60.9, 56.2, 53.6, 50.8; IR (KBr) 1770, 1591, 1508, 1459, 1426, 1351, 1243, 1126, 1013, 760 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{19}\text{H}_{20}\text{NaO}_5$ 351.1203; Found 351.1203.

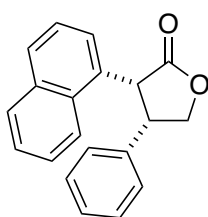
Intramolecular C–H Insertion of **11i**

To a refluxing solution of cat. (*R*)-**10b** (3.43 mg, 1.50 μmol , 2.00 mol%) in CH_2Cl_2 (4.5 mL), a solution of **11i** (23.7 mg, 75.0 μmol , 1.00 equiv.) in CH_2Cl_2 (0.75 mL) was added dropwise over 1.5 h via a syringe pump under a N_2 atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12i**:*trans*-**12i** were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (87% yield, *cis*-**12i** only).

To a solution of the residue in CH_2Cl_2 (1.0 mL), DBU (22.4 μL , 0.150 mmol, 2.00 equiv.) was added at rt under an Ar atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The yield of *trans*-**12i** was determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (85% yield). The residue was purified by recycled prep. HPLC to afford pure *trans*-**12i**; HPLC (COSMOSIL SSL-II (20 mm \times 250 mm), *n*-hexane/AcOEt = 4/1, flow rate = 20 mL/min, $\lambda = 254$ nm). The enantiomeric excess of *trans*-**12i** was determined to be 85% ee by HPLC analysis; HPLC (CHIRALPAK IC (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, $\lambda = 254$ nm) $t_{\text{R}} = 21.9$ min (for *trans*-(3*R*,4*R*)-**12i**), 27.2 min (for *trans*-(3*S*,4*S*)-**12i**).

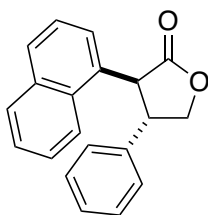
For physical data collection, *cis*-**12i** and *trans*-**12i** were synthesized alternatively by $\text{Rh}_2(\text{TPA})_4$ -catalyzed intramolecular C–H insertion of **11i** and successive epimerization (for *trans*-**12i**). Each diastereomer was separated by recycled prep. HPLC under the same conditions as mentioned above.

Cis-3-(1-Naphthyl)-4-phenyldihydrofuran-2(3*H*)-one (*cis*-**12i**)



Colorless oil; ^1H NMR (300 MHz, CDCl_3) δ 7.91–7.76 (m, 2H), 7.64 (d, J = 8.3 Hz, 1H), 7.53–7.41 (m, 2H), 7.18 (dd, J = 8.2, 7.3 Hz, 1H), 7.02–6.88 (m, 4H), 6.71–6.63 (m, 2H), 5.03 (d, J = 8.5 Hz, 1H), 4.89–4.74 (m, 2H), 4.24 (ddd, J = 8.6, 6.3, 3.4 Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3) δ 176.8, 137.3, 133.5, 132.1, 129.2, 129.1, 128.3, 128.1, 127.48, 127.45, 127.3, 126.4, 125.5, 125.1, 122.4, 71.7, 48.1, 47.0; IR (neat) 1766, 1371, 1209, 1142, 1038, 1021, 790, 774, 757, 702 cm^{-1} ; HRMS (EI) m/z : $[\text{M}]^+$ Calcd for $\text{C}_{20}\text{H}_{16}\text{O}_2$ 288.1150; Found 288.1151.

Trans-3-(1-Naphthyl)-4-phenyldihydrofuran-2(3*H*)-one (*trans*-**12i**)



Colorless oil; $[\alpha]_{\text{D}}^{20}$ = +93.5 (c 0.3, CH_2Cl_2 , 85% ee for (3*S*,4*S*)); ^1H NMR (300 MHz, CDCl_3) δ 7.90–7.77 (m, 2H), 7.73–7.65 (m, 1H), 7.52–7.37 (m, 3H), 7.37–7.18 (m, 6H), 4.81 (dd, J = 9.2, 7.7 Hz, 1H), 4.59 (d, J = 8.8 Hz, 1H), 4.49 (dd, J = 9.2, 7.9 Hz, 1H), 3.99 (q, J = 8.1 Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3) δ 177.1, 138.9, 134.3, 132.1, 131.5, 129.34, 129.26, 128.9, 128.0, 127.1, 126.6, 126.0, 125.5, 123.3, 72.5, 51.4, 49.9 (One carbon signal was overlapped); IR (neat) 1768, 1349, 1142, 1018, 795, 776, 754, 697, 665, 630 cm^{-1} ; HRMS (EI) m/z : $[\text{M}]^+$ Calcd for $\text{C}_{20}\text{H}_{16}\text{O}_2$ 288.1150; Found 288.1153.

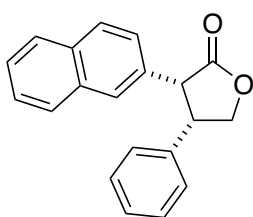
Intramolecular C–H Insertion of **11j**

To a refluxing solution of cat. (*R*)-**10b** (3.43 mg, 1.50 μmol , 2.00 mol%) in CH_2Cl_2 (4.5 mL), a solution of **11j** (23.7 mg, 75.0 μmol , 1.00 equiv.) in CH_2Cl_2 (0.75 mL) was added dropwise over 1.5 h via a syringe pump under a N_2 atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12j**:*trans*-**12j** were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (90% yield, *cis*-**12j** only).

To a solution of the residue in CH_2Cl_2 (1.0 mL), DBU (22.4 μL , 0.150 mmol, 2.00 equiv.) was added at rt under an Ar atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The yield of *trans*-**12j** was determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (85% yield). The residue was purified by recycled prep. HPLC to afford pure *trans*-**12j**; HPLC (COSMOSIL SSL-II (20 mm \times 250 mm), *n*-hexane/AcOEt = 4/1, flow rate = 20 mL/min, λ = 254 nm). The enantiomeric excess of *trans*-**12j** was determined to be 96% ee by HPLC analysis; HPLC (CHIRALPAK IC (4.6 mm \times 250 mm), *n*-hexane/IPA = 7/3, flow rate = 1.0 mL/min, λ = 254 nm) t_{R} = 17.0 min (for *trans*-(3*R*,4*R*)-**12j**), 20.9 min (for *trans*-(3*S*,4*S*)-**12j**).

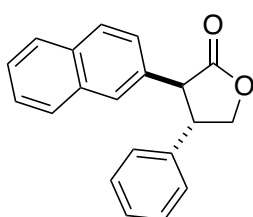
For physical data collection, *cis*-**12j** and *trans*-**12j** were synthesized alternatively by $\text{Rh}_2(\text{TPA})_4$ -catalyzed intramolecular C–H insertion of **11j** and successive epimerization (for *trans*-**12j**). Each diastereomer was separated by recycled prep. HPLC under the same conditions as mentioned above.

Cis-3-(2-Naphthyl)-4-phenyldihydrofuran-2(3*H*)-one (*cis*-**12j**)



White solid; M.p. 177–178 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.68 (ddt, $J = 24.2, 6.9, 3.5$ Hz, 2H), 7.55 (d, $J = 8.5$ Hz, 1H), 7.45–7.38 (m, 3H), 7.13–7.04 (m, 3H), 6.91–6.84 (m, 2H), 6.79 (dd, $J = 8.5, 1.8$ Hz, 1H), 4.81–4.73 (m, 2H), 4.42 (d, $J = 8.5$ Hz, 1H), 4.09 (ddd, $J = 8.5, 6.1, 4.5$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 176.6, 136.8, 133.2, 132.5, 130.7, 128.8, 128.6, 128.1, 127.9, 127.8, 127.64, 127.62, 127.2, 126.2, 71.5, 52.3, 48.0 (One carbon signal was overlapped); IR (KBr) 1769, 1370, 1210, 1143, 1021, 965, 911, 821, 747, 702, 478 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{20}\text{H}_{16}\text{NaO}_2$ 311.1043; Found 311.1041.

Trans-3-(2-Naphthyl)-4-phenyldihydrofuran-2(3*H*)-one (*trans*-**12j**)



Colorless oil; $[\alpha]_{\text{D}}^{20} = +237.5$ (c 1.1, CH_2Cl_2 , 96% ee for (3*S*,4*S*)); ^1H NMR (500 MHz, CDCl_3) δ 7.86–7.72 (m, 3H), 7.65 (d, $J = 1.8$ Hz, 1H), 7.50–7.43 (m, 2H), 7.36–7.27 (m, 4H), 7.25–7.20 (m, 2H), 4.77 (dd, $J = 9.2, 7.9$ Hz, 1H), 4.40 (dd, $J = 10.1, 9.1$ Hz, 1H), 4.12 (d, $J = 11.4$ Hz, 1H), 4.02–3.93 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 176.4, 137.2, 133.5, 132.9, 132.8, 129.3, 129.0, 128.1, 128.0, 127.9, 127.8, 127.4, 126.5, 126.3, 125.9, 71.9, 53.6, 50.6; IR (neat) 1771, 1602, 1504, 1350, 1145, 1019, 816, 752, 698, 477 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{20}\text{H}_{16}\text{NaO}_2$ 311.1043; Found 311.1044.

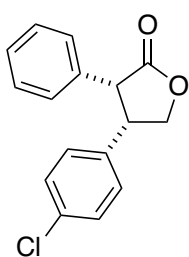
Intramolecular C–H Insertion of **11k**

To a refluxing solution of cat. (*R*)-**10b** (3.43 mg, 1.50 μmol , 2.00 mol%) in CH_2Cl_2 (4.5 mL), a solution of **11k** (22.6 mg, 75.0 μmol , 1.00 equiv.) in CH_2Cl_2 (0.75 mL) was added dropwise over 1.5 h via a syringe pump under a N_2 atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12k**:*trans*-**12k** were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (52% yield, *cis*-**12k** only).

To a solution of the residue in CH_2Cl_2 (1.0 mL), DBU (22.4 μL , 0.150 mmol, 2.00 equiv.) was added at rt under an Ar atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The yield of *trans*-**12k** was determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (47% yield). The residue was purified by recycled prep. HPLC to afford pure *trans*-**12k**; HPLC (COSMOSIL SSL-II (20 mm \times 250 mm), *n*-hexane/AcOEt = 4/1, flow rate = 20 mL/min, $\lambda = 254$ nm). The enantiomeric excess of *trans*-**12k** was determined to be 90% ee by HPLC analysis; HPLC (CHIRAL 5C (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, $\lambda = 254$ nm) $t_{\text{R}} = 17.5$ min (for *trans*-(3*R*,4*R*)-**12k**), 22.5 min (for *trans*-(3*S*,4*S*)-**12k**).

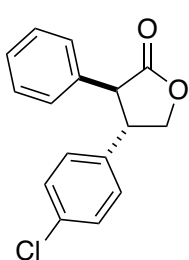
For physical data collection, *cis*-**12k** and *trans*-**12k** were synthesized alternatively by $\text{Rh}_2(\text{TPA})_4$ -catalyzed intramolecular C–H insertion of **11k** and successive epimerization (for *trans*-**12k**). Each diastereomer was separated by recycled prep. HPLC under the same conditions as mentioned above.

Cis-4-(4-Chlorophenyl)-3-phenyldihydrofuran-2(3*H*)-one (*cis*-**12k**)



Colorless oil; ^1H NMR (500 MHz, CDCl_3) δ 7.19–7.06 (m, 5H), 6.86–6.80 (m, 2H), 6.79–6.74 (m, 2H), 4.73–4.58 (m, 2H), 4.25 (d, $J = 8.5$ Hz, 1H), 3.97 (ddd, $J = 8.5, 6.3, 4.2$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 176.2, 135.4, 133.4, 132.8, 129.41, 129.35, 128.7, 128.5, 127.6, 71.1, 51.9, 47.3; IR (neat) 1771, 1494, 1373, 1212, 1144, 1092, 1029, 826, 750, 700 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{16}\text{H}_{13}\text{ClNaO}_2$ 295.0496; Found 295.0489.

Trans-4-(4-Chlorophenyl)-3-phenyldihydrofuran-2(3*H*)-one (*trans*-**12k**)



Colorless oil; $[\alpha]_{\text{D}}^{20} = +182.6$ (c 0.6, CH_2Cl_2 , 90% ee for (3*S*,4*S*)); ^1H NMR (500 MHz, CDCl_3) δ 7.38–7.22 (m, 5H), 7.21–7.07 (m, 4H), 4.70 (dd, $J = 9.2, 7.5$ Hz, 1H), 4.30 (t, $J = 9.5$ Hz, 1H), 3.92–3.77 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 176.0, 135.7, 135.0, 134.0, 129.5, 129.1, 128.7, 128.5, 128.1, 71.5, 53.4, 50.2; IR (neat) 1775, 1495, 1146, 1091, 1056, 1017, 822, 753, 700, 517 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{16}\text{H}_{13}\text{ClNaO}_2$ 295.0496; Found 295.0507.

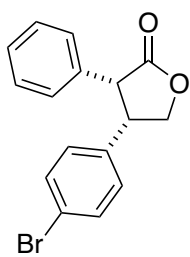
Intramolecular C–H Insertion of **11l**

To a refluxing solution of cat. (*R*)-**10b** (3.43 mg, 1.50 μmol , 2.00 mol%) in CH_2Cl_2 (4.5 mL), a solution of **11l** (25.9 mg, 75.0 μmol , 1.00 equiv.) in CH_2Cl_2 (0.75 mL) was added dropwise over 1.5 h via a syringe pump under a N_2 atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12l**:*trans*-**12l** were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (58% yield, *cis*-**12l** only).

To a solution of the residue in CH_2Cl_2 (1.0 mL), DBU (22.4 μL , 0.150 mmol, 2.00 equiv.) was added at rt under an Ar atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The yield of *trans*-**12l** was determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (55% yield). The residue was purified by recycled prep. HPLC to afford pure *trans*-**12l**; HPLC (COSMOSIL 5SL-II (20 mm \times 250 mm), *n*-hexane/AcOEt = 4/1, flow rate = 20 mL/min, $\lambda = 254$ nm). The enantiomeric excess of *trans*-**12l** was determined to be 89% ee by HPLC analysis; HPLC (CHIRAL 5C (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, $\lambda = 254$ nm) $t_{\text{R}} = 17.7$ min (for *trans*-(3*R*,4*R*)-**12l**), 22.6 min (for *trans*-(3*S*,4*S*)-**12l**).

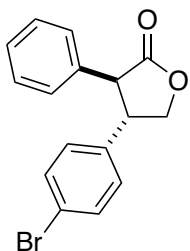
For physical data collection, *cis*-**12l** and *trans*-**12l** were synthesized alternatively by $\text{Rh}_2(\text{TPA})_4$ -catalyzed intramolecular C–H insertion of **11l** and successive epimerization (for *trans*-**12l**). Each diastereomer was separated by recycled prep. HPLC under the same conditions as mentioned above.

Cis-4-(4-Bromophenyl)-3-phenyldihydrofuran-2(3*H*)-one (*cis*-**12l**)



White solid; M.p. 122–123 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.27–7.21 (m, 2H), 7.18–7.10 (m, 3H), 6.85–6.78 (m, 2H), 6.74–6.67 (m, 2H), 4.72–4.58 (m, 2H), 4.24 (d, J = 8.5 Hz, 1H), 3.96 (ddd, J = 8.5, 6.4, 4.2 Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 176.2, 135.9, 132.8, 131.6, 129.7, 129.4, 128.5, 127.7, 121.5, 71.1, 51.8, 47.3; IR (KBr) 1770, 1490, 1373, 1211, 1146, 1075, 1028, 970, 822, 745, 698 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{16}\text{H}_{13}\text{BrNaO}_2$ 338.9991; Found 338.9973.

Trans-4-(4-Bromophenyl)-3-phenyldihydrofuran-2(3*H*)-one (*trans*-**12l**)



Colorless oil; $[\alpha]_{\text{D}}^{20}$ = +186.2 (c 0.6, CH_2Cl_2 , 89% ee for (3*S*,4*S*)); ^1H NMR (500 MHz, CDCl_3) δ 7.51–7.42 (m, 2H), 7.36–7.26 (m, 3H), 7.18–7.12 (m, 2H), 7.12–7.04 (m, 2H), 4.70 (dd, J = 9.2, 7.7 Hz, 1H), 4.30 (dd, J = 9.9, 9.2 Hz, 1H), 3.88 (d, J = 11.6 Hz, 1H), 3.81 (ddd, J = 11.6, 10.0, 7.7 Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 176.0, 136.2, 135.0, 132.4, 129.13, 129.05, 128.5, 128.1, 122.0, 71.4, 53.4, 50.2; IR (neat) 1775, 1493, 1145, 1073, 1055, 1015, 818, 752, 700, 512 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{16}\text{H}_{13}\text{BrNaO}_2$ 338.9991; Found 338.9999.

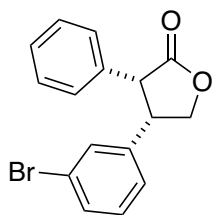
Intramolecular C–H Insertion of 11m

To a refluxing solution of cat. (*R*)-**10b** (3.43 mg, 1.50 μmol , 2.00 mol%) in CH_2Cl_2 (4.5 mL), a solution of **11m** (25.9 mg, 75.0 μmol , 1.00 equiv.) in CH_2Cl_2 (0.75 mL) was added dropwise over 1.5 h via a syringe pump under a N_2 atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12m**:*trans*-**12m** were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (46% yield, *cis*-**12m** only).

To a solution of the residue in CH_2Cl_2 (1.0 mL), DBU (22.4 μL , 0.150 mmol, 2.00 equiv.) was added at rt under an Ar atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The yield of *trans*-**12m** was determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (42% yield). The residue was purified by recycled prep. HPLC to afford pure *trans*-**12m**; HPLC (COSMOSIL SSL-II (20 mm \times 250 mm), *n*-hexane/AcOEt = 4/1, flow rate = 20 mL/min, λ = 254 nm). The enantiomeric excess of *trans*-**12m** was determined to be 87% ee by HPLC analysis; HPLC (CHIRAL 5C (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, λ = 254 nm) t_{R} = 17.3 min (for *trans*-(3*R*,4*R*)-**12m**), 24.8 min (for *trans*-(3*S*,4*S*)-**12m**).

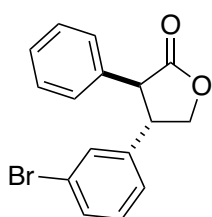
For physical data collection, *cis*-**12m** and *trans*-**12m** were synthesized alternatively by $\text{Rh}_2(\text{TPA})_4$ -catalyzed intramolecular C–H insertion of **11m** and successive epimerization (for *trans*-**12m**). Each diastereomer was separated by recycled prep. HPLC under the same conditions as mentioned above.

Cis-4-(3-Bromophenyl)-3-phenyldihydrofuran-2(3*H*)-one (*cis*-**12m**)



Colorless oil; ^1H NMR (500 MHz, CDCl_3) δ 7.30–7.24 (m, 1H), 7.20–7.12 (m, 3H), 7.03–6.95 (m, 2H), 6.87–6.80 (m, 2H), 6.76 (dt, $J = 7.8, 1.4$ Hz, 1H), 4.74–4.61 (m, 2H), 4.26 (d, $J = 8.5$ Hz, 1H), 3.96 (ddd, $J = 8.5, 6.4, 4.3$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 176.1, 139.2, 132.7, 131.2, 130.7, 130.0, 129.4, 128.5, 127.8, 126.7, 122.6, 71.0, 51.9, 47.6; IR (neat) 1771, 1567, 1477, 1372, 1211, 1144, 1077, 1030, 750, 698 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{16}\text{H}_{13}\text{BrNaO}_2$ 338.9991; Found 338.9979.

Trans-4-(3-Bromophenyl)-3-phenyldihydrofuran-2(3*H*)-one (*trans*-**12m**)



Colorless oil; $[\alpha]_{\text{D}}^{20} = +163.9$ (c 0.6, CH_2Cl_2 , 87% ee for (3*S*,4*S*)); ^1H NMR (500 MHz, CDCl_3) δ 7.43 (dt, $J = 7.9, 1.5$ Hz, 1H), 7.40–7.27 (m, 4H), 7.24–7.11 (m, 4H), 4.71 (dd, $J = 9.2, 7.8$ Hz, 1H), 4.31 (t, $J = 9.6$ Hz, 1H), 3.91 (d, $J = 11.4$ Hz, 1H), 3.82 (ddd, $J = 11.4, 9.9, 7.8$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 175.9, 139.6, 135.0, 131.3, 130.9, 130.5, 129.2, 128.4, 128.2, 126.0, 123.3, 71.5, 53.2, 50.2; IR (neat) 1773, 1595, 1567, 1476, 1145, 1021, 785, 753, 694, 506, 461 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{16}\text{H}_{13}\text{BrNaO}_2$ 338.9991; Found 339.0000.

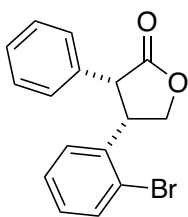
Intramolecular C–H Insertion of **11n**

To a refluxing solution of cat. (*R*)-**10b** (3.43 mg, 1.50 μmol , 2.00 mol%) in CH_2Cl_2 (4.5 mL), a solution of **11n** (25.9 mg, 75.0 μmol , 1.00 equiv.) in CH_2Cl_2 (0.75 mL) was added dropwise over 1.5 h via a syringe pump under a N_2 atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12n**:*trans*-**12n** were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (34% yield, *cis*-**12n** only).

To a solution of the residue in CH_2Cl_2 (1.0 mL), DBU (22.4 μL , 0.150 mmol, 2.00 equiv.) was added at rt under an Ar atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The yield of *trans*-**12n** was determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (31% yield). The residue was purified by recycled prep. HPLC to afford pure *trans*-**12n**; HPLC (COSMOSIL SSL-II (20 mm \times 250 mm), *n*-hexane/AcOEt = 4/1, flow rate = 20 mL/min, λ = 254 nm). The enantiomeric excess of *trans*-**12n** was determined to be 93% ee by HPLC analysis; HPLC (CHIRAL 5A (4.6 mm \times 250 mm), *n*-hexane/IPA = 9/1, flow rate = 1.0 mL/min, λ = 225 nm) t_{R} = 12.6 min (for *trans*-(3*R*,4*R*)-**12n**), 15.3 min (for *trans*-(3*S*,4*S*)-**12n**).

For physical data collection, *cis*-**12n** and *trans*-**12n** were synthesized alternatively by $\text{Rh}_2(\text{TPA})_4$ -catalyzed intramolecular C–H insertion of **11n** and successive epimerization (for *trans*-**12n**). Each diastereomer was separated by recycled prep. HPLC under the same conditions as mentioned above.

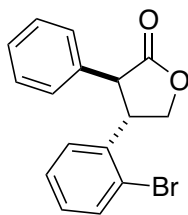
Cis-4-(2-Bromophenyl)-3-phenyldihydrofuran-2(3*H*)-one (*cis*-**12n**)



As *cis*-**12n** was easily epimerized during the purification, only ^1H and ^{13}C NMR signals, and HRMS of *cis/trans*-mixture of **12n** were measured.

HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{16}\text{H}_{13}\text{BrNaO}_2$ 338.9991; Found 338.9972.

Trans-4-(2-Bromophenyl)-3-phenyldihydrofuran-2(3*H*)-one (*trans*-**12n**)



White solid; M.p. 116–117 °C; $[\alpha]_{\text{D}}^{20} = +67.9$ (c 0.3, CH_2Cl_2 , 93% ee for (3*S*,4*S*)); ^1H NMR (500 MHz, CDCl_3) δ 7.58 (dd, $J = 8.1, 1.3$ Hz, 1H), 7.41 (dd, $J = 7.9, 1.8$ Hz, 1H), 7.39–7.31 (m, 3H), 7.31–7.24 (m, 3H), 7.16 (td, $J = 7.6, 1.7$ Hz, 1H), 4.83 (dd, $J = 9.1, 7.6$ Hz, 1H), 4.44 (ddd, $J = 10.4, 8.7, 7.6$ Hz, 1H), 4.21 (t, $J = 8.9$ Hz, 1H), 4.07 (d, $J = 10.3$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 176.1, 136.7, 134.9, 133.8, 129.5, 129.1, 128.43, 128.36, 128.1, 127.4, 125.1, 71.0, 51.9, 48.8; IR (KBr) 1776, 1474, 1190, 1146, 1054, 1022, 752, 698, 624, 443 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{16}\text{H}_{13}\text{BrNaO}_2$ 338.9991; Found 338.9997.

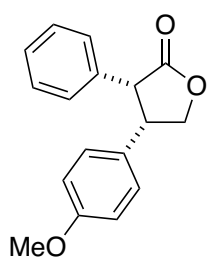
Intramolecular C–H Insertion of **11o**

To a refluxing solution of cat. (*R*)-**10b** (3.43 mg, 1.50 μmol , 2.00 mol%) in CH_2Cl_2 (4.5 mL), a solution of **11o** (22.2 mg, 75.0 μmol , 1.00 equiv.) in CH_2Cl_2 (0.75 mL) was added dropwise over 1.5 h via a syringe pump under a N_2 atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12o**:*trans*-**12o** were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (98% yield, *cis*-**12o** only).

To a solution of the residue in CH_2Cl_2 (1.0 mL), DBU (22.4 μL , 0.150 mmol, 2.00 equiv.) was added at rt under an Ar atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The yield of *trans*-**12o** was determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (95% yield). The residue was purified by recycled prep. HPLC to afford pure *trans*-**12o**; HPLC (COSMOSIL 5SL-II (20 mm \times 250 mm), *n*-hexane/AcOEt = 3/1, flow rate = 20 mL/min, $\lambda = 254$ nm). The enantiomeric excess of *trans*-**12o** was determined to be 92% ee by HPLC analysis; HPLC (CHIRAL 5C (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, $\lambda = 254$ nm) $t_{\text{R}} = 17.3$ min (for *trans*-(3*R*,4*R*)-**12o**), 19.9 min (for *trans*-(3*S*,4*S*)-**12o**).

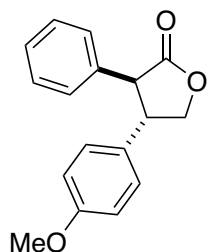
For physical data collection, *cis*-**12o** and *trans*-**12o** were synthesized alternatively by $\text{Rh}_2(\text{TPA})_4$ -catalyzed intramolecular C–H insertion of **11o** and successive epimerization (for *trans*-**12o**). Each diastereomer was separated by recycled prep. HPLC under the same conditions as mentioned above.

Cis-4-(4-Methoxyphenyl)-3-phenyldihydrofuran-2(3*H*)-one (*cis*-**12o**)



White solid; M.p. 131–132 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.17–7.11 (m, 3H), 6.86–6.79 (m, 2H), 6.78–6.73 (m, 2H), 6.68–6.62 (m, 2H), 4.72–4.61 (m, 2H), 4.20 (d, J = 8.4 Hz, 1H), 3.96 (ddd, J = 8.4, 6.4, 4.6 Hz, 1H), 3.72 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 176.8, 158.9, 133.3, 129.5, 129.2, 128.7, 128.4, 127.4, 113.9, 71.6, 55.3, 52.2, 47.2; IR (KBr) 1769, 1611, 1514, 1373, 1300, 1254, 1145, 1030, 830, 752, 701 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{17}\text{H}_{16}\text{NaO}_3$ 291.0992; Found 291.0969.

Trans-4-(4-Methoxyphenyl)-3-phenyldihydrofuran-2(3*H*)-one (*trans*-**12o**)



Colorless oil; $[\alpha]_{\text{D}}^{20}$ = +203.6 (c 0.9, CH_2Cl_2 , 92% ee for (3*S*,4*S*)); ^1H NMR (500 MHz, CDCl_3) δ 7.35–7.24 (m, 3H), 7.20–7.14 (m, 2H), 7.14–7.09 (m, 2H), 6.90–6.83 (m, 2H), 4.68 (dd, J = 9.1, 7.8 Hz, 1H), 4.29 (dd, J = 10.2, 9.2 Hz, 1H), 3.88 (d, J = 11.6 Hz, 1H), 3.83–3.75 (m, 4H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 176.5, 159.3, 135.4, 129.01, 128.99, 128.5, 128.4, 127.9, 114.6, 72.0, 55.4, 53.5, 50.0; IR (neat) 1773, 1611, 1515, 1455, 1252, 1181, 1144, 1020, 828, 751, 699 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{17}\text{H}_{16}\text{NaO}_3$ 291.0992; Found 291.1008.

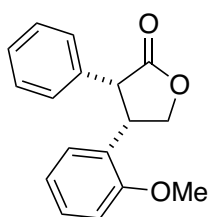
Intramolecular C–H Insertion of **11p**

To a refluxing solution of cat. (*R*)-**10b** (3.43 mg, 1.50 μmol , 2.00 mol%) in CH_2Cl_2 (4.5 mL), a solution of **11p** (22.2 mg, 75.0 μmol , 1.00 equiv.) in CH_2Cl_2 (0.75 mL) was added dropwise over 1.5 h via a syringe pump under a N_2 atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12p**:*trans*-**12p** were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (100% yield, *cis*-**12p** only).

To a solution of the residue in CH_2Cl_2 (1.0 mL), DBU (22.4 μL , 0.150 mmol, 2.00 equiv.) was added at rt under an Ar atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The yield of *trans*-**12p** was determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (97% yield). The residue was purified by recycled prep. HPLC to afford pure *trans*-**12p**; HPLC (COSMOSIL SSL-II (20 mm \times 250 mm), *n*-hexane/AcOEt = 3/1, flow rate = 20 mL/min, λ = 254 nm). The enantiomeric excess of *trans*-**12p** was determined to be 89% ee by HPLC analysis; HPLC (CHIRAL 5A (4.6 mm \times 250 mm), *n*-hexane/IPA = 9/1, flow rate = 1.0 mL/min, λ = 254 nm) t_{R} = 11.6 min (for *trans*-(3*R*,4*R*)-**12p**), 14.0 min (for *trans*-(3*S*,4*S*)-**12p**).

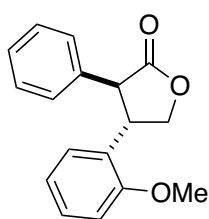
For physical data collection, *cis*-**12p** and *trans*-**12p** were synthesized alternatively by $\text{Rh}_2(\text{TPA})_4$ -catalyzed intramolecular C–H insertion of **12p** and successive epimerization (for *trans*-**12p**). Each diastereomer was separated by recycled prep. HPLC under the same conditions as mentioned above.

Cis-4-(2-Methoxyphenyl)-3-phenyldihydrofuran-2(3*H*)-one (*cis*-**12p**)



Colorless oil; ^1H NMR (500 MHz, CDCl_3) δ 7.15–7.04 (m, 4H), 6.94 (dd, J = 7.6, 1.7 Hz, 1H), 6.88–6.82 (m, 2H), 6.79 (td, J = 7.5, 1.2 Hz, 1H), 6.61 (dd, J = 8.3, 1.1 Hz, 1H), 4.68 (d, J = 5.9 Hz, 2H), 4.43 (dt, J = 8.8, 5.9 Hz, 1H), 4.30 (d, J = 8.8 Hz, 1H), 3.50 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 177.3, 157.0, 133.7, 129.3, 128.7, 127.8, 127.3, 127.1, 125.7, 120.6, 110.2, 70.5, 55.0, 50.8, 41.1; IR (neat) 1771, 1602, 1496, 1460, 1376, 1250, 1147, 1027, 755, 701 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{17}\text{H}_{16}\text{NaO}_3$ 291.0992; Found 291.0978.

Trans-4-(2-Methoxyphenyl)-3-phenyldihydrofuran-2(3*H*)-one (*trans*-**12p**)



Colorless oil; $[\alpha]_{\text{D}}^{20}$ = +165.8 (c 0.5, CH_2Cl_2 , 89% ee for (3*S*,4*S*)); ^1H NMR (500 MHz, CDCl_3) δ 7.35–7.20 (m, 6H), 7.14 (dd, J = 7.7, 1.7 Hz, 1H), 6.93–6.86 (m, 2H), 4.71 (t, J = 8.4 Hz, 1H), 4.34 (t, J = 8.9 Hz, 1H), 4.21 (d, J = 10.5 Hz, 1H), 4.09 (dt, J = 10.5, 8.6 Hz, 1H), 3.82 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 177.3, 157.7, 136.3, 129.1, 128.9, 128.6, 128.4, 127.7, 125.5, 121.0, 111.1, 70.8, 55.4, 50.7, 46.3; IR (neat) 1773, 1602, 1496, 1461, 1249, 1183, 1146, 1120, 1021, 753, 700 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{17}\text{H}_{16}\text{NaO}_3$ 291.0992; Found 291.1003.

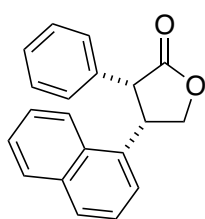
Intramolecular C–H Insertion of **11q**

To a refluxing solution of cat. (*R*)-**10b** (3.43 mg, 1.50 μmol , 2.00 mol%) in CH_2Cl_2 (4.5 mL), a solution of **11q** (23.7 mg, 75.0 μmol , 1.00 equiv.) in CH_2Cl_2 (0.75 mL) was added dropwise over 1.5 h via a syringe pump under a N_2 atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12q**:*trans*-**12q** were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (74% yield, *cis*-**12q** only).

To a solution of the residue in CH_2Cl_2 (1.0 mL), DBU (22.4 μL , 0.150 mmol, 2.00 equiv.) was added at rt under an Ar atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The yield of *trans*-**12q** was determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (70% yield). The residue was purified by recycled prep. HPLC to afford pure *trans*-**12q**; HPLC (COSMOSIL SSL-II (20 mm \times 250 mm), *n*-hexane/AcOEt = 4/1, flow rate = 20 mL/min, λ = 254 nm). The enantiomeric excess of *trans*-**12q** was determined to be 90% ee by HPLC analysis; HPLC (CHIRAL 5A (4.6 mm \times 250 mm), *n*-hexane/IPA = 9/1, flow rate = 1.0 mL/min, λ = 254 nm) t_{R} = 17.0 min (for *trans*-(3*R*,4*R*)-**12q**), 21.4 min (for *trans*-(3*S*,4*S*)-**12q**).

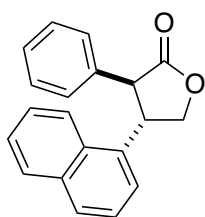
For physical data collection, *cis*-**12q** and *trans*-**12q** were synthesized alternatively by $\text{Rh}_2(\text{TPA})_4$ -catalyzed intramolecular C–H insertion of **11q** and successive epimerization (for *trans*-**12q**). Each diastereomer was separated by recycled prep. HPLC under the same conditions as mentioned above.

Cis-4-(1-Naphthyl)-3-phenyldihydrofuran-2(3*H*)-one (*cis*-**12q**)



White solid; M.p. 169–170 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.83–7.71 (m, 2H), 7.68–7.63 (m, 1H), 7.43–7.36 (m, 2H), 7.28–7.22 (m, 1H), 7.06 (d, J = 7.3 Hz, 1H), 6.95–6.84 (m, 3H), 6.66–6.60 (m, 2H), 4.91–4.83 (m, 2H), 4.81–4.74 (m, 1H), 4.46–4.41 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 177.0, 133.6, 133.0, 132.4, 131.9, 129.0, 128.9, 128.3, 128.0, 127.4, 126.3, 125.7, 125.2, 124.1, 122.7, 70.8, 51.9, 42.4; IR (KBr) 1771, 1453, 1372, 1218, 1145, 1022, 957, 780, 752, 700 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{20}\text{H}_{16}\text{NaO}_2$ 311.1043; Found 311.1025.

Trans-4-(1-Naphthyl)-3-phenyldihydrofuran-2(3*H*)-one (*trans*-**12q**)



Colorless oil; $[\alpha]_{\text{D}}^{20}$ = +25.5 (c 1, CH_2Cl_2 , 90% ee for (3*S*,4*S*)); ^1H NMR (500 MHz, CDCl_3) δ 7.94–7.84 (m, 2H), 7.81 (d, J = 8.1 Hz, 1H), 7.56 (d, J = 7.3 Hz, 1H), 7.53–7.45 (m, 3H), 7.35–7.22 (m, 5H), 4.94 (dd, J = 9.2, 7.7 Hz, 1H), 4.76–4.67 (m, 1H), 4.34 (t, J = 9.0 Hz, 1H), 4.25 (d, J = 10.2 Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 176.6, 135.5, 134.2, 133.4, 131.8, 129.4, 129.1, 128.6, 128.4, 128.0, 126.9, 126.2, 125.7, 123.2, 122.5, 72.1, 51.9, 45.5; IR (neat) 1773, 1500, 1146, 1020, 799, 778, 748, 699, 627, 462, 409 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{20}\text{H}_{16}\text{NaO}_2$ 311.1043; Found 311.1049.

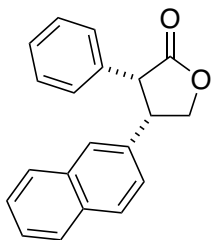
Intramolecular C–H Insertion of **11r**

To a refluxing solution of cat. (*R*)-**10b** (3.43 mg, 1.50 μmol , 2.00 mol%) in CH_2Cl_2 (4.5 mL), a solution of **11r** (23.7 mg, 75.0 μmol , 1.00 equiv.) in CH_2Cl_2 (0.75 mL) was added dropwise over 1.5 h via a syringe pump under a N_2 atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12r**:*trans*-**12r** were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (82% yield, *cis*-**12r** only).

To a solution of the residue in CH_2Cl_2 (1.0 mL), DBU (22.4 μL , 0.150 mmol, 2.00 equiv.) was added at rt under an Ar atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The yield of *trans*-**12r** was determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (80% yield). The residue was purified by recycled prep. HPLC to afford pure *trans*-**12r**; HPLC (COSMOSIL 5SL-II (20 mm \times 250 mm), *n*-hexane/AcOEt = 4/1, flow rate = 20 mL/min, λ = 254 nm). The enantiomeric excess of *trans*-**12r** was determined to be 89% ee by HPLC analysis; HPLC (CHIRAL 5C (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, λ = 254 nm) t_{R} = 19.8 min (for *trans*-(3*R*,4*R*)-**12r**), 27.1 min (for *trans*-(3*S*,4*S*)-**12r**).

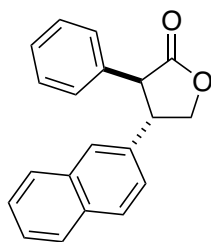
For physical data collection, *cis*-**12r** and *trans*-**12r** were synthesized alternatively by $\text{Rh}_2(\text{TPA})_4$ -catalyzed intramolecular C–H insertion of **11r** and successive epimerization (for *trans*-**12r**). Each diastereomer was separated by recycled prep. HPLC under the same conditions as mentioned above.

Cis-4-(2-Naphthyl)-3-phenyldihydrofuran-2(3*H*)-one (*cis*-**12r**)



White solid; M.p. 154–155 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.77–7.64 (m, 2H), 7.58 (d, $J = 8.5$ Hz, 1H), 7.48–7.38 (m, 3H), 7.12–7.02 (m, 3H), 6.87 (td, $J = 8.1, 1.9$ Hz, 3H), 4.83–4.75 (m, 2H), 4.33 (d, $J = 8.5$ Hz, 1H), 4.16 (ddd, $J = 8.5, 5.9, 4.7$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 176.6, 134.4, 133.2, 133.1, 132.5, 129.5, 128.3, 128.1, 127.8, 127.6, 127.5, 126.7, 126.3, 126.2, 126.1, 71.5, 52.1, 47.9; IR (KBr) 1770, 1501, 1453, 1375, 1143, 1029, 971, 819, 748, 699, 478 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{20}\text{H}_{16}\text{NaO}_2$ 311.1043; Found 311.1024.

Trans-4-(2-Naphthyl)-3-phenyldihydrofuran-2(3*H*)-one (*trans*-**12r**)



Colorless oil; $[\alpha]_{\text{D}}^{20} = +225.7$ (c 1.1, CH_2Cl_2 , 89% ee for (3*S*,4*S*)); ^1H NMR (500 MHz, CDCl_3) δ 7.87–7.79 (m, 2H), 7.79–7.72 (m, 1H), 7.63 (d, $J = 1.9$ Hz, 1H), 7.51–7.43 (m, 2H), 7.36–7.22 (m, 4H), 7.22–7.15 (m, 2H), 4.75 (dd, $J = 9.2, 7.6$ Hz, 1H), 4.42 (t, $J = 9.5$ Hz, 1H), 4.08–3.94 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 176.4, 135.4, 134.5, 133.5, 133.0, 129.2, 129.0, 128.5, 128.0, 127.8, 126.74, 126.70, 126.4, 124.7, 71.8, 53.3, 50.9 (One carbon signal was overlapped); IR (neat) 1773, 1503, 1362, 1144, 1058, 1019, 820, 749, 699, 478 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{20}\text{H}_{16}\text{NaO}_2$ 311.1043; Found 311.1055.

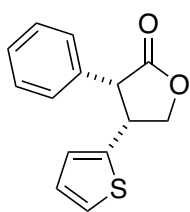
Intramolecular C–H Insertion of **11s**

To a refluxing solution of cat. (*R*)-**10b** (3.43 mg, 1.50 μmol , 2.00 mol%) in CH_2Cl_2 (4.5 mL), a solution of **11s** (20.4 mg, 75.0 μmol , 1.00 equiv.) in CH_2Cl_2 (0.75 mL) was added dropwise over 1.5 h via a syringe pump under a N_2 atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12s**:*trans*-**12s** were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (50% yield, *cis*-**12s** only).

To a solution of the residue in CH_2Cl_2 (1.0 mL), DBU (22.4 μL , 0.150 mmol, 2.00 equiv.) was added at rt under an Ar atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The yield of *trans*-**12s** was determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (46% yield). The residue was purified by recycled prep. HPLC to afford pure *trans*-**12s**; HPLC (COSMOSIL 5SL-II (20 mm \times 250 mm), *n*-hexane/AcOEt = 4/1, flow rate = 20 mL/min, $\lambda = 254$ nm). The enantiomeric excess of *trans*-**12s** was determined to be 77% ee by HPLC analysis; HPLC (CHIRALPAK IC (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, $\lambda = 254$ nm) $t_{\text{R}} = 17.7$ min (for *trans*-(3*R*,4*S*)-**12s**), 21.5 min (for *trans*-(3*S*,4*R*)-**12s**).

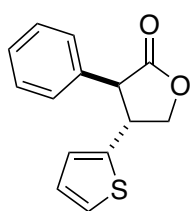
For physical data collection, *cis*-**12s** and *trans*-**12s** were synthesized alternatively by $\text{Rh}_2(\text{TPA})_4$ -catalyzed intramolecular C–H insertion of **11s** and successive epimerization (for *trans*-**12s**). Each diastereomer was separated by recycled prep. HPLC under the same conditions as mentioned above.

Cis-3-Phenyl-4-(thiophen-2-yl)dihydrofuran-2(3*H*)-one (*cis*-**12s**)



White solid; M.p. 116–117 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.24–7.16 (m, 3H), 7.05 (dd, J = 5.1, 1.2 Hz, 1H), 6.96–6.88 (m, 2H), 6.81 (dd, J = 5.1, 3.5 Hz, 1H), 6.61 (dt, J = 3.6, 0.9 Hz, 1H), 4.72 (dd, J = 9.3, 6.6 Hz, 1H), 4.60 (dd, J = 9.3, 5.6 Hz, 1H), 4.33–4.26 (m, 1H), 4.18 (d, J = 8.3 Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 176.2, 138.7, 133.0, 129.2, 128.6, 127.8, 126.9, 125.9, 125.0, 72.0, 52.3, 43.6; IR (KBr) 1767, 1497, 1453, 1371, 1211, 1153, 1011, 942, 848, 750, 699 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{14}\text{H}_{12}\text{NaO}_2\text{S}$ 267.0450; Found 267.0456.

Trans-3-Phenyl-4-(thiophen-2-yl)dihydrofuran-2(3*H*)-one (*trans*-**12s**)



Colorless oil; $[\alpha]_{\text{D}}^{20}$ = +150.3 (c 0.4, CH_2Cl_2 , 77% ee for (3*S*,4*R*)); ^1H NMR (500 MHz, CDCl_3) δ 7.38–7.29 (m, 3H), 7.25–7.19 (m, 3H), 6.95 (dd, J = 5.1, 3.5 Hz, 1H), 6.84 (dt, J = 3.5, 1.0 Hz, 1H), 4.75 (dd, J = 9.1, 7.8 Hz, 1H), 4.34 (dd, J = 10.3, 9.1 Hz, 1H), 4.15–4.08 (m, 1H), 3.88 (d, J = 11.7 Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 175.8, 140.1, 134.8, 129.1, 128.7, 128.2, 127.4, 125.5, 124.9, 71.9, 54.7, 46.3; IR (neat) 1774, 1498, 1449, 1358, 1307, 1243, 1135, 1020, 849, 750, 699 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{14}\text{H}_{12}\text{NaO}_2\text{S}$ 267.0450; Found 267.0449.

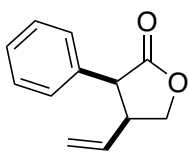
Intramolecular C–H Insertion of **2**

To a refluxing solution of cat. (*S*)-**10b** (6.86 mg, 3.00 μmol , 2.00 mol%) in CH_2Cl_2 (9.0 mL), a solution of **2** (43.2 mg, 150 μmol , 1.00 equiv.) in CH_2Cl_2 (1.5 mL) was added dropwise over 1.5 h via a syringe pump under a N_2 atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**48**:*trans*-**48** were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (31% yield, *cis*-**48** only).

To a solution of the residue in CH_2Cl_2 (2.0 mL), DBU (449 μL , 0.300 mmol, 2.00 equiv.) was added at rt under an Ar atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The yield of *trans*-**48** was determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (28% yield). The residue was purified by recycled prep. HPLC to afford pure *trans*-**48**; HPLC (COSMOSIL 5SL-II (20 mm \times 250 mm), *n*-hexane/AcOEt = 4/1, flow rate = 20 mL/min, λ = 254 nm). The enantiomeric excess of *trans*-**48** was determined to be 75% ee by HPLC analysis; HPLC (CHIRAL 5A (4.6 mm \times 250 mm), *n*-hexane/IPA = 19/1, flow rate = 1.0 mL/min, λ = 254 nm) t_{R} = 12.8 min (for *trans*-(3*S*,4*R*)-**48**), 14.2 min (for *trans*-(3*R*,4*S*)-**48**).

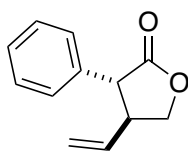
For physical data collection, *cis*-**48** and *trans*-**48** were synthesized alternatively by $\text{Rh}_2(\text{TPA})_4$ -catalyzed intramolecular C–H insertion of **2** and successive epimerization (for *trans*-**48**). Each diastereomer was separated by recycled prep. HPLC under the same conditions as mentioned above.

Cis-3-Phenyl-4-vinyldihydrofuran-2(3*H*)-one (*cis*-**48**)



The spectral data was identical to our previous data.¹³

Trans-3-Phenyl-4-vinyldihydrofuran-2(3*H*)-one (*trans*-**48**)



Colorless oil; $[\alpha]_D^{20} = -61.0$ (*c* 0.1, CH₂Cl₂, 75% ee for (3*R*,4*S*)); ¹H NMR (500 MHz, CDCl₃) δ 7.38–7.32 (m, 2H), 7.32–7.27 (m, 1H), 7.18–7.12 (m, 2H), 5.31 (ddd, *J* = 17.1, 10.2, 8.6 Hz, 1H), 5.11–5.00 (m, 2H), 4.49 (dd, *J* = 9.2, 7.0 Hz, 1H), 4.24 (dd, *J* = 9.3, 6.5 Hz, 1H), 3.99 (d, *J* = 8.7 Hz, 1H), 3.51–3.41 (m, 1H); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 177.0, 133.5, 133.4, 129.3, 128.8, 127.8, 118.8, 70.6, 50.6, 45.8; IR (neat) 1772, 1497, 1453, 1370, 1211, 1149, 1032, 1014, 924, 740, 704 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₁₂H₁₂NaO₂ 211.0730; Found 211.0730.

Intramolecular C–H Insertion of **11t**

To a refluxing solution of cat. (*S*)-**10b** (3.43 mg, 1.50 μ mol, 2.00 mol%) in CH₂Cl₂ (4.5 mL), a solution of **11t** (28.1 mg, 75.0 μ mol, 1.00 equiv.) in CH₂Cl₂ (0.75 mL) was added dropwise over 1.5 h via a syringe pump under a N₂ atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12t**:*trans*-**12t** were determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard (98% yield, *cis*-**12t** only).

To a solution of the residue in CH₂Cl₂ (1.0 mL), DBU (22.4 μ L, 0.150 mmol, 2.00 equiv.) was added at rt under an Ar atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The yield of *trans*-**12t** was determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard (98% yield). The residue was purified by recycled prep. HPLC to afford pure *trans*-**12t**; HPLC (COSMOSIL 5SL-II (20 mm \times 250 mm), *n*-hexane/AcOEt = 3/1, flow rate = 20 mL/min, λ = 254 nm). The enantiomeric excess of *trans*-**12t** was determined to be 93% ee by HPLC analysis; HPLC (CHIRAL 5B (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 25.6 min (for *trans*-(3*R*,4*R*)-**12t**), 28.8 min (for *trans*-(3*S*,4*S*)-**12t**).

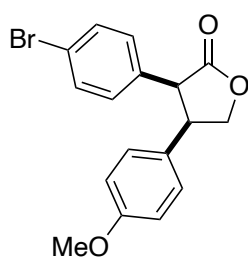
For physical data collection, *cis*-**12t** and *trans*-**12t** were synthesized alternatively by Rh₂(TPA)₄-catalyzed intramolecular C–H insertion of **11t** and successive epimerization (for *trans*-**12t**). Each diastereomer was separated by recycled prep. HPLC under the same conditions as mentioned above.

Intramolecular C–H Insertion of **11t in Gram-Scale**

To a refluxing solution of cat. (*S*)-**10b** (34.3 mg, 15.0 μ mol, 0.50 mol%) in CH₂Cl₂ (30 mL), a solution of **11t** (1.13 g, 3.00 mmol, 1.00 equiv.) in CH₂Cl₂ (18 mL) was added dropwise over 3 h via a syringe pump under a N₂ atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12t**:*trans*-**12t** were determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard (100% yield, *cis*-**12t** only).

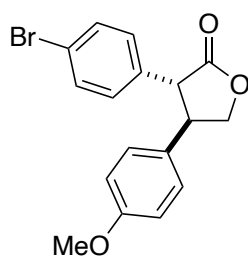
To a solution of the residue in CH₂Cl₂ (10 mL), DBU (896 μ L, 6.00 mmol, 2.00 equiv.) was added at rt under an Ar atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The yield of *trans*-**12t** was determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard (99% yield). The residue was purified by column chromatography (SiO₂, *n*-hexane:AcOEt = 7:3) to afford *trans*-**12t** (941 mg, 90% yield in 2 steps from **11t**). The enantiomeric excess of *trans*-**12t** was determined to be 93% ee by chiral HPLC analysis under the same conditions as mentioned above.

Cis-3-(4-Bromophenyl)-4-(4-methoxyphenyl)dihydrofuran-2(3*H*)-one (*cis*-**12t**)



Colorless oil; ¹H NMR (500 MHz, CDCl₃) δ 7.30–7.21 (m, 2H), 6.80–6.74 (m, 2H), 6.73–6.65 (m, 4H), 4.74–4.59 (m, 2H), 4.18 (d, *J* = 8.3 Hz, 1H), 3.93 (ddd, *J* = 8.4, 6.2, 3.6 Hz, 1H), 3.73 (s, 3H); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 176.2, 159.0, 132.4, 131.4, 131.3, 129.0, 128.6, 121.6, 114.1, 71.8, 55.3, 51.7, 47.0; IR (neat) 1772, 1612, 1514, 1489, 1301, 1254, 1181, 1146, 1032, 831, 756 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₁₇H₁₅BrNaO₃ 369.0097; Found 369.0078.

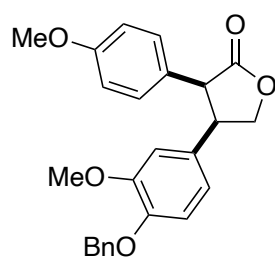
Trans-3-(4-Bromophenyl)-4-(4-methoxyphenyl)dihydrofuran-2(3*H*)-one (*trans*-**12t**)



Colorless oil; [α]_D²⁰ = –201.1 (*c* 0.7, CH₂Cl₂, 93% ee for (3*R*,4*R*)); ¹H NMR (500 MHz, CDCl₃) δ 7.47–7.39 (m, 2H), 7.15–7.07 (m, 2H), 7.07–7.00 (m, 2H), 6.90–6.83 (m, 2H), 4.66 (dd, *J* = 9.2, 7.9 Hz, 1H), 4.28 (dd, *J* = 10.5, 9.2 Hz, 1H), 3.85 (d, *J* = 12.1 Hz, 1H), 3.79 (s, 3H), 3.73 (ddd, *J* = 12.1, 10.5, 7.9 Hz, 1H); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 175.9, 159.4, 134.3, 132.1, 130.2, 128.4, 128.3, 122.0, 114.7, 71.9, 55.4, 52.9, 50.1; IR (neat) 1776, 1612, 1515, 1490, 1294, 1252, 1180, 1146, 1015, 829, 811 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₁₇H₁₅BrNaO₃ 369.0097; Found 369.0106.

Intramolecular C–H Insertion of **11u**

Cis-4-(4-(Benzyloxy)-3-methoxyphenyl)-3-(4-methoxyphenyl)dihydrofuran-2(3*H*)-one (*cis*-**12u**)

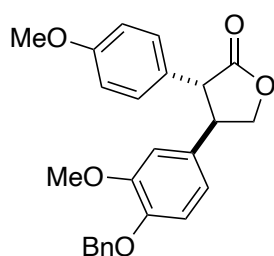


To a refluxing solution of cat. (*S*)-**10b** (3.43 mg, 1.50 μ mol, 2.00 mol%) in CH₂Cl₂ (4.5 mL), a solution of **11u** (32.4 mg, 75.0 μ mol, 1.00 equiv.) in CH₂Cl₂ (0.75 mL) was added dropwise over 1.5 h via a syringe pump under a N₂ atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12u**:*trans*-**12u** were determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard (91% yield, *cis*-**12u** only). The residue was purified by prep. TLC (SiO₂, CHCl₃:MeOH = 49:1) to afford *cis*-**12u** (28.6 mg, 94% yield). The enantiomeric excess of *cis*-**12u** was determined to be 96% ee by HPLC analysis; HPLC (CHIRALPAK ID (4.6 mm \times 250 mm), *n*-hexane/IPA = 3/2, flow rate = 1.0 mL/min, λ = 254 nm) *t*_R = 27.9 min (for *cis*-(3*S*,4*R*)-**12u**), 47.7 min (for *cis*-(3*R*,4*S*)-**12u**).

White solid; M.p. 132–133 °C; [α]_D²⁵ = –86.2 (*c* 0.4, CHCl₃, 96% ee for (3*S*,4*R*)); ¹H NMR (500 MHz, CDCl₃) δ 7.41–7.24 (m, 5H), 6.76–6.64 (m, 5H), 6.44 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.21 (d, *J* = 2.1 Hz, 1H), 5.08 (s, 2H),

4.71–4.59 (m, 2H), 4.16 (d, $J = 8.3$ Hz, 1H), 3.88 (ddd, $J = 8.3, 6.2, 4.4$ Hz, 1H), 3.72 (s, 3H), 3.60 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 177.0, 159.0, 149.5, 147.5, 137.0, 130.6, 129.8, 128.7, 128.0, 127.4, 125.3, 120.2, 114.0, 113.9, 112.1, 71.5, 71.0, 56.0, 55.4, 51.6, 47.6; IR (neat) 1761, 1517, 1254, 1239, 1218, 1135, 1028, 973, 787, 694 cm^{-1} ; HRMS (EI) m/z : $[\text{M}]^+$ Calcd for $\text{C}_{25}\text{H}_{24}\text{O}_5$ 404.1624; Found 404.1622.

Trans-4-(4-(Benzyloxy)-3-methoxyphenyl)-3-(4-methoxyphenyl)dihydrofuran-2(3*H*)-one (*trans*-**12u**)



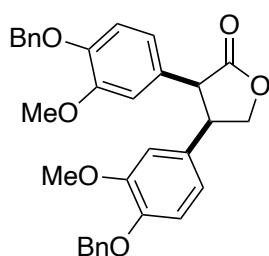
To a refluxing solution of cat. (*S*)-**10b** (3.43 mg, 1.50 μmol , 2.00 mol%) in CH_2Cl_2 (4.5 mL), a solution of **11u** (32.4 mg, 75.0 μmol , 1.00 equiv.) in CH_2Cl_2 (0.75 mL) was added dropwise over 1.5 h via a syringe pump under a N_2 atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12u**:*trans*-**12u** were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (91% yield, *cis*-**12u** only).

To a solution of the residue in CH_2Cl_2 (1.0 mL), DBU (22.4 μL , 0.150 mmol, 2.00 equiv.) was added at rt under a N_2 atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The residue was purified by prep. TLC (SiO_2 , CHCl_3 :MeOH = 49:1) to afford *trans*-**12u** (27.8 mg, 92% yield in 2 steps from **11u**). The enantiomeric excess of *trans*-**12u** was determined to be 96% ee by HPLC analysis; HPLC (CHIRAL 5C (4.6 mm \times 250 mm), *n*-hexane/IPA = 7/3, flow rate = 0.8 mL/min, $\lambda = 254$ nm) $t_R = 53.9$ min (for *trans*-(3*S*,4*S*)-**12u**), 58.7 min (for *trans*-(3*R*,4*R*)-**12u**).

Colorless oil; $[\alpha]_D^{25} = -170.9$ (c 0.7, CHCl_3 , 96% ee for (3*R*,4*R*)); ^1H NMR (500 MHz, CDCl_3) δ 7.45–7.27 (m, 5H), 7.12–7.06 (m, 2H), 6.89–6.79 (m, 3H), 6.71–6.63 (m, 2H), 5.12 (s, 2H), 4.67 (dd, $J = 9.1, 7.8$ Hz, 1H), 4.28 (t, $J = 9.6$ Hz, 1H), 3.86–3.68 (m, 8H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 176.8, 159.3, 150.0, 147.9, 137.0, 130.2, 129.6, 128.7, 128.1, 127.41, 127.36, 119.2, 114.5, 114.3, 111.1, 71.8, 71.1, 56.2, 55.4, 52.7, 50.3; IR (neat) 1766, 1513, 1454, 1248, 1140, 1015, 825, 808, 747, 698 cm^{-1} ; HRMS (EI) m/z : $[\text{M}]^+$ Calcd for $\text{C}_{25}\text{H}_{24}\text{O}_5$ 404.1624; Found 404.1626.

Intramolecular C–H Insertion of **11v**

Cis-3,4-Bis(4-(benzyloxy)-3-methoxyphenyl)dihydrofuran-2(3*H*)-one (*cis*-**12v**)



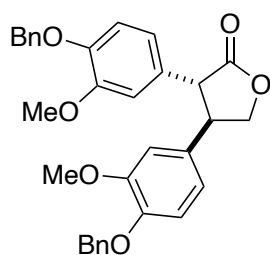
To a refluxing solution of cat. (*S*)-**10b** (3.43 mg, 1.50 μmol , 2.00 mol%) in CH_2Cl_2 (4.5 mL), a solution of **11v** (40.4 mg, 75.0 μmol , 1.00 equiv.) in CH_2Cl_2 (0.75 mL) was added dropwise over 1.5 h via a syringe pump under a N_2 atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12v**:*trans*-**12v** were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (90% yield, *cis*-**12v** only). The

residue was purified by prep. TLC (SiO_2 , CHCl_3 :MeOH = 49:1) to afford *cis*-**12v** (32.6 mg, 85% yield). The enantiomeric excess of *cis*-**12v** was determined to be 95% ee by HPLC analysis; HPLC (CHIRAL 5C (4.6 mm \times 250 mm), *n*-hexane/IPA = 3/2, flow rate = 1.0 mL/min, $\lambda = 254$ nm) $t_R = 33.0$ min (for *cis*-(3*S*,4*R*)-**12v**), 64.8 min (for *cis*-(3*R*,4*S*)-**12v**).

White solid; M.p. 135–136 $^\circ\text{C}$; $[\alpha]_D^{25} = -81.7$ (c 0.6, CHCl_3 , 95% ee for (3*S*,4*R*)); ^1H NMR (300 MHz, CDCl_3) δ

7.47–7.22 (m, 10H), 6.70 (dd, $J = 8.3, 0.8$ Hz, 2H), 6.45 (ddd, $J = 8.2, 4.9, 2.1$ Hz, 2H), 6.23 (d, $J = 2.1$ Hz, 1H), 6.13 (d, $J = 2.1$ Hz, 1H), 5.08 (s, 2H), 5.08 (s, 2H), 4.71–4.56 (m, 2H), 4.13 (d, $J = 8.3$ Hz, 1H), 3.86 (ddd, $J = 8.3, 6.0, 4.4$ Hz, 1H), 3.59 (s, 3H), 3.54 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3) δ 176.8, 149.5, 149.3, 147.6, 137.1, 137.0, 129.9, 128.7, 128.6, 128.0, 127.9, 127.29, 127.27, 126.2, 121.8, 120.0, 113.8, 113.6, 113.3, 112.2, 71.5, 71.0, 56.0, 55.9, 51.9, 47.6 (Two carbon signals were overlapped); IR (neat) 1751, 1517, 1450, 1261, 1246, 1229, 1143, 1136, 972, 725 cm^{-1} ; HRMS (EI) m/z : $[\text{M}]^+$ Calcd for $\text{C}_{32}\text{H}_{30}\text{O}_6$ 510.2042; Found 510.2041.

Trans-3,4-Bis(4-(benzyloxy)-3-methoxyphenyl)dihydrofuran-2(3*H*)-one (*trans*-**12v**)



To a refluxing solution of cat. (*S*)-**10b** (3.43 mg, 1.50 μmol , 2.00 mol%) in CH_2Cl_2 (4.5 mL), a solution of **11v** (40.4 mg, 75.0 μmol , 1.00 equiv.) in CH_2Cl_2 (0.75 mL) was added dropwise over 1.5 h via a syringe pump under a N_2 atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12v**:*trans*-**12v** were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (89% yield, *cis*-**12v** only).

To a solution of the residue in CH_2Cl_2 (1.0 mL), DBU (22.4 μL , 0.150 mmol, 2.00 equiv.) was added at rt under a N_2 atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The residue was purified by prep. TLC (SiO_2 , CHCl_3 :MeOH = 49:1) to afford *trans*-**12v** (33.7 mg, 88% yield in 2 steps from **11v**). The enantiomeric excess of *trans*-**12v** was determined to be 95% ee by HPLC analysis; HPLC (CHIRAL 5C (4.6 mm \times 250 mm), *n*-hexane/IPA = 3/2, flow rate = 1.0 mL/min, $\lambda = 254$ nm) $t_R = 61.3$ min (for *trans*-(3*S*,4*S*)-**12v**), 94.0 min (for *trans*-(3*R*,4*R*)-**12v**).

White solid; M.p. 160–161 $^\circ\text{C}$; $[\alpha]_D^{25} = -138.8$ (c 1.3, CHCl_3 , 95% ee for (3*R*,4*R*)); ^1H NMR (300 MHz, CDCl_3) δ 7.45–7.25 (m, 10H), 6.82 (dd, $J = 8.2, 7.4$ Hz, 2H), 6.72–6.61 (m, 4H), 5.13 (s, 2H), 5.12 (s, 2H), 4.66 (dd, $J = 9.1, 7.5$ Hz, 1H), 4.34–4.24 (m, 1H), 3.86–3.65 (m, 8H); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3) δ 176.6, 150.0, 149.9, 147.91, 147.87, 137.1, 137.0, 130.3, 128.69, 128.65, 128.3, 128.04, 127.95, 127.32, 127.29, 120.7, 119.2, 114.3, 114.1, 112.1, 111.1, 71.6, 71.1, 71.0, 56.2, 56.1, 53.0, 50.2; IR (neat) 1759, 1518, 1454, 1250, 1221, 1143, 1005, 755, 728, 701 cm^{-1} ; HRMS (EI) m/z : $[\text{M}]^+$ Calcd for $\text{C}_{32}\text{H}_{30}\text{O}_6$ 510.2042; Found 510.2043.

Intramolecular C–H Insertion of **11w**

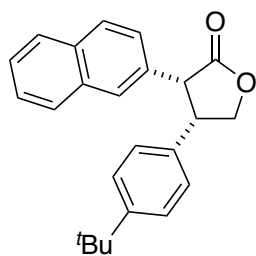
To a refluxing solution of cat. (*R*)-**10b** (3.43 mg, 1.50 μmol , 2.00 mol%) in CH_2Cl_2 (4.5 mL), a solution of **11w** (27.9 mg, 75.0 μmol , 1.00 equiv.) in CH_2Cl_2 (0.75 mL) was added dropwise over 1.5 h via a syringe pump under a N_2 atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12w**:*trans*-**12w** were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (99% yield, *cis*-**12w** only).

To a solution of the residue in CH_2Cl_2 (1.0 mL), DBU (22.4 μL , 0.150 mmol, 2.00 equiv.) was added at rt under an Ar atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The yield of *trans*-**12w** was determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (97% yield). The residue was purified by recycled prep. HPLC to afford pure *trans*-**12w**; HPLC (COSMOSIL SSL-II (20 mm \times 250 mm), *n*-hexane/AcOEt = 5/1, flow rate = 20 mL/min, $\lambda = 254$ nm). The

enantiomeric excess of *trans*-**12w** was determined to be 92% ee by HPLC analysis; HPLC (CHIRAL 5C (4.6 mm × 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 18.9 min (for *trans*-(3*R*,4*R*)-**12w**), 25.0 min (for *trans*-(3*S*,4*S*)-**12w**).

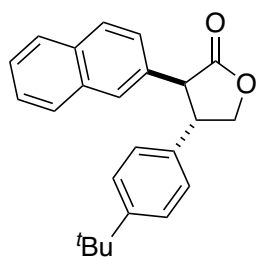
For physical data collection, *cis*-**12w** and *trans*-**12w** were synthesized alternatively by Rh₂(TPA)₄-catalyzed intramolecular C–H insertion of **11w** and successive epimerization (for *trans*-**12w**). Each diastereomer was separated by recycled prep. HPLC under the same conditions as mentioned above.

Cis-4-(4-*tert*-Butylphenyl)-3-(2-naphthyl)dihydrofuran-2(3*H*)-one (*cis*-**12w**)



White solid; M.p. 153–154 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.76–7.68 (m, 1H), 7.66–7.59 (m, 1H), 7.54 (d, J = 8.5 Hz, 1H), 7.45–7.37 (m, 2H), 7.33 (d, J = 1.8 Hz, 1H), 7.12–7.05 (m, 2H), 6.84–6.75 (m, 3H), 4.76 (d, J = 5.2 Hz, 2H), 4.39 (d, J = 8.4 Hz, 1H), 4.04 (dt, J = 8.4, 5.2 Hz, 1H), 1.20 (s, 9H); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 176.8, 150.7, 133.7, 133.1, 132.5, 130.8, 128.8, 127.9, 127.7, 127.61, 127.55, 127.3, 126.1, 126.0, 125.4, 71.6, 52.4, 47.6, 34.5, 31.3; IR (KBr) 2960, 1763, 1364, 1205, 1146, 1026, 963, 810, 702, 481 cm⁻¹; HRMS (ESI) m/z : [M+Na]⁺ Calcd for C₂₄H₂₄NaO₂ 367.1669; Found 367.1650.

Trans-4-(4-*tert*-Butylphenyl)-3-(2-naphthyl)dihydrofuran-2(3*H*)-one (*trans*-**12w**)



White solid; M.p. 135–136 °C; [α]_D²⁰ = +230.8 (c 0.7, CH₂Cl₂, 92% ee for (3*S*,4*S*)); ¹H NMR (500 MHz, CDCl₃) δ 7.87–7.74 (m, 3H), 7.67 (d, J = 1.8 Hz, 1H), 7.47 (dt, J = 6.3, 3.4 Hz, 2H), 7.38–7.29 (m, 3H), 7.20–7.12 (m, 2H), 4.76 (dd, J = 9.1, 7.9 Hz, 1H), 4.38 (dd, J = 10.0, 9.1 Hz, 1H), 4.12 (d, J = 11.4 Hz, 1H), 3.99 (ddd, J = 11.5, 10.1, 7.9 Hz, 1H), 1.29 (s, 9H); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 176.6, 151.1, 134.1, 133.5, 132.93, 132.91, 129.0, 128.0, 127.9, 127.8, 127.0, 126.4, 126.3, 126.2, 126.0, 72.1, 53.4, 49.9, 34.7, 31.4; IR (KBr) 2962, 1775, 1513, 1364, 1217, 1146, 1057, 1019, 815, 751, 476 cm⁻¹; HRMS (ESI) m/z : [M+Na]⁺ Calcd for C₂₄H₂₄NaO₂ 367.1669; Found 367.1680.

Intramolecular C–H Insertion of **11x**

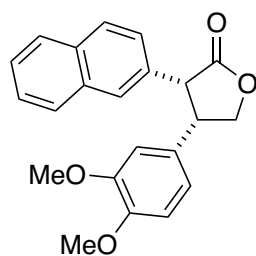
To a refluxing solution of cat. (*R*)-**10b** (3.43 mg, 1.50 μ mol, 2.00 mol%) in CH₂Cl₂ (4.5 mL), a solution of **11x** (28.2 mg, 75.0 μ mol, 1.00 equiv.) in CH₂Cl₂ (0.75 mL) was added dropwise over 1.5 h via a syringe pump under a N₂ atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12x**:*trans*-**12x** were determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard (98% yield, *cis*-**12x** only).

To a solution of the residue in CH₂Cl₂ (1.0 mL), DBU (22.4 μ L, 0.150 mmol, 2.00 equiv.) was added at rt under an Ar atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The yield of *trans*-**12x** was determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard (97% yield). The residue was purified by recycled prep. HPLC to afford pure *trans*-**12x**; HPLC (COSMOSIL 5SL-II (20 mm × 250 mm), *n*-hexane/AcOEt = 3/2, flow rate = 20 mL/min, λ = 254 nm). The

enantiomeric excess of *trans*-**12x** was determined to be 95% ee by HPLC analysis; HPLC (CHIRAL 5C (4.6 mm × 250 mm), *n*-hexane/IPA = 2/3, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 17.4 min (for *trans*-(3*S*,4*S*)-**12x**), 23.2 min (for *trans*-(3*R*,4*R*)-**12x**).

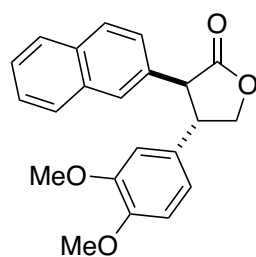
For physical data collection, *cis*-**12x** and *trans*-**12x** were synthesized alternatively by Rh₂(TPA)₄-catalyzed intramolecular C–H insertion of **11x** and successive epimerization (for *trans*-**12x**). Each diastereomer was separated by recycled prep. HPLC under the same conditions as mentioned above.

Cis-4-(3,4-Dimethoxyphenyl)-3-(2-naphthyl)dihydrofuran-2(3*H*)-one (*cis*-**12x**)



White solid; M.p. 136–137 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.75–7.64 (m, 2H), 7.57 (d, J = 8.5 Hz, 1H), 7.48 (d, J = 1.7 Hz, 1H), 7.45–7.39 (m, 2H), 6.80 (dd, J = 8.5, 1.8 Hz, 1H), 6.61 (d, J = 8.2 Hz, 1H), 6.52 (dd, J = 8.3, 2.1 Hz, 1H), 6.12 (d, J = 2.1 Hz, 1H), 4.77–4.64 (m, 2H), 4.37 (d, J = 8.4 Hz, 1H), 4.02 (ddd, J = 8.4, 6.5, 4.9 Hz, 1H), 3.75 (s, 3H), 3.33 (s, 3H); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 176.7, 148.7, 148.4, 133.1, 132.5, 131.0, 128.8, 128.5, 127.9, 127.8, 127.6, 127.2, 126.3, 126.2, 120.3, 111.5, 111.0, 71.6, 55.9, 55.6, 52.3, 47.6; IR (KBr) 1770, 1595, 1516, 1463, 1370, 1263, 1144, 1026, 755, 478 cm⁻¹; HRMS (ESI) m/z : [M+Na]⁺ Calcd for C₂₂H₂₀NaO₄ 371.1254; Found 371.1262.

Trans-4-(3,4-Dimethoxyphenyl)-3-(2-naphthyl)dihydrofuran-2(3*H*)-one (*trans*-**12x**)



Colorless oil; [α]_D²⁰ = +208.9 (c 0.9, CH₂Cl₂, 95% ee for (3*S*,4*S*)); ¹H NMR (500 MHz, CDCl₃) δ 7.86–7.72 (m, 3H) 7.64 (s, 1H), 7.50–7.42 (m, 2H), 7.29 (dt, J = 8.5, 1.6 Hz, 1H), 6.84–6.74 (m, 2H), 6.66 (s, 1H), 4.75 (td, J = 8.3, 7.6 Hz, 1H), 4.42–4.33 (m, 1H), 4.06 (d, J = 11.5 Hz, 1H), 3.93–3.82 (m, 4H), 3.78 (s, 3H); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 176.5, 149.5, 148.8, 133.5, 132.9, 129.6, 129.0, 128.0, 127.9, 127.8, 126.5, 126.4, 126.0, 119.4, 111.7, 110.5, 72.0, 56.0, 53.8, 50.5 (Two carbon signals were overlapped); IR (neat) 1770, 1595, 1517, 1462, 1262, 1144, 1022, 817, 756, 477 cm⁻¹; HRMS (ESI) m/z : [M+Na]⁺ Calcd for C₂₂H₂₀NaO₄ 371.1254; Found 371.1255.

Intramolecular C–H Insertion of **11y**

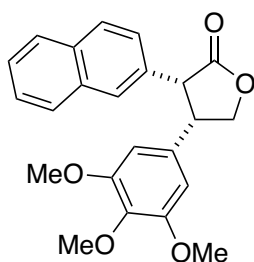
To a refluxing solution of cat. (*R*)-**10b** (3.43 mg, 1.50 μ mol, 2.00 mol%) in CH₂Cl₂ (4.5 mL), a solution of **11y** (30.5 mg, 75.0 μ mol, 1.00 equiv.) in CH₂Cl₂ (0.75 mL) was added dropwise over 1.5 h via a syringe pump under a N₂ atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12y**:*trans*-**12y** were determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard (100% yield, *cis*-**12y** only).

To a solution of the residue in CH₂Cl₂ (1.0 mL), DBU (22.4 μ L, 0.150 mmol, 2.00 equiv.) was added at rt under an Ar atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The yield of *trans*-**12y** was determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard (99% yield). The residue was purified by recycled prep. HPLC to afford pure *trans*-**12y**; HPLC (COSMOSIL 5SL-II (20 mm × 250 mm), *n*-hexane/AcOEt = 1/1, flow rate = 20 mL/min, λ = 254 nm). The

enantiomeric excess of *trans*-**12y** was determined to be 94% ee by HPLC analysis; HPLC (CHIRAL 5C (4.6 mm × 250 mm), *n*-hexane/IPA = 2/3, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 17.0 min (for *trans*-(3*S*,4*S*)-**12y**), 35.3 min (for *trans*-(3*R*,4*R*)-**12y**).

For physical data collection, *cis*-**12y** and *trans*-**12y** were synthesized alternatively by Rh₂(TPA)₄-catalyzed intramolecular C–H insertion of **11y** and successive epimerization (for *trans*-**12y**). Each diastereomer was separated by recycled prep. HPLC under the same conditions as mentioned above.

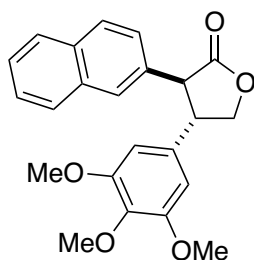
Cis-3-(2-Naphthyl)-4-(3,4,5-trimethoxyphenyl)dihydrofuran-2(3*H*)-one (*cis*-**12y**)



Colorless oil; ¹H NMR (500 MHz, CDCl₃) δ 7.75–7.64 (m, 2H), 7.59 (d, J = 8.5 Hz, 1H), 7.45–7.38 (m, 3H), 6.84 (dd, J = 8.5, 1.8 Hz, 1H), 5.97 (s, 2H), 4.77–4.66 (m, 2H), 4.38 (d, J = 8.4 Hz, 1H), 3.98 (ddd, J = 8.4, 6.5, 4.9 Hz, 1H), 3.68 (s, 3H), 3.42 (s, 6H); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 176.5, 153.1, 137.6, 133.1, 132.5, 131.9, 130.8, 128.5, 127.9, 127.8, 127.6, 127.1, 126.4, 126.3, 105.5, 71.4, 60.9, 56.0, 52.3, 48.2; IR (neat) 1770, 1591, 1509, 1461, 1426, 1350, 1325, 1241, 1128, 1012, 752 cm⁻¹;

HRMS (ESI) m/z : [M+Na]⁺ Calcd for C₂₃H₂₂NaO₅ 401.1359; Found 401.1363.

Trans-3-(2-Naphthyl)-4-(3,4,5-trimethoxyphenyl)dihydrofuran-2(3*H*)-one (*trans*-**12y**)

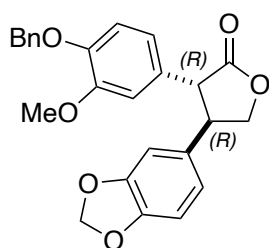


Colorless oil; [α]_D²⁰ = +218.1 (c 0.3, CH₂Cl₂, 94% ee for (3*S*,4*S*)); ¹H NMR (500 MHz, CDCl₃) δ 7.89–7.74 (m, 3H), 7.66 (s, 1H), 7.52–7.44 (m, 2H), 7.30 (d, J = 8.5 Hz, 1H), 6.40 (s, 2H), 4.77 (t, J = 8.6 Hz, 1H), 4.42–4.36 (m, 1H), 4.08 (d, J = 11.2 Hz, 1H), 3.94–3.72 (m, 10H); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 176.4, 153.8, 137.8, 133.5, 133.1, 133.0, 132.9, 129.1, 128.0, 127.9, 127.8, 126.6, 126.4, 125.9, 104.3, 72.0, 61.0, 56.3, 53.7, 51.0; IR (neat) 1771, 1592, 1510, 1461, 1426, 1348, 1243, 1127, 1016, 821,

752 cm⁻¹; HRMS (ESI) m/z : [M+Na]⁺ Calcd for C₂₃H₂₂NaO₅ 401.1359; Found 401.1363.

Total Syntheses of Cinnamomumolide (**13**) and Cinnassin A₇ (*ent*-**13**) (Scheme 15)

Trans-4-(Benzo[*d*][1,3]dioxol-5-yl)-3-(4-(benzyloxy)-3-methoxyphenyl)dihydrofuran-2(3*H*)-one (*trans*-**12a**)



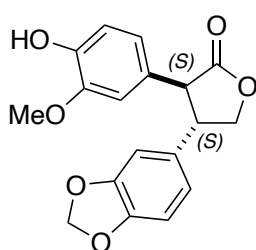
To a refluxing solution of cat. (*S*)-**10b** (3.43 mg, 1.50 μ mol, 2.00 mol%) in CH₂Cl₂ (4.5 mL), a solution of **11a** (33.5 mg, 75.0 μ mol, 1.00 equiv.) in CH₂Cl₂ (0.75 mL) was added dropwise over 1.5 h via a syringe pump under an Ar atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12a**:*trans*-**12a** were determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard (84% yield, *cis*-**12a** only).

To a solution of the residue in CH₂Cl₂ (1.0 mL), DBU (22.4 μ L, 0.150 mmol, 2.00 equiv.) was added at rt under an Ar atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The residue was purified by prep. TLC (SiO₂, CHCl₃:MeOH = 49:1) to afford *trans*-**12a** (25.3 mg, 81% yield in 2 steps from **11a**, 96% ee for (3*R*,4*R*)). The enantiomeric excess of *trans*-**12a** was determined by HPLC analysis; HPLC (CHIRALPAK IC (4.6 mm \times 250 mm), *n*-hexane/IPA = 3/2, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 77.9 min (for *trans*-(3*S*,4*S*)-**12a**), 103.5 min (for *trans*-(3*R*,4*R*)-**12a**). The absolute configuration of the major enantiomer was determined to be (3*R*,4*R*) by the asymmetric synthesis of cinnassin A₇ (*trans*-(3*R*,4*R*)-**13**) as shown in **Scheme 15**.

$[\alpha]_D^{20}$ = -204.0 (*c* 0.5, CH₂Cl₂, 96% ee for (3*R*,4*R*)).

Trans-4-(Benzo[*d*][1,3]dioxol-5-yl)-3-(4-hydroxy-3-methoxyphenyl)dihydrofuran-2(3*H*)-one (**13**)

For cinnamomumolide (*trans*-(3*S*,4*S*)-**13**)²⁴

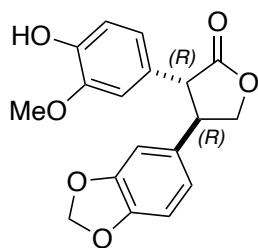


To Pd/C (10 wt%) in the flask, a solution of *trans*-(3*S*,4*S*)-**12a** (29.9 mg, 71.5 μ mol, 95% ee) in CHCl₃/EtOH (1:1, 2.0 mL) was added at rt, and stirred at rt for 25 min under a H₂ atmosphere. Then, the reaction mixture was filtered, and concentrated *in vacuo* to give a residue. The residue was purified by prep. TLC (SiO₂, CHCl₃:MeOH = 49:1) to afford **13** (23.4 mg, quant., 95% ee). The enantiomeric excess of synthetic **13** was determined by HPLC analysis; HPLC (CHIRALPAK IC (4.6 mm \times 250 mm), *n*-hexane/IPA = 3/2, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 34.9 min (for *trans*-(3*R*,4*R*)-**13**), 46.8 min (for *trans*-(3*S*,4*S*)-**13**).

$[\alpha]_D^{20}$ = +201.7 (*c* 0.4, CH₂Cl₂, 95% ee for (3*S*,4*S*)); CD (MeOH, 95% ee for (3*S*,4*S*)) λ_{ext} ($\Delta\epsilon$): 288.5 (6.15), 237.5 (12.5), 211 (25.6) nm; UV (MeOH) λ_{max} (log ϵ): 285 (3.93), 233 (4.10), 208 (4.51) nm.

The absolute configuration of synthetic **13** was determined to be (3*S*,4*S*) by comparing with the sign of the specific rotation of cinnamomumolide (**13**) { $[\alpha]_D^{25}$ = +161.5 (*c* 0.4, CH₂Cl₂, 97% ee for (3*S*,4*S*))} synthesized by Hou, X.-L. *et al.*^{24b}

For cinnassins A₇ (*trans*-(3*R*,4*R*)-**13**)²⁵



To Pd/C (10 wt%) in the flask, a solution of *trans*-(3*R*,4*R*)-**12a** (29.2 mg, 69.8 μ mol, 96% ee) in CHCl₃/EtOH (1:1, 2.0 mL) was added at rt, and stirred at rt for 1 h under a H₂ atmosphere. Then, the reaction mixture was filtered, and concentrated *in vacuo* to give a residue. The residue was purified by prep. TLC (SiO₂, CHCl₃:MeOH = 49:1) to afford *ent*-**13** (23.0 mg, quant., 96% ee). The enantiomeric excess of synthetic *ent*-**13** was determined by HPLC analysis; HPLC (CHIRALPAK IC (4.6 mm \times 250 mm), *n*-hexane/IPA = 3/2, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 32.2 min (for *trans*-(3*R*,4*R*)-**13**), 41.7 min (for *trans*-(3*S*,4*S*)-**13**).

$[\alpha]_D^{20}$ = -175.5 (*c* 0.4, CH₂Cl₂, 96% ee for (3*R*,4*R*)); $[\alpha]_D^{16}$ = -213.4 (*c* 0.3, MeOH, 96% ee for (3*R*,4*R*)); CD (MeOH, 96% ee for (3*R*,4*R*)) λ_{ext} ($\Delta\epsilon$): 289 (-6.2), 237.5 (-12.4), 210.5 (-31.1) nm; UV (MeOH) λ_{max} (log ϵ): 285 (3.93), 233 (4.08), 208 (4.56) nm.

Cinnassins A₇ (*trans*-(3*R*,4*R*)-**13**)²⁵ from natural source: $[\alpha]_D^{25}$ = -193 (*c* 0.4, MeOH); CD (MeOH) λ_{ext} ($\Delta\epsilon$): 285 (-0.34), 240 (-0.60), 207 (-2.45) nm; UV (MeOH) λ_{max} (log ϵ): 285 (4.09), 235 (4.16), 200 (4.02) nm.

White solid; M.p. 138–140 °C; ¹H NMR (400 MHz, CDCl₃) δ 6.84 (d, *J* = 8.1 Hz, 1H), 6.75 (d, *J* = 8.0 Hz, 1H), 6.68 (dd, *J* = 10.8, 1.9 Hz, 2H), 6.64 (dd, *J* = 8.0, 2.0 Hz, 2H), 5.95 (s, 2H), 5.60 (s, 1H), 4.65 (dd, *J* = 9.1, 7.3 Hz, 1H), 4.24 (t, *J* = 9.5 Hz, 1H), 3.84 (s, 3H), 3.81–3.68 (m, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 176.6, 148.4, 147.4, 146.9, 145.4, 130.8, 126.9, 121.5, 120.9, 114.8, 110.8, 108.8, 107.4, 101.4, 71.8, 56.1, 53.1, 50.5; ¹H NMR (500 MHz, CD₃OD) δ 6.88 (s, 1H), 6.77–6.69 (m, 4H), 6.63 (dd, *J* = 8.2, 2.0 Hz, 1H), 5.92 (q, *J* = 1.3 Hz, 2H), 4.64 (t, *J* = 8.3 Hz, 1H), 4.29 (dd, *J* = 10.8, 8.8 Hz, 1H), 4.00 (d, *J* = 12.3 Hz, 1H), 3.88–3.77 (m, 4H); ¹³C{¹H} NMR (126 MHz, CD₃OD) δ 179.5, 149.6, 149.1, 148.6, 147.2, 132.4, 128.3, 122.5, 122.4, 116.3, 113.3, 109.4, 108.6, 102.5, 73.2, 56.4, 54.2, 51.8; IR (KBr) 3447, 1768, 1516, 1447, 1365, 1251, 1155, 1126, 1035, 931, 731 cm⁻¹; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₁₈H₁₆NaO₆ 351.0839; Found 351.0843.

Table S3. Comparison of ¹H NMR of Synthetic Cinnamomumolide (13) with Reported Data (δ (ppm)).

Synthetic 13 (400 MHz, CDCl ₃)	Isolated 13 (400 MHz, CDCl ₃) ^{24a}	Synthetic 13 (400 MHz, CDCl ₃) ^{24b}
3.68–3.81 (m, 2H)	3.70–3.75 (dt, <i>J</i> = 11.4, 7.8 Hz, 1H)	3.71–3.80 (m, 2H)
	3.78 (d, <i>J</i> = 11.4 Hz, 1H)	
3.84 (s, 3H)	3.85 (s, 3H)	3.85 (s, 3H)
4.24 (t, <i>J</i> = 9.5 Hz, 1H)	4.43 (t, <i>J</i> = 9.0, 7.8 Hz, 1H)*	4.25 (t, <i>J</i> = 9.2 Hz, 1H)
4.65 (dd, <i>J</i> = 9.1, 7.3 Hz, 1H)	4.65 (dd, <i>J</i> = 9.0, 7.8 Hz, 1H)	4.66 (t, <i>J</i> = 9.0 Hz, 1H)
5.60 (s, 1H)		5.60 (s, 1H)
5.95 (s, 2H)	5.96 (s, 2H)	5.96 (s, 2H)
6.64 (dd, <i>J</i> = 8.0, 2.0 Hz, 2H)	6.64 (dd, <i>J</i> = 8.4, 1.8 Hz, 1H)	6.63–6.70 (m, 4H)
	6.64 (dd, <i>J</i> = 7.8, 1.8 Hz, 1H)	
6.68 (dd, <i>J</i> = 10.8, 1.9 Hz, 2H)	6.67 (d, <i>J</i> = 1.8 Hz, 1H)	
	6.70 (d, <i>J</i> = 1.8 Hz, 1H)	
6.75 (d, <i>J</i> = 8.0 Hz, 1H)	6.75 (d, <i>J</i> = 7.8 Hz, 1H)	6.76 (d, <i>J</i> = 8.0 Hz, 1H)
6.84 (d, <i>J</i> = 8.1 Hz, 1H)	6.84 (d, <i>J</i> = 8.4 Hz, 1H)	6.84 (d, <i>J</i> = 8.0 Hz, 1H)

*This signal might be misassigned.

Table S4. Comparison of ¹³C NMR of Synthetic Cinnamomumolide (13) with Reported Data (δ (ppm)).

Synthetic 13 (101 MHz, CDCl ₃)	Isolated 13 (101 MHz, CDCl ₃) ^{24a}	Synthetic 13 (101 MHz, CDCl ₃) ^{24b}
50.5	51.3	50.3
53.1	53.0	53.0
56.1	55.9	55.9
71.8	71.7	71.6
101.4	101.3	101.3
107.4	107.2	107.2
108.8	108.7	108.7
110.8	110.7	110.6
114.8	114.6	114.6
120.9	120.7	120.7
121.5	121.3	121.3
126.9	126.8	126.7
130.8	130.7	130.6
145.4	145.3	145.3
146.9	146.8	146.7
147.4	147.3	147.2
148.4	148.3	148.2
176.6	176.5	176.4

Table S5. Comparison of ^1H NMR of Synthetic Cinnacassin A₇ (*ent*-13) with Reported Data (δ (ppm)).

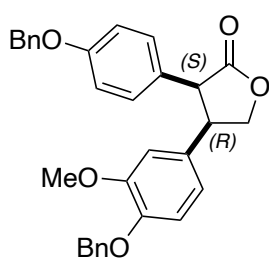
Synthetic <i>ent</i> -13 (500 MHz, CD ₃ OD)	Isolated <i>ent</i> -13 (600 MHz, CD ₃ OD) ²⁵
3.77–3.88 (m, 4H)	3.83 (m, 4H)
4.00 (d, $J = 12.3$ Hz, 1H)	3.99 (d, $J = 12.0$ Hz, 1H)
4.29 (dd, $J = 10.8, 8.8$ Hz, 1H)	4.28 (dd, $J = 10.8, 9.0$ Hz, 1H)
4.64 (t, $J = 8.3$ Hz, 1H)	4.63 (dd, $J = 9.0, 7.8$ Hz, 1H)
5.92 (q, $J = 1.3$ Hz, 2H)	5.91 (s, 2H)
6.63 (dd, $J = 8.2, 2.0$ Hz, 1H)	6.63 (dd, $J = 7.8, 1.8$ Hz, 1H)
6.69–6.77 (m, 4H)	6.72 (d, $J = 7.8$ Hz, 1H)
	6.73 (overlapped, 1H)
	6.73 (overlapped, 1H)
	6.75 (d, $J = 1.8$ Hz, 1H)
6.88 (s, 1H)	6.87 (s, 1H)

Table S6. Comparison of ^{13}C NMR of Synthetic Cinnacassin A₇ (*ent*-13) with Reported Data (δ (ppm)).

Synthetic <i>ent</i> -13 (126 MHz, CD ₃ OD)	Isolated <i>ent</i> -13 (151 MHz, CD ₃ OD) ²⁵
51.8	51.7
54.2	54.1
56.4	56.4
73.2	73.2
102.5	102.5
108.6	108.6
109.4	109.3
113.3	113.3
116.3	116.3
122.4	122.3
122.5	122.5
128.3	128.3
132.4	132.3
147.2	147.2
148.6	148.5
149.1	149.1
149.6	149.5
179.5	179.5

Total Synthesis of Cinnamomulactone (14) (Scheme 16)

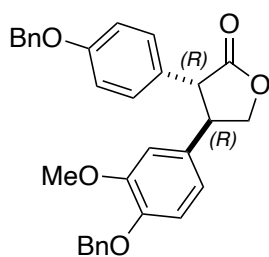
Cis-4-(4-(Benzyloxy)-3-methoxyphenyl)-3-(4-(benzyloxy)phenyl)dihydrofuran-2(3*H*)-one (*cis*-**12z**)



To a refluxing solution of cat. (*S*)-**10b** (3.43 mg, 1.50 μ mol, 2.00 mol%) in CH_2Cl_2 (4.5 mL), a solution of **11z** (38.1 mg, 75.0 μ mol, 1.00 equiv.) in CH_2Cl_2 (0.75 mL) was added dropwise over 1.5 h via a syringe pump under an Ar atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12z**:*trans*-**12z** were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (92% yield, *cis*-**12z** only). The residue was purified by prep. TLC (SiO_2 , CHCl_3 :MeOH = 49:1) to afford *cis*-**12z** (32.9 mg, 91% yield).

White solid; M.p. 150–151 $^\circ\text{C}$; ^1H NMR (600 MHz, CDCl_3) δ 7.40–7.33 (m, 8H), 7.33–7.27 (m, 2H), 6.77–6.71 (m, 4H), 6.69 (d, J = 8.3 Hz, 1H), 6.45 (dd, J = 8.3, 2.1 Hz, 1H), 6.20 (d, J = 2.1 Hz, 1H), 5.08 (s, 2H), 4.98 (s, 2H), 4.67 (dd, J = 9.4, 6.3 Hz, 1H), 4.63 (dd, J = 9.4, 4.5 Hz, 1H), 4.15 (d, J = 8.3 Hz, 1H), 3.88 (ddd, J = 8.3, 6.3, 4.5 Hz, 1H), 3.59 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 176.9, 158.2, 149.5, 147.5, 137.1, 137.0, 130.7, 129.8, 128.72, 128.66, 128.1, 128.0, 127.5, 127.4, 125.6, 120.2, 114.8, 114.0, 112.1, 71.5, 71.1, 70.1, 56.0, 51.6, 47.6; IR (KBr) 1769, 1609, 1514, 1457, 1378, 1248, 1142, 1024, 913, 736, 698 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{31}\text{H}_{28}\text{NaO}_5$ 503.1829; Found 503.1829.

Trans-4-(4-(Benzyloxy)-3-methoxyphenyl)-3-(4-(benzyloxy)phenyl)dihydrofuran-2(3*H*)-one (*trans*-**12z**)



To a refluxing solution of cat. (*S*)-**10b** (3.43 mg, 1.50 μ mol, 2.00 mol%) in CH_2Cl_2 (4.5 mL), a solution of **11z** (38.1 mg, 75.0 μ mol, 1.00 equiv.) in CH_2Cl_2 (0.75 mL) was added dropwise over 1.5 h via a syringe pump under an Ar atmosphere. After being refluxed for 1 h, the reaction mixture was concentrated *in vacuo* to give a residue. The yield and the ratio for *cis*-**12z**:*trans*-**12z** were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (92% yield, *cis*-**12z** only).

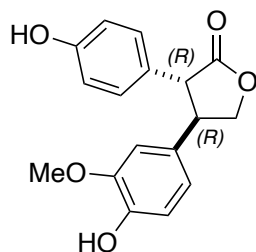
To a solution of the residue in CH_2Cl_2 (1.0 mL), DBU (22.4 μ L, 0.150 mmol, 2.00 equiv.) was added at rt under an Ar atmosphere. After being refluxed for 0.5 h, the resulting mixture was concentrated *in vacuo* to give a residue. The residue was purified by prep. TLC (SiO_2 , CHCl_3 :MeOH = 49:1) to afford *trans*-**12z** (31.7 mg, 88% yield in 2 steps from **11z**, 96% ee for (3*R*,4*R*)). The enantiomeric excess of *trans*-**12z** was determined by HPLC analysis; HPLC (CHIRALPAK IC (4.6 mm \times 250 mm), *n*-hexane/IPA = 3/2, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 51.0 min (for *trans*-(3*S*,4*S*)-**12z**), 65.7 min (for *trans*-(3*R*,4*R*)-**12z**). The absolute configuration of the major enantiomer was determined to be (3*R*,4*R*) by the asymmetric synthesis of cinnamomulactone (*trans*-(3*R*,4*R*)-**14**) as shown in **Scheme 16** and the comparison of CD spectra of synthetic γ -lactones as shown in **Figure 19**.

White solid; M.p. 124–125 $^\circ\text{C}$; $[\alpha]_D^{20}$ = -177.8 (c 0.7, CH_2Cl_2 , 96% ee for (3*R*,4*R*)); ^1H NMR (600 MHz, CDCl_3) δ 7.43–7.39 (m, 4H), 7.39–7.35 (m, 4H), 7.34–7.29 (m, 2H), 7.11–7.08 (m, 2H), 6.95–6.91 (m, 2H), 6.83 (d, J = 8.3 Hz, 1H), 6.69 (dd, J = 8.3, 2.1 Hz, 1H), 6.65 (d, J = 2.1 Hz, 1H), 5.13 (s, 2H), 5.03 (s, 2H), 4.67 (dd, J = 9.1, 7.8 Hz, 1H), 4.28 (dd, J = 10.2, 9.1 Hz, 1H), 3.83–3.80 (m, 4H), 3.73 (ddd, J = 11.7, 10.3, 7.8 Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 176.7, 158.5, 150.1, 148.0, 137.1, 137.0, 130.3, 129.7, 128.8, 128.7, 128.2, 128.1, 127.7, 127.6, 127.4, 119.2, 115.4, 114.4, 111.1, 71.8, 71.2, 70.2, 56.2, 52.7, 50.3; IR (KBr) 1770, 1610, 1515,

1454, 1382, 1242, 1143, 1018, 737, 697 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{31}\text{H}_{28}\text{NaO}_5$ 503.1829; Found 503.1824.

Trans-4-(4-Hydroxy-3-methoxyphenyl)-3-(4-hydroxyphenyl)dihydrofuran-2(3*H*)-one (**14**)

Cinnamomulactone (*trans*-(3*R*,4*R*)-**14**)²⁶



To Pd/C (10 wt%) in the flask, a solution of *trans*-(3*R*,4*R*)-**12z** (31.2 mg, 65.0 μmol , 96% ee) in $\text{CHCl}_3/\text{EtOH}$ (1:1, 2.0 mL) was added at rt, and stirred at rt for 4.5 h under a H_2 atmosphere. Then, the reaction mixture was filtered, and concentrated *in vacuo* to give a residue. The residue was purified by prep. TLC (SiO_2 , $\text{CHCl}_3:\text{MeOH}$ = 49:1) to afford **14** (20.9 mg, quant., 96% ee for (3*R*,4*R*)). The enantiomeric excess of synthetic **14** was determined by HPLC analysis; HPLC (CHIRALPAK ID (4.6 mm \times 250 mm),

n-hexane/IPA = 17/3, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 45.3 min (for *trans*-(3*S*,4*S*)-**14**), 51.2 min (for *trans*-(3*R*,4*R*)-**14**).

$[\alpha]_D^{20}$ = -257.8 (c 0.2, MeOH, 96% ee for (3*R*,4*R*)); CD (MeOH, 96% ee for (3*R*,4*R*)) λ_{ext} ($\Delta\epsilon$): 284 (-2.86), 232 (-20.8), 208 (-20.9) nm; UV (MeOH) λ_{max} ($\log\epsilon$): 281 (3.70), 228 (4.19), 209 (4.42) nm.

The absolute configuration of synthetic **14** was determined to be (3*R*,4*R*) by comparing the sign of the specific rotation of isolated cinnamomulactone (**14**) $\{[\alpha]_D^{25} = -280.5$ (c 0.1, MeOH) $\}^{26}$ and CD spectra of synthetic cinnamomumolide (**13**) and cinncassin A₇ (*ent*-**13**).

White solid; M.p. 80–81 $^\circ\text{C}$; ^1H NMR (400 MHz, CD_3OD) δ 7.05–6.96 (m, 2H), 6.84 (s, 1H), 6.76–6.68 (m, 4H), 4.64 (dd, J = 8.7, 7.9 Hz, 1H), 4.31 (dd, J = 10.8, 8.7 Hz, 1H), 4.01 (d, J = 12.3 Hz, 1H), 3.83–3.68 (m, 4H); $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CD_3OD) δ 179.9, 158.1, 149.3, 147.2, 130.9, 129.9, 128.1, 121.2, 116.49, 116.47, 112.2, 73.4, 56.4, 53.9, 52.0; IR (KBr) 2917, 1754, 1613, 1518, 1449, 1373, 1267, 1218, 1013, 762 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{17}\text{H}_{16}\text{NaO}_5$ 323.0890; Found 323.0892.

Table S7. Comparison of ^1H NMR of Synthetic Cinnamomulactone (14) with Reported Data (δ (ppm)).

Synthetic 14 (400 MHz, CD_3OD)	Isolated 14 (250 MHz, CD_3OD) ²⁶
3.68–3.83 (m, 4H)	3.76 (ddd, $J = 12.3, 10.8, 8.0$ Hz, 1H)
	3.79 (s, 3H)
4.01 (d, $J = 12.3$ Hz, 1H)	4.01 (d, $J = 12.3$ Hz, 1H)
4.31 (dd, $J = 10.8, 8.7$ Hz, 1H)	4.31 (dd, $J = 10.8, 8.6$ Hz, 1H)
4.64 (dd, $J = 8.7, 7.9$ Hz, 1H)	4.63 (dd, $J = 8.6, 8.0$ Hz, 1H)
6.68–6.76 (m, 4H)	6.72 (d, $J = 8.6$ Hz, 2H)
	6.72 (m, 2H)
6.84 (s, 1H)	6.84 (s, 1H)
6.96–7.05 (m, 2H)	7.00 (d, $J = 8.6$ Hz, 2H)

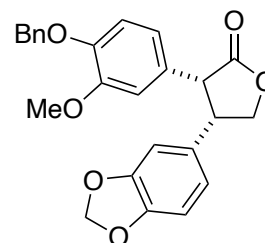
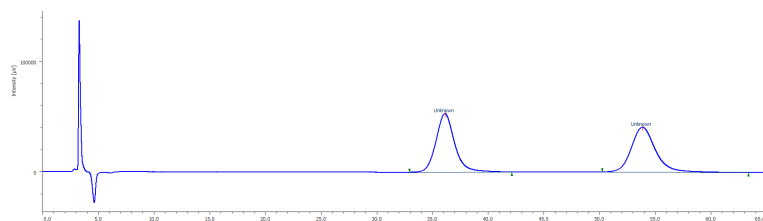
Table S8. Comparison of ^{13}C NMR of Synthetic Cinnamomulactone (14) with Reported Data (δ (ppm)).

Synthetic 14 (151 MHz, CD_3OD)	Isolated 14 (63 MHz, CD_3OD) ²⁶
52.0	52.0
53.9	53.8
56.4	56.3
73.4	73.4
112.2	112.1
116.47	116.4
116.49	116.4
121.2	121.1
128.1	128.0
129.9	129.9
130.9	130.9
147.2	147.1
149.3	149.2
158.1	158.1
179.9	179.9

HPLC Analysis for Determination of the Enantiomeric Excess of C–H Adducts

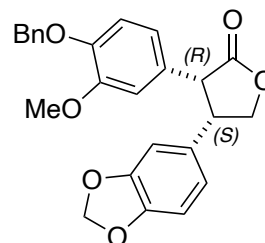
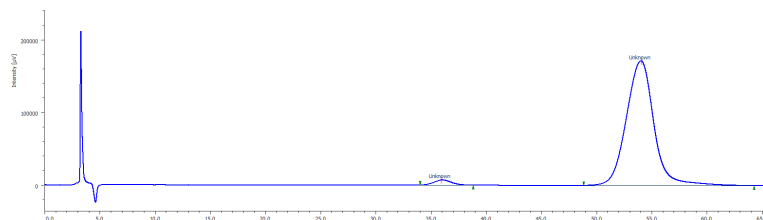
For γ -lactone *cis*-**12a**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHIRALPAK IC (4.6 mm \times 250 mm), *n*-hexane/IPA = 3/2, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic *cis*-**12a**



	Retention time (min)	Peak area (%)
1	36.1	50.17
2	53.8	49.83

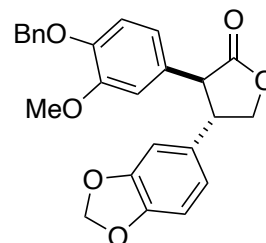
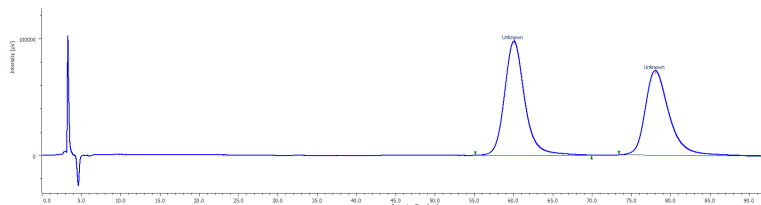
(2) Chromatogram of *cis*-**12a** (95% ee for (3*R*,4*S*))



	Retention time (min)	Peak area (%)
1	35.9	2.56
2	54.0	97.44

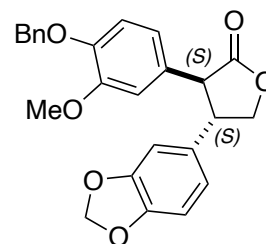
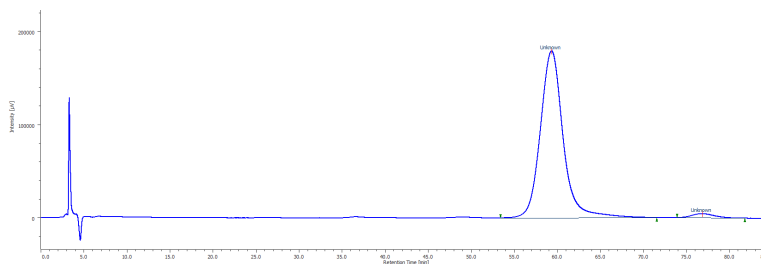
For γ -lactone *trans*-**12a**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHIRALPAK IC (4.6 mm \times 250 mm), *n*-hexane/IPA = 3/2, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic *trans*-**12a**



	Retention time (min)	Peak area (%)
1	60.0	53.14
2	78.0	46.86

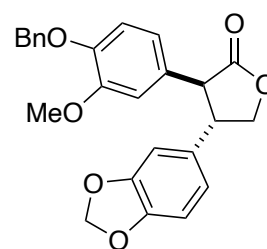
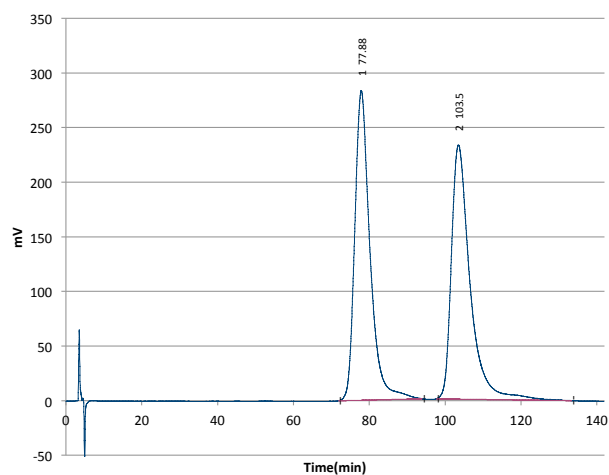
(2) Chromatogram of *trans*-**12a** (95% ee for (3*S*,4*S*))



	Retention time (min)	Peak area (%)
1	59.3	97.59
2	76.8	2.41

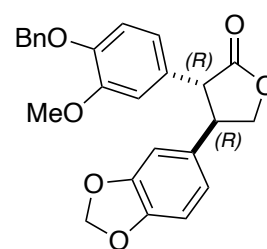
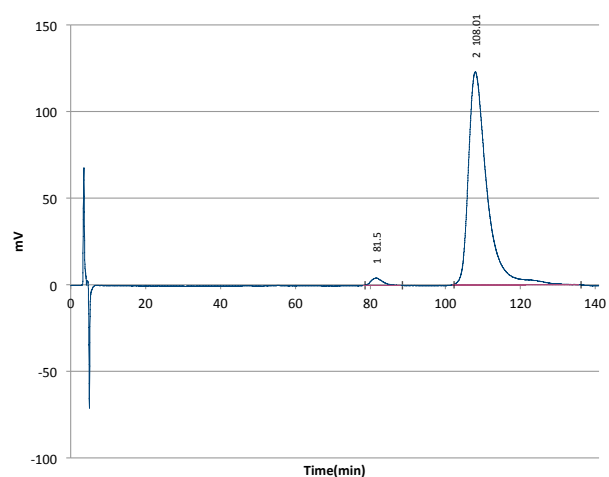
For γ -lactone *trans*-**12a**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHIRALPAK IC (4.6 mm \times 250 mm), *n*-hexane/IPA = 3/2, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic *trans*-**12a**



	Retention time (min)	Peak area (%)
1	77.9	49.95
2	103.5	50.05

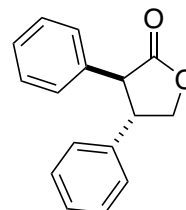
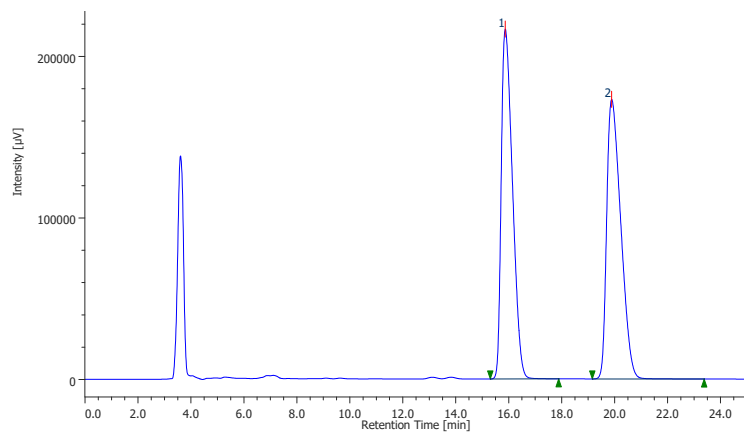
(2) Chromatogram of *trans*-**12a** (96% ee for (3*R*,4*R*))



	Retention time (min)	Peak area (%)
1	81.5	2.20
2	108.0	97.80

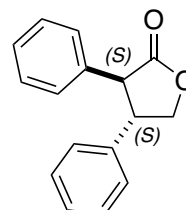
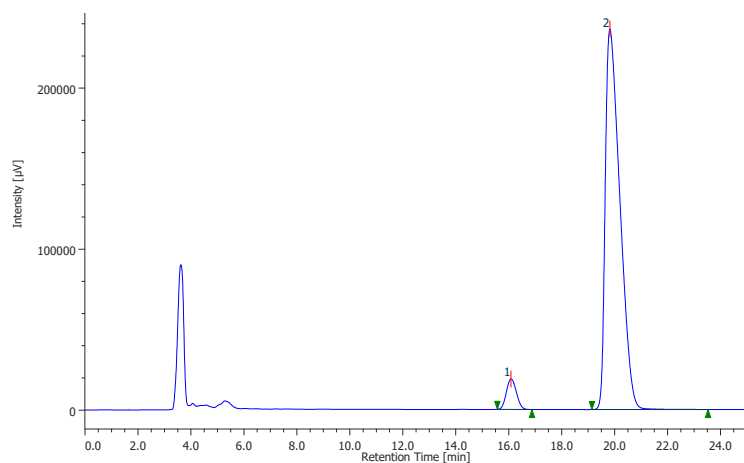
For γ -lactone *trans*-**12b**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHiRAL 5C (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic *trans*-**12b**



	Retention time (min)	Peak area (%)
1	15.9	49.96
2	19.9	50.04

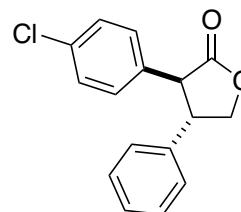
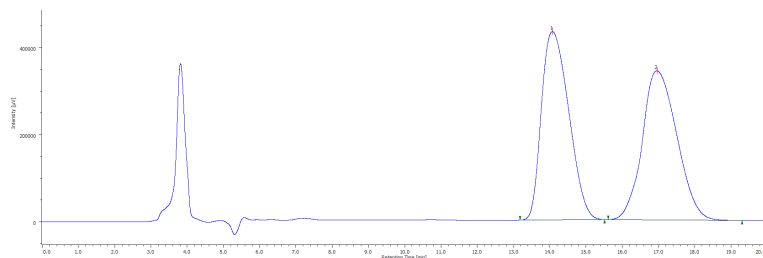
(2) Chromatogram of *trans*-**12b** (90% ee for (3*S*,4*S*))



	Retention time (min)	Peak area (%)
1	16.1	5.21
2	19.8	94.79

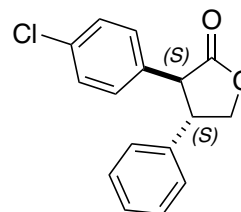
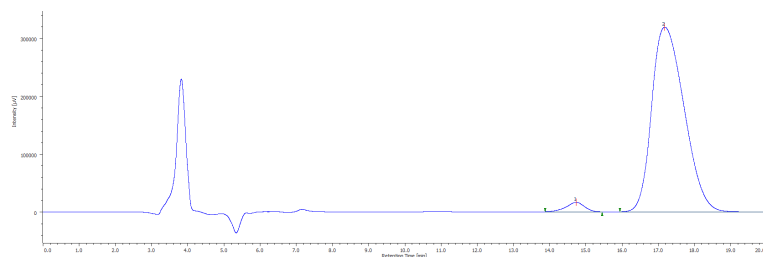
For γ -lactone *trans*-**12c**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHIRALPAK IC (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic *trans*-**12c**



	Retention time (min)	Peak area (%)
1	14.1	49.95
2	17.0	50.05

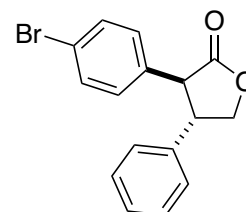
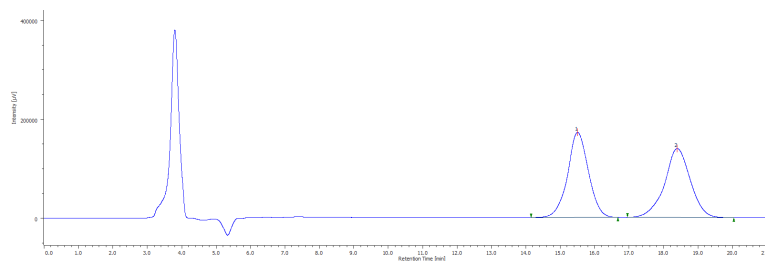
(2) Chromatogram of *trans*-**12c** (94% ee for (3*S*,4*S*))



	Retention time (min)	Peak area (%)
1	14.7	2.82
2	17.2	97.18

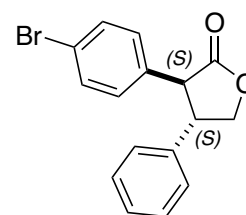
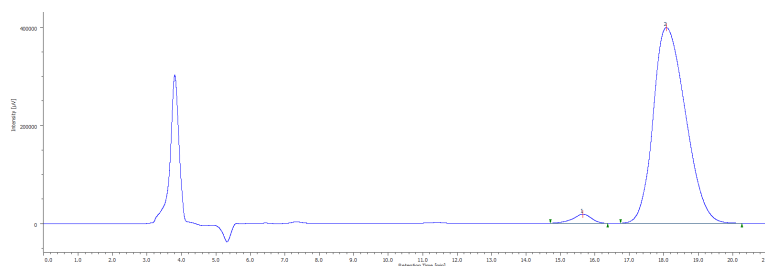
For γ -lactone *trans*-**12d**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHIRALPAK IC (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic *trans*-**12d**



	Retention time (min)	Peak area (%)
1	15.5	49.94
2	18.4	50.06

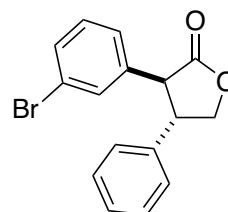
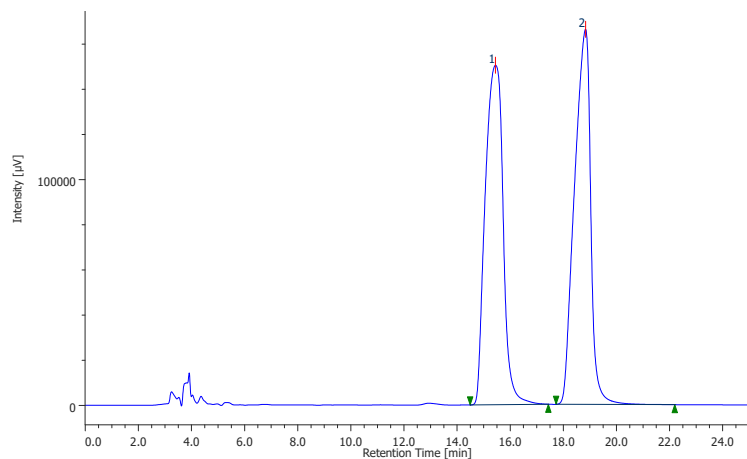
(2) Chromatogram of *trans*-**12d** (95% ee for (3*S*,4*S*))



	Retention time (min)	Peak area (%)
1	15.7	2.60
2	18.1	97.40

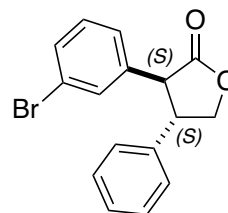
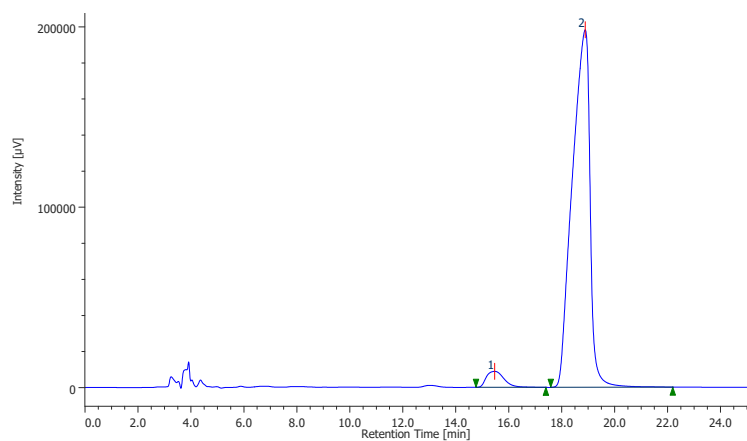
For γ -lactone *trans*-**12e**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHiRAL 5A (4.6 mm \times 250 mm), *n*-hexane/IPA = 9/1, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic *trans*-**12e**



	Retention time (min)	Peak area (%)
1	15.4	50.12
2	18.8	49.88

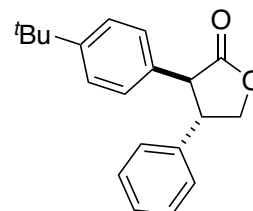
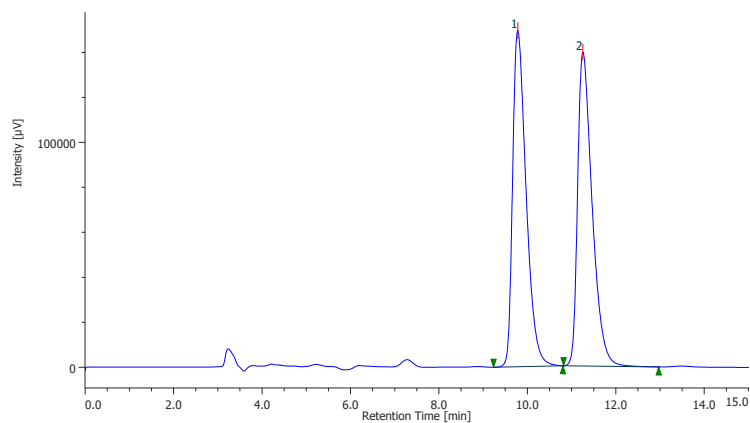
(2) Chromatogram of *trans*-**12e** (91% ee for (3*S*,4*S*))



	Retention time (min)	Peak area (%)
1	15.5	4.30
2	18.9	95.70

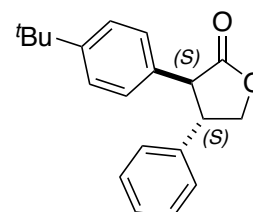
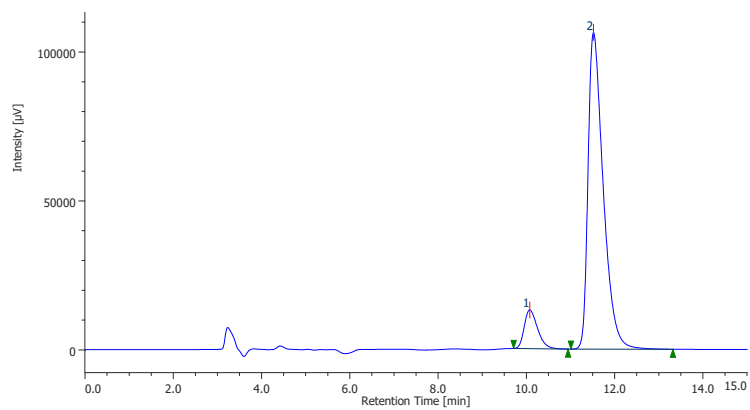
For γ -lactone *trans*-**12f**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHiRAL 5A (4.6 mm \times 250 mm), *n*-hexane/IPA = 9/1, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic *trans*-**12f**



	Retention time (min)	Peak area (%)
1	9.8	49.94
2	11.3	50.06

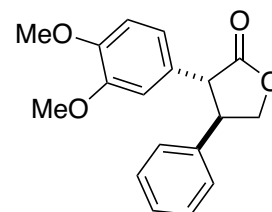
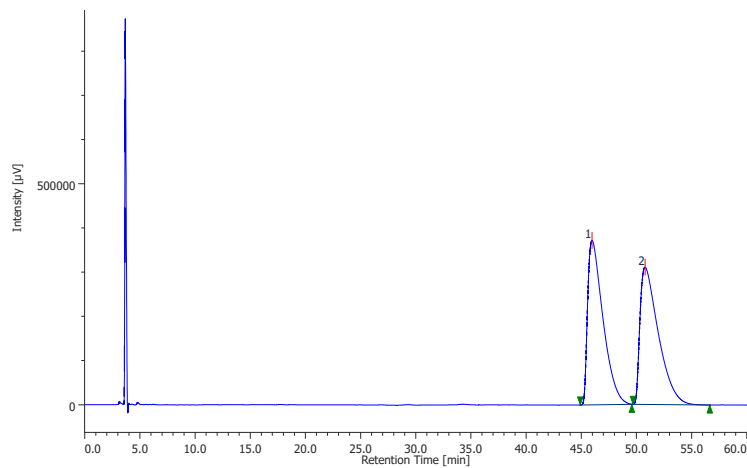
(2) Chromatogram of *trans*-**12f** (81% ee for (3*S*,4*S*))



	Retention time (min)	Peak area (%)
1	10.1	9.70
2	11.5	90.30

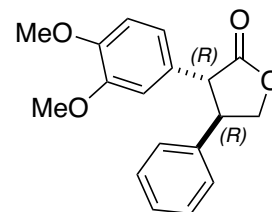
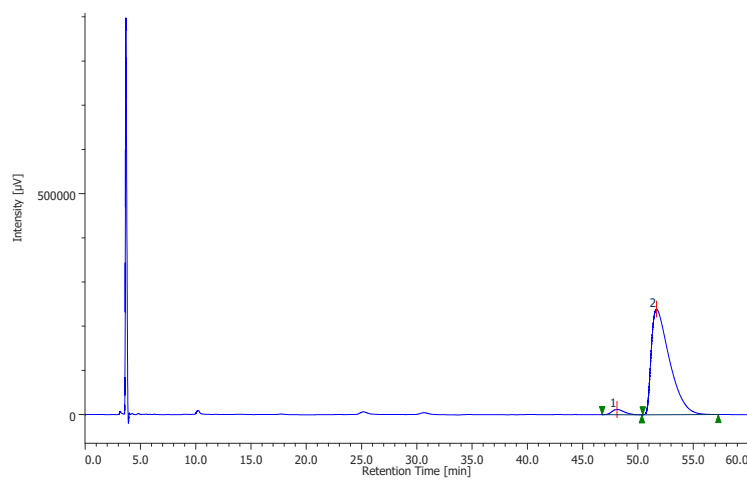
For γ -lactone *trans*-**12g**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHiRAL 5B (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, λ = 230 nm).

(1) Chromatogram of racemic *trans*-**12g**



	Retention time (min)	Peak area (%)
1	46.0	50.02
2	50.8	49.98

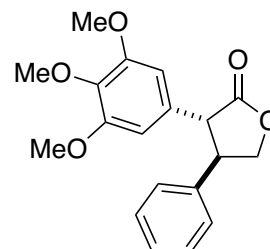
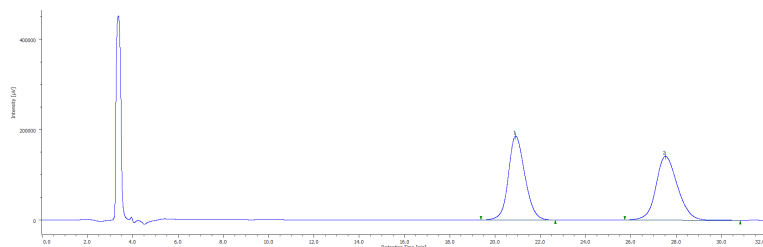
(2) Chromatogram of *trans*-**12g** (93% ee for (3*R*,4*R*))



	Retention time (min)	Peak area (%)
1	48.1	3.31
2	51.7	96.69

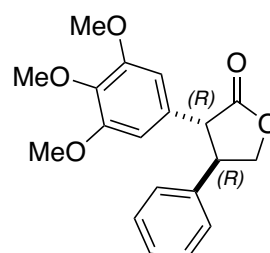
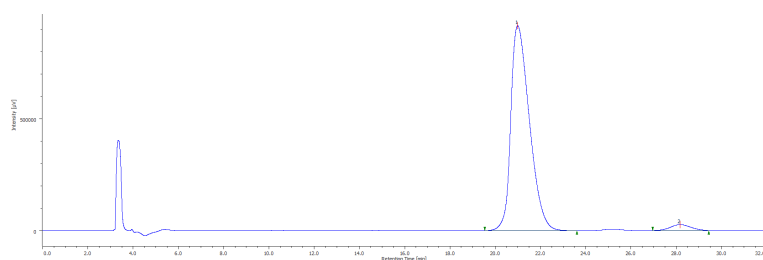
For γ -lactone *trans*-**12h**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHIRALPAK IC (4.6 mm \times 250 mm), *n*-hexane/IPA = 3/2, flow rate = 1.0 mL/min, λ = 230 nm).

(1) Chromatogram of racemic *trans*-**12h**



	Retention time (min)	Peak area (%)
1	20.9	50.21
2	27.5	49.79

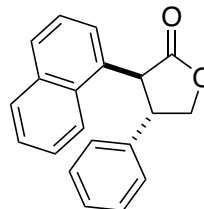
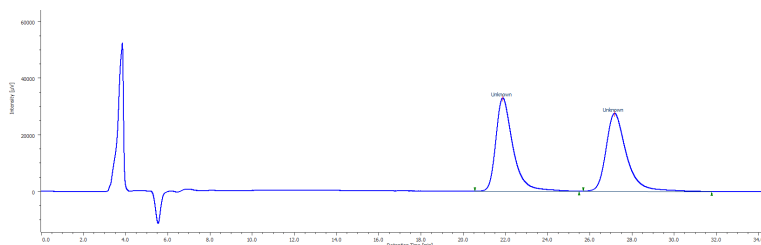
(2) Chromatogram of *trans*-**12h** (94% ee for (3*R*,4*R*))



	Retention time (min)	Peak area (%)
1	21.0	96.93
2	28.2	3.07

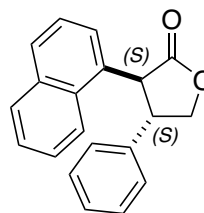
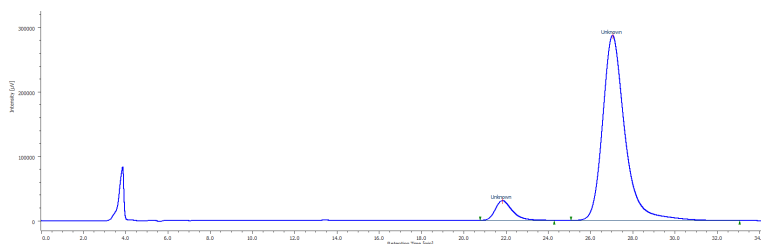
For γ -lactone *trans*-**12i**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHIRALPAK IC (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic *trans*-**12i**



	Retention time (min)	Peak area (%)
1	21.9	50.07
2	27.2	49.93

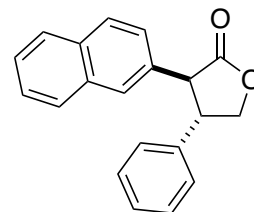
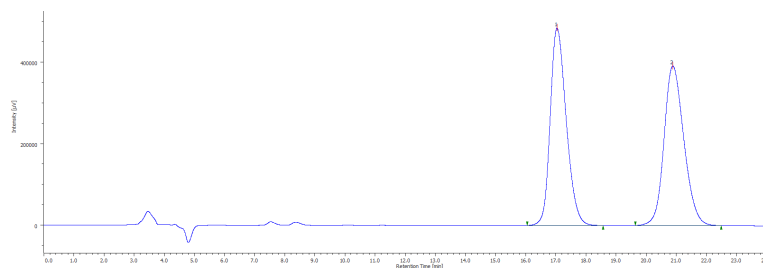
(2) Chromatogram of *trans*-**12i** (85% ee for (3*S*,4*S*))



	Retention time (min)	Peak area (%)
1	21.8	7.52
2	27.0	92.48

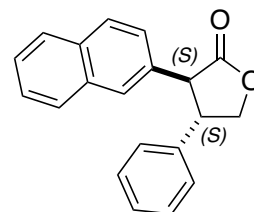
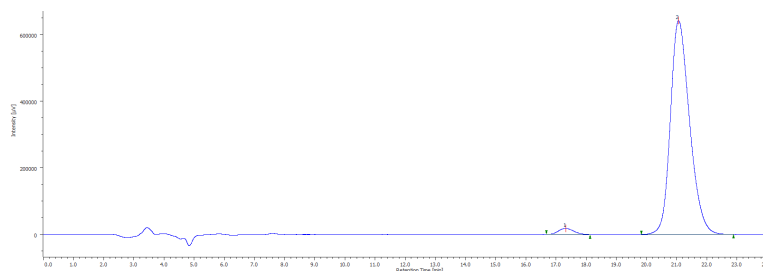
For γ -lactone *trans*-**12j**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHIRALPAK IC (4.6 mm \times 250 mm), *n*-hexane/IPA = 7/3, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic *trans*-**12j**



	Retention time (min)	Peak area (%)
1	17.0	50.03
2	20.9	49.97

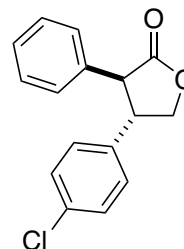
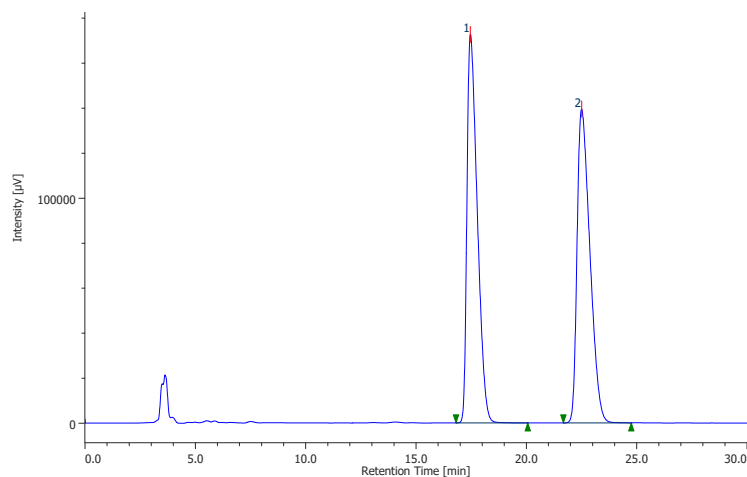
(2) Chromatogram of *trans*-**12j** (96% ee for (3*S*,4*S*))



	Retention time (min)	Peak area (%)
1	17.3	2.22
2	21.1	97.78

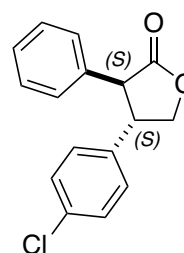
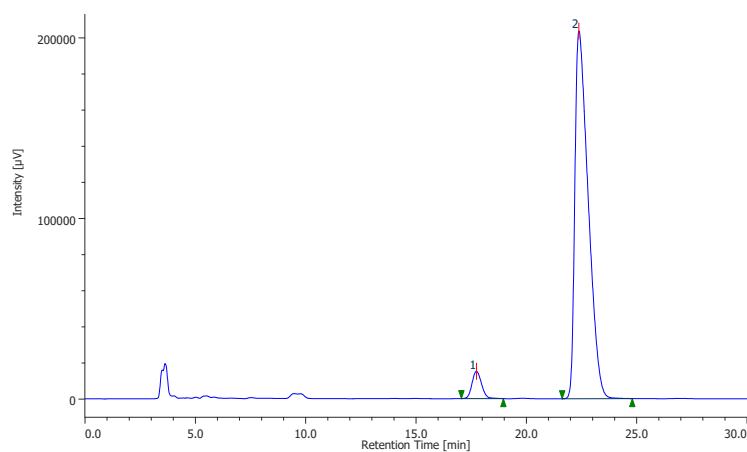
For γ -lactone *trans*-**12k**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHiRAL 5C (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic *trans*-**12k**



	Retention time (min)	Peak area (%)
1	17.5	49.98
2	22.5	50.02

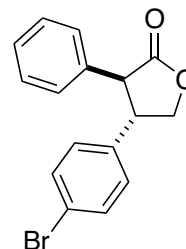
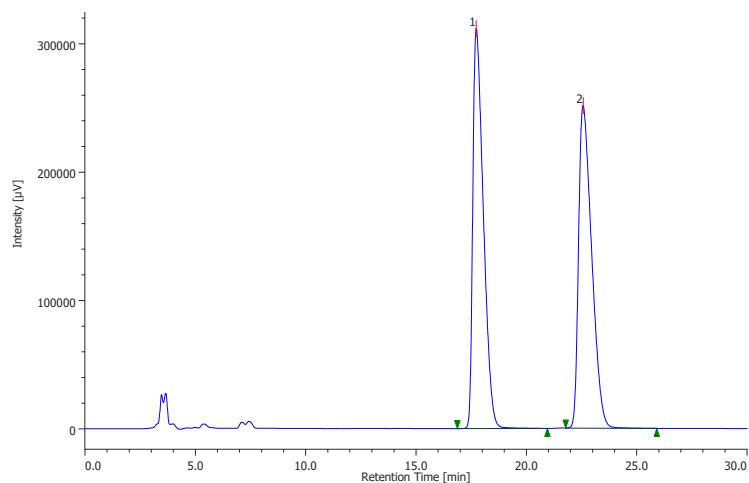
(2) Chromatogram of *trans*-**12k** (90% ee for (3*S*,4*S*))



	Retention time (min)	Peak area (%)
1	17.7	5.04
2	22.4	94.96

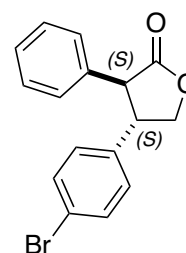
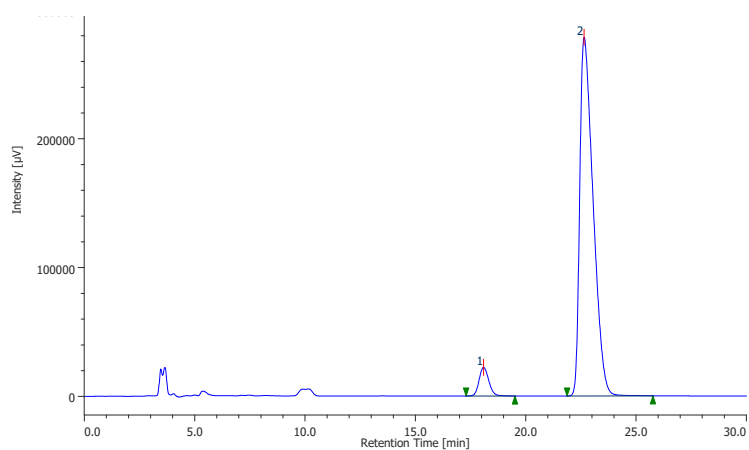
For γ -lactone *trans*-**12l**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHIRAL 5C (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic *trans*-**12l**



	Retention time (min)	Peak area (%)
1	17.7	50.05
2	22.6	49.95

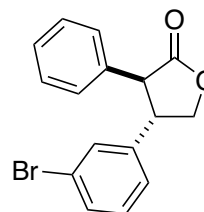
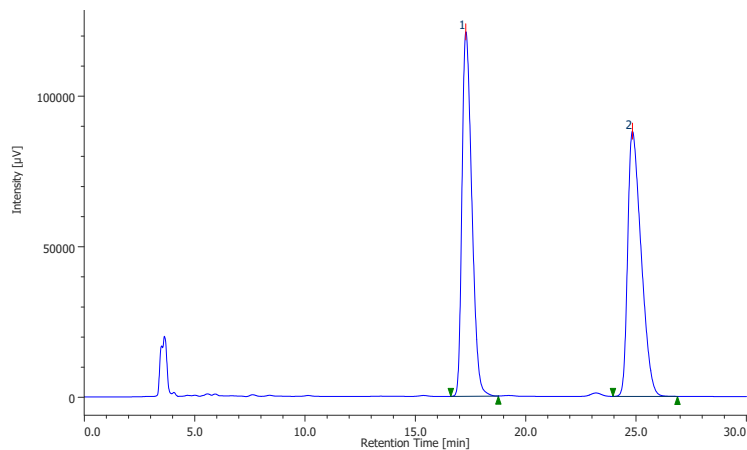
(2) Chromatogram of *trans*-**12l** (89% ee for (3*S*,4*S*))



	Retention time (min)	Peak area (%)
1	18.1	5.52
2	22.6	94.48

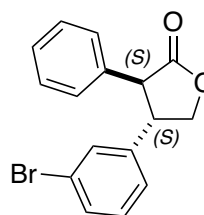
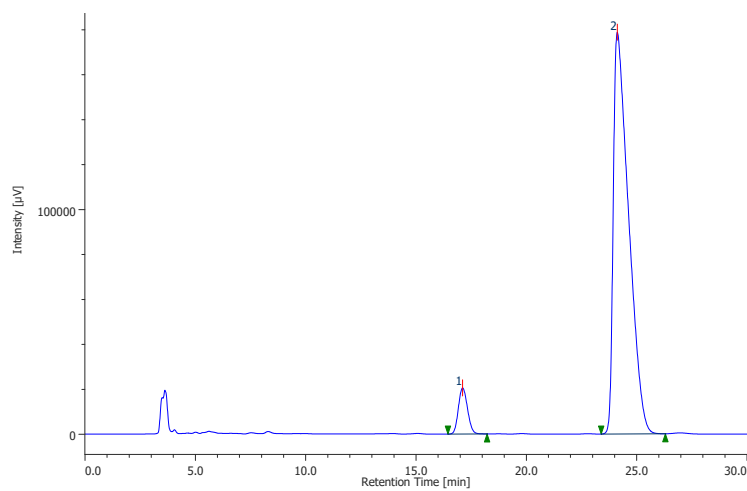
For γ -lactone *trans*-**12m**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHIRAL 5C (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic *trans*-**12m**



	Retention time (min)	Peak area (%)
1	17.3	50.17
2	24.8	49.83

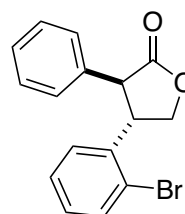
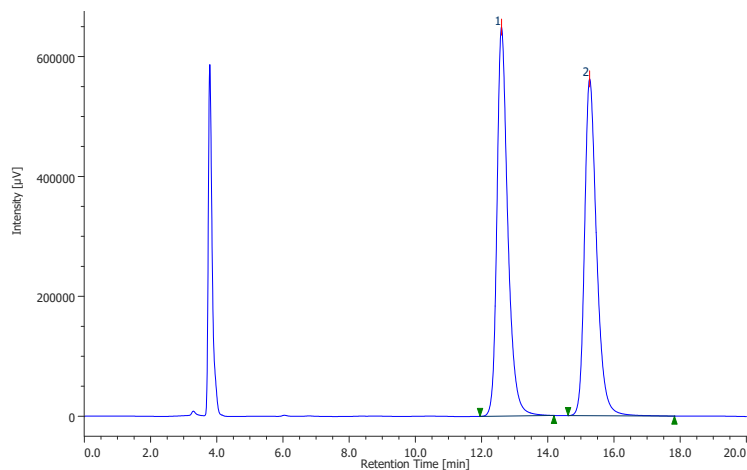
(2) Chromatogram of *trans*-**12m** (87% ee for (3*S*,4*S*))



	Retention time (min)	Peak area (%)
1	17.1	6.41
2	24.1	93.59

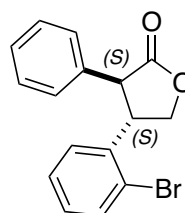
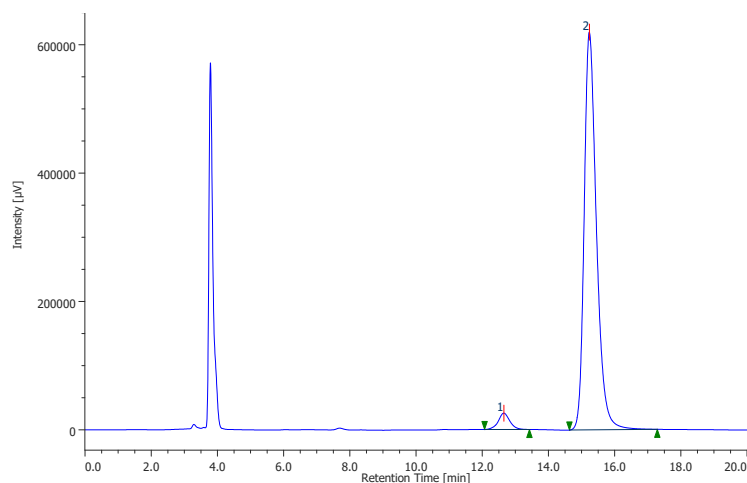
For γ -lactone *trans*-**12n**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHiRAL 5A (4.6 mm \times 250 mm), *n*-hexane/IPA = 9/1, flow rate = 1.0 mL/min, λ = 225 nm).

(1) Chromatogram of racemic *trans*-**12n**



	Retention time (min)	Peak area (%)
1	12.6	50.98
2	15.3	49.02

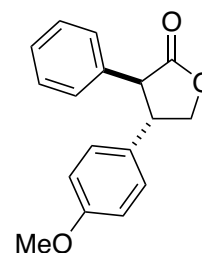
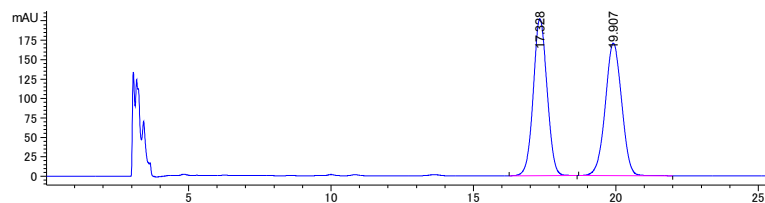
(2) Chromatogram of *trans*-**12n** (93% ee for (3*S*,4*S*))



	Retention time (min)	Peak area (%)
1	12.7	3.72
2	15.2	96.28

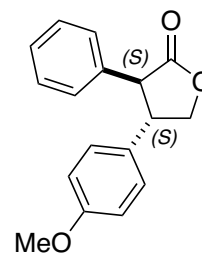
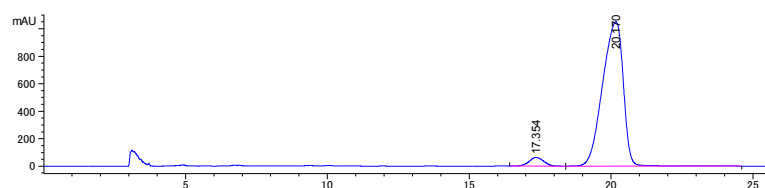
For γ -lactone *trans*-**12o**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHiRAL 5C (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic *trans*-**12o**



	Retention time (min)	Peak area (%)
1	17.3	49.92
2	19.9	50.08

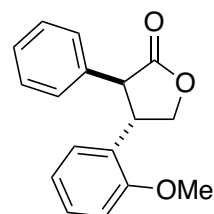
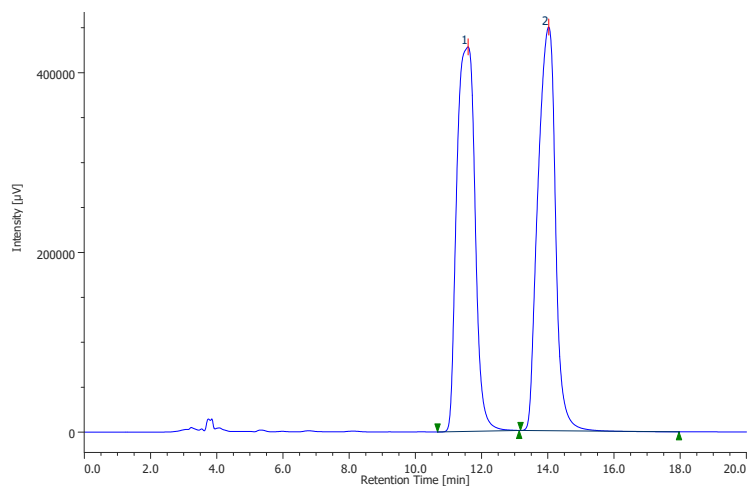
(2) Chromatogram of *trans*-**12o** (92% ee for (3*S*,4*S*))



	Retention time (min)	Peak area (%)
1	17.4	4.04
2	20.2	95.96

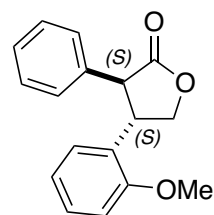
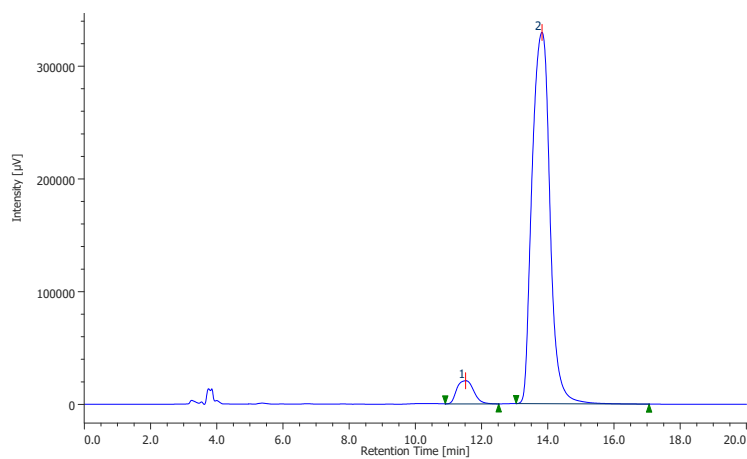
For γ -lactone *trans*-**12p**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHIRAL 5C (4.6 mm \times 250 mm), *n*-hexane/IPA = 9/1, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic *trans*-**12p**



	Retention time (min)	Peak area (%)
1	11.6	49.94
2	14.0	50.06

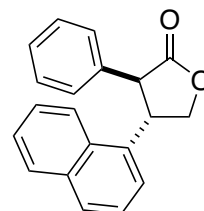
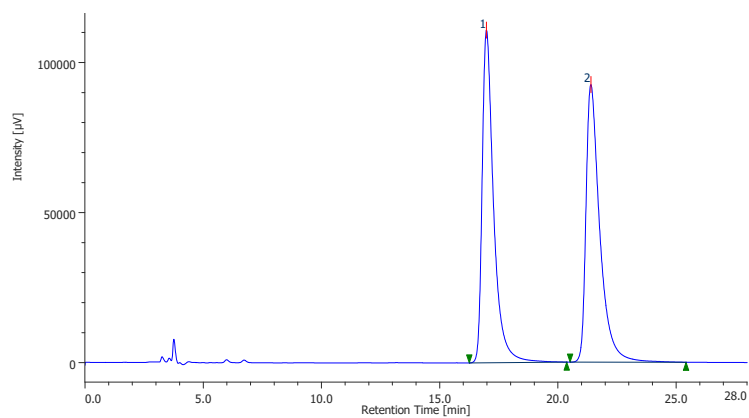
(2) Chromatogram of *trans*-**12p** (89% ee for (3*S*,4*S*))



	Retention time (min)	Peak area (%)
1	11.5	5.56
2	13.8	94.44

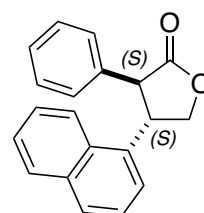
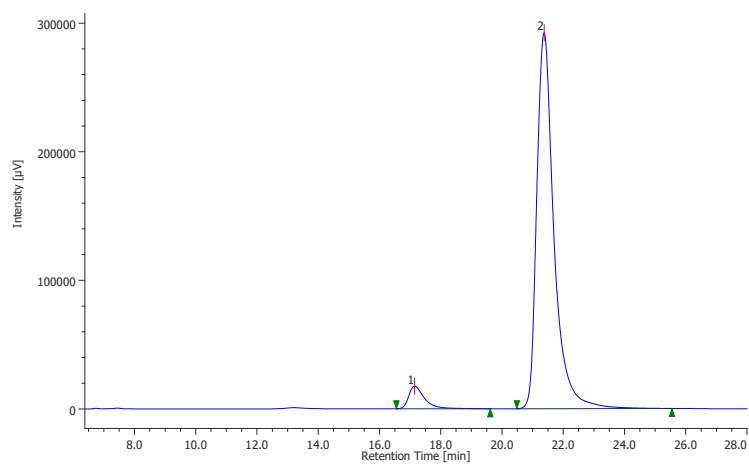
For γ -lactone *trans*-**12q**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHiRAL 5A (4.6 mm \times 250 mm), *n*-hexane/IPA = 9/1, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic *trans*-**12q**



	Retention time (min)	Peak area (%)
1	17.0	49.93
2	21.4	50.07

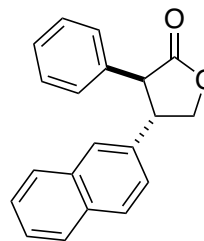
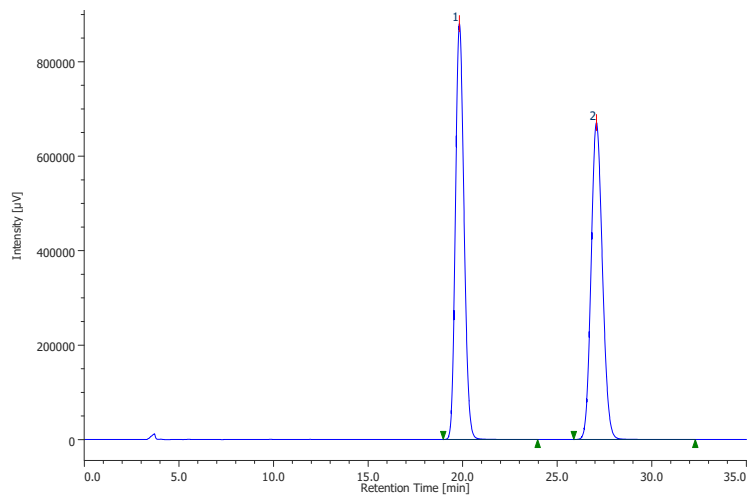
(2) Chromatogram of *trans*-**12q** (90% ee for (3*S*,4*S*))



	Retention time (min)	Peak area (%)
1	17.1	5.25
2	21.4	94.75

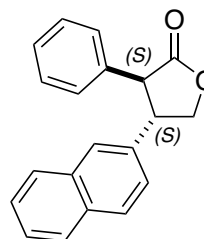
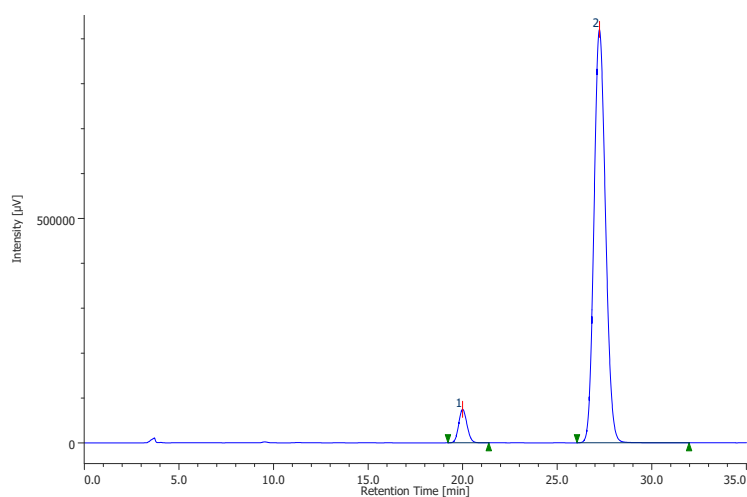
For γ -lactone *trans*-**12r**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHiRAL 5C (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic *trans*-**12r**



	Retention time (min)	Peak area (%)
1	19.8	49.92
2	27.1	50.08

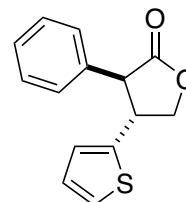
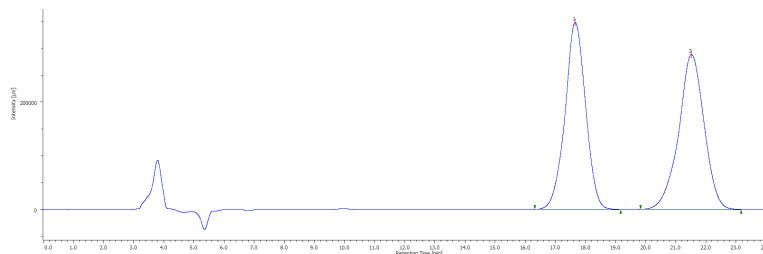
(2) Chromatogram of *trans*-**12r** (89% ee for (3*S*,4*S*))



	Retention time (min)	Peak area (%)
1	20.0	5.53
2	27.2	94.47

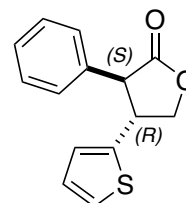
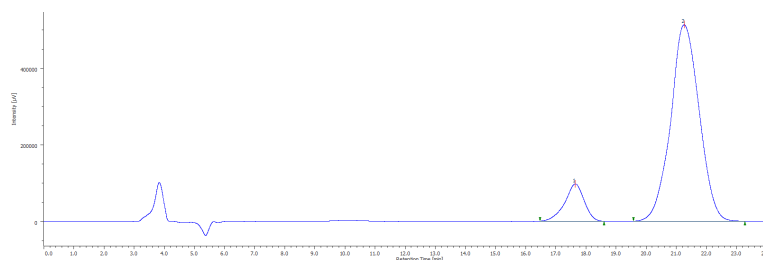
For γ -lactone *trans*-**12s**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHIRALPAK IC (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic *trans*-**12s**



	Retention time (min)	Peak area (%)
1	17.7	49.47
2	21.5	50.53

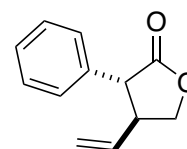
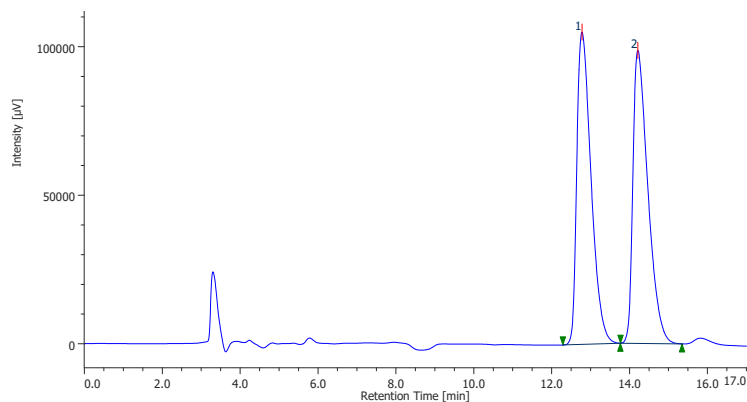
(2) Chromatogram of *trans*-**12s** (77% ee for (3*S*,4*R*))



	Retention time (min)	Peak area (%)
1	17.6	11.40
2	21.3	88.60

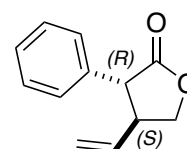
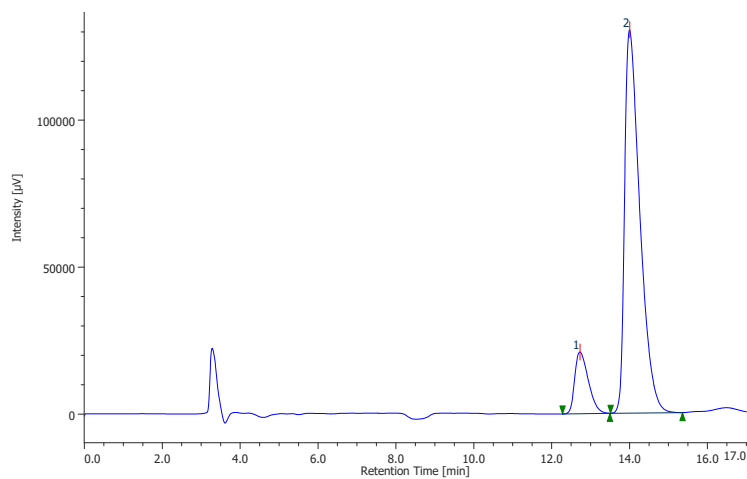
For γ -lactone *trans*-**48**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHIRAL 5A (4.6 mm \times 250 mm), *n*-hexane/IPA = 19/1, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic *trans*-**48**



	Retention time (min)	Peak area (%)
1	12.8	50.25
2	14.2	49.75

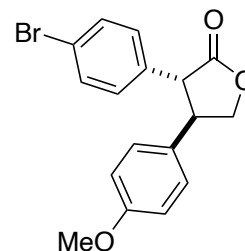
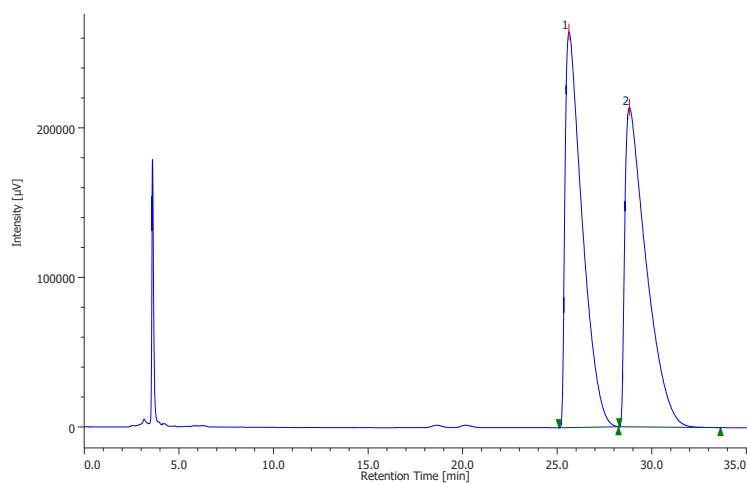
(2) Chromatogram of *trans*-**48** (75% ee for (3*R*,4*S*))



	Retention time (min)	Peak area (%)
1	12.7	12.50
2	14.0	87.50

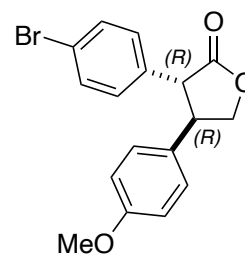
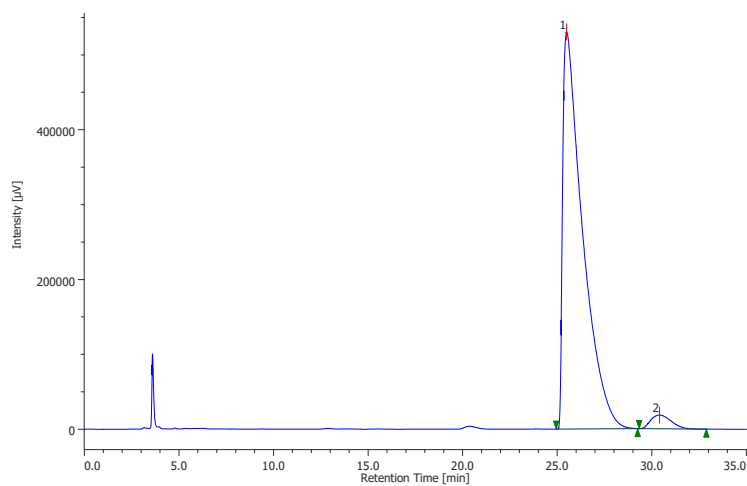
For γ -lactone *trans*-**12t**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHiRAL 5B (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic *trans*-**12t**



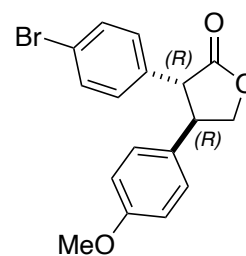
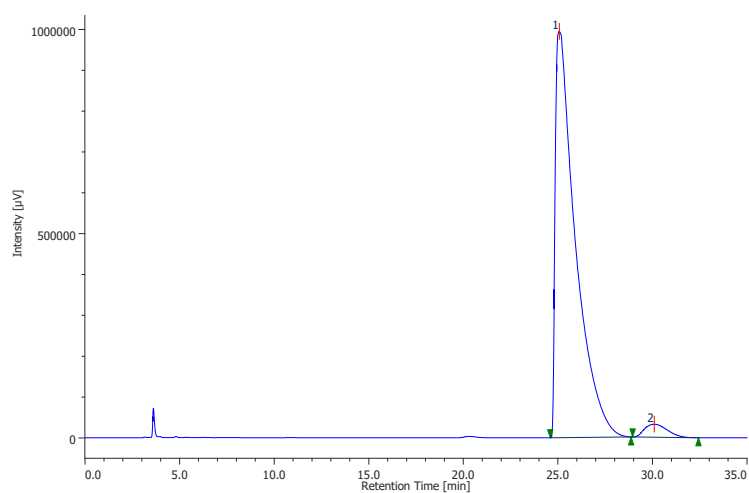
	Retention time (min)	Peak area (%)
1	25.6	49.97
2	28.8	50.03

(2) Chromatogram of *trans*-**12t** (93% ee for (3*R*,4*R*))



	Retention time (min)	Peak area (%)
1	25.5	96.56
2	30.4	3.44

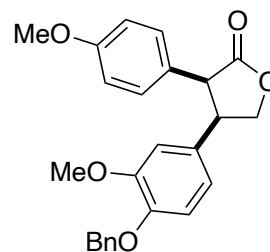
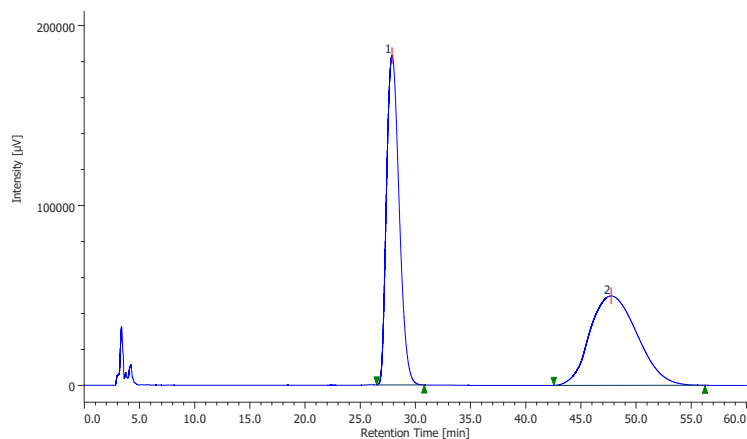
(3) Chromatogram of *trans*-**12t** in gram-scale synthesis (93% ee for (3*R*,4*R*))



	Retention time (min)	Peak area (%)
1	25.1	96.52
2	30.1	3.48

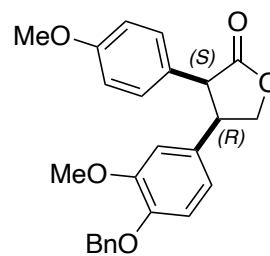
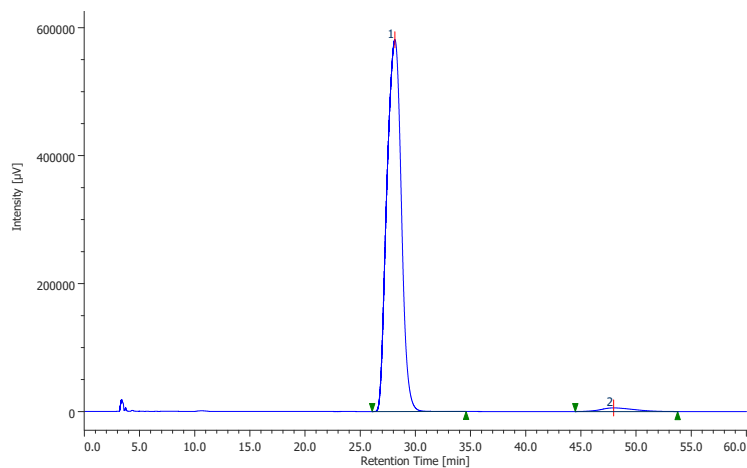
For γ -lactone *cis*-**12u**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHIRALPAK ID (4.6 mm \times 250 mm), *n*-hexane/IPA = 3/2, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic *cis*-**12u**



	Retention time (min)	Peak area (%)
1	27.9	49.56
2	47.7	50.44

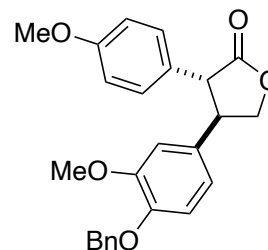
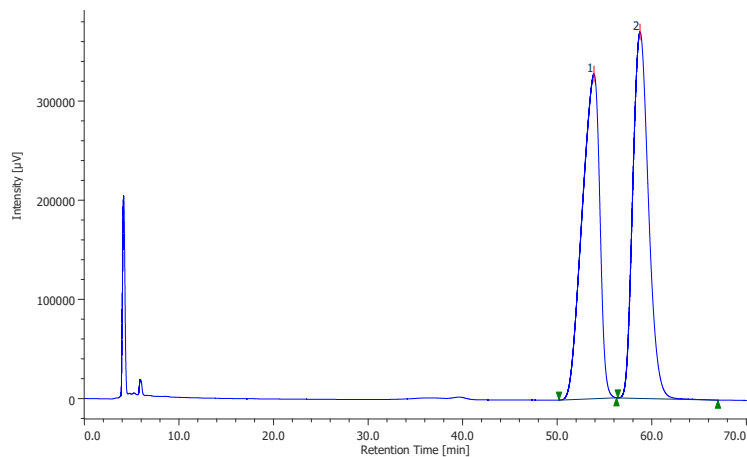
(2) Chromatogram of *cis*-**12u** (96% ee for (3*S*,4*R*))



	Retention time (min)	Peak area (%)
1	28.1	97.78
2	48.0	2.22

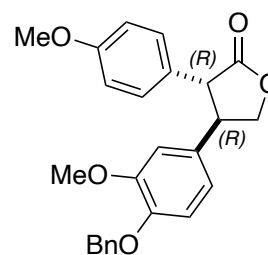
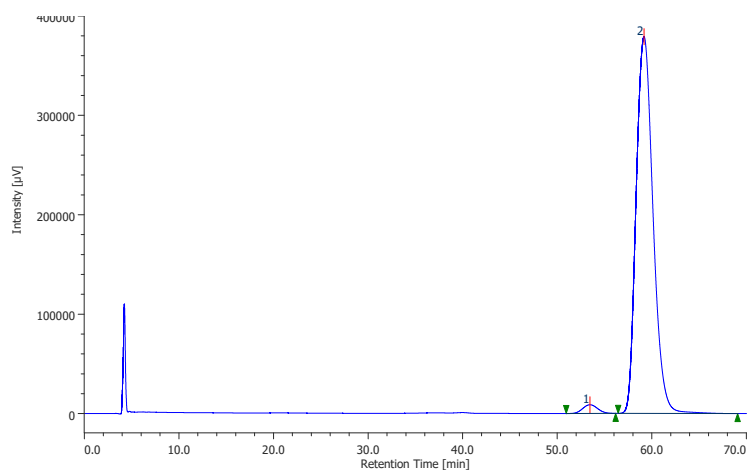
For γ -lactone *trans*-**12u**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHiRAL 5C (4.6 mm \times 250 mm), *n*-hexane/IPA = 7/3, flow rate = 0.8 mL/min, λ = 254 nm).

(1) Chromatogram of racemic *trans*-**12u**



	Retention time (min)	Peak area (%)
1	53.9	49.98
2	58.7	50.02

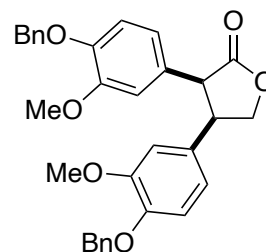
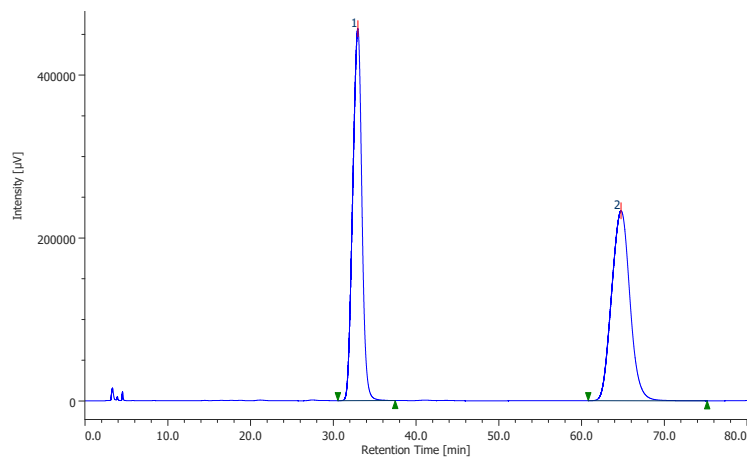
(2) Chromatogram of *trans*-**12u** (96% ee for (3*R*,4*R*))



	Retention time (min)	Peak area (%)
1	53.4	2.01
2	59.2	97.99

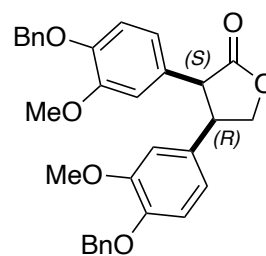
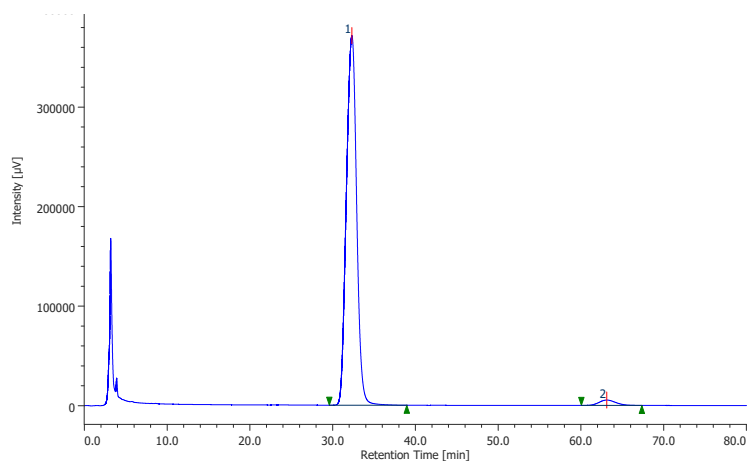
For γ -lactone *cis*-**12v**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHiRAL 5C (4.6 mm \times 250 mm), *n*-hexane/IPA = 3/2, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic *cis*-**12v**



	Retention time (min)	Peak area (%)
1	33.0	49.45
2	64.8	50.55

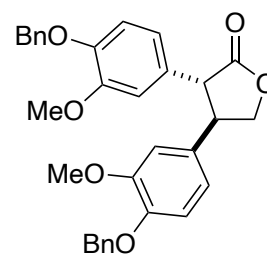
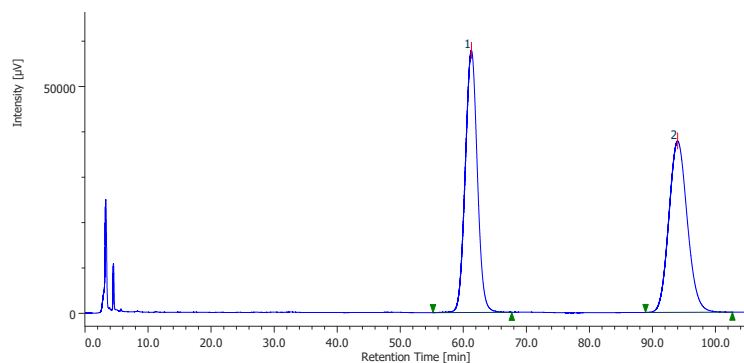
(2) Chromatogram of *cis*-**12v** (95% ee for (3*S*,4*R*))



	Retention time (min)	Peak area (%)
1	32.3	97.66
2	63.1	2.34

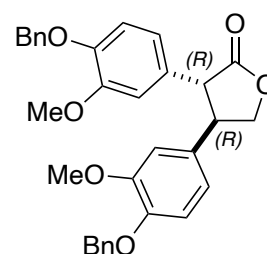
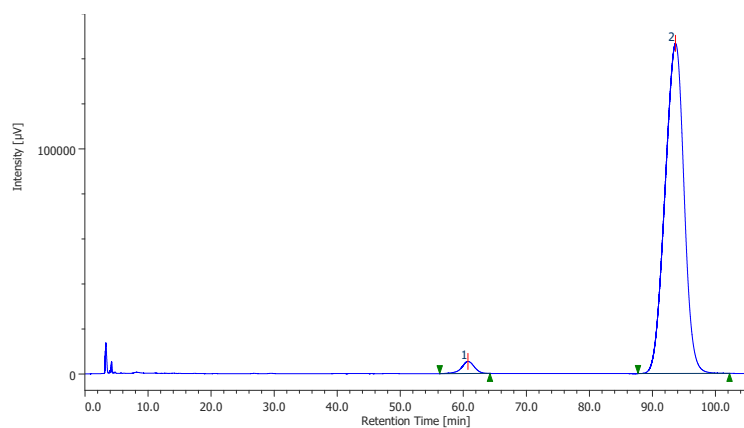
For γ -lactone *trans*-**12v**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHIRAL 5C (4.6 mm \times 250 mm), *n*-hexane/IPA = 3/2, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic *trans*-**12v**



	Retention time (min)	Peak area (%)
1	61.3	50.05
2	94.0	49.95

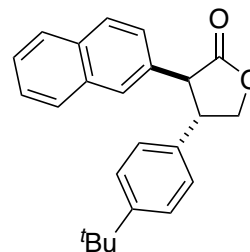
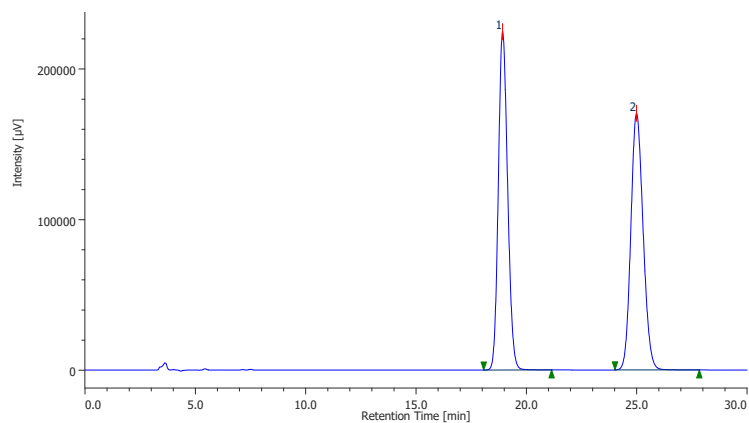
(2) Chromatogram of *trans*-**12v** (95% ee for (3*R*,4*R*))



	Retention time (min)	Peak area (%)
1	60.7	2.41
2	93.6	97.59

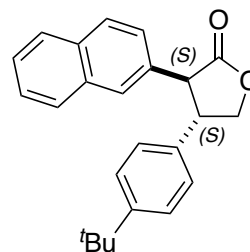
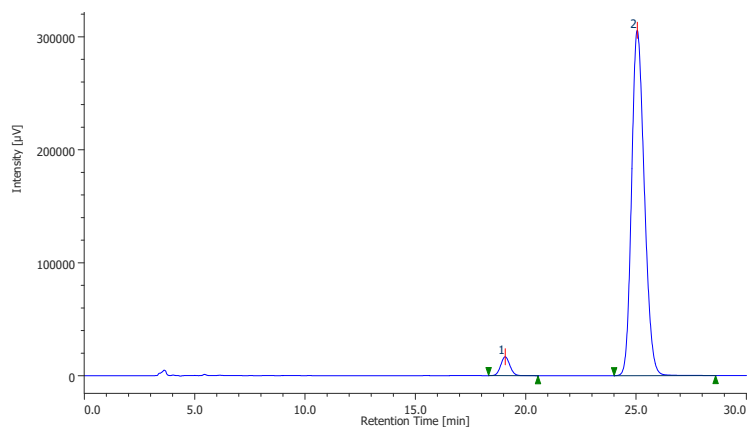
For γ -lactone *trans*-**12w**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHiRAL 5C (4.6 mm \times 250 mm), *n*-hexane/IPA = 4/1, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic *trans*-**12w**



	Retention time (min)	Peak area (%)
1	18.9	49.97
2	25.0	50.03

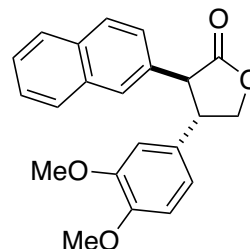
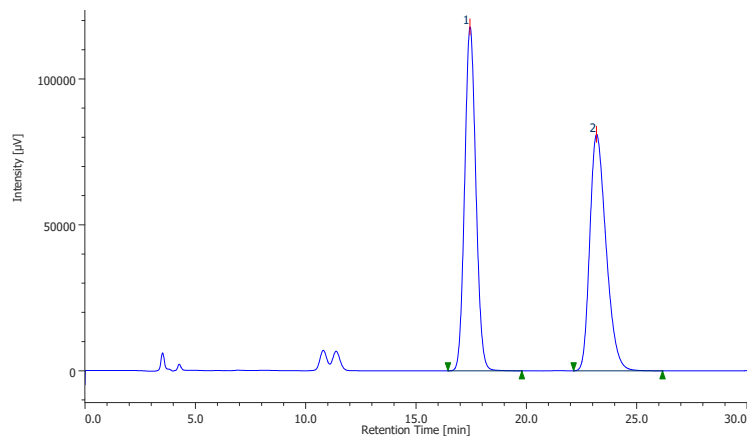
(2) Chromatogram of *trans*-**12w** (92% ee for (3*S*,4*S*))



	Retention time (min)	Peak area (%)
1	19.1	3.80
2	25.1	96.20

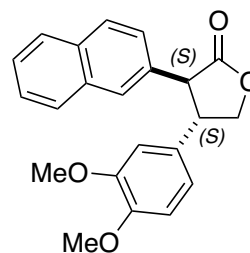
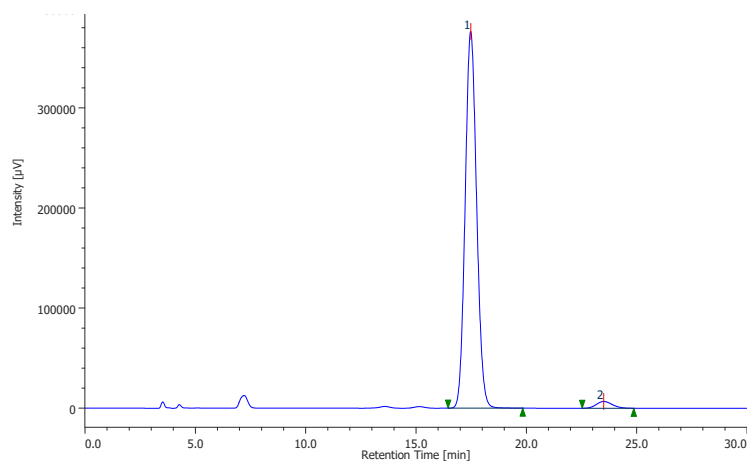
For γ -lactone *trans*-**12x**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHiRAL 5C (4.6 mm \times 250 mm), *n*-hexane/IPA = 2/3, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic *trans*-**12x**



	Retention time (min)	Peak area (%)
1	17.4	50.06
2	23.2	49.94

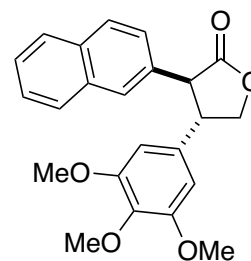
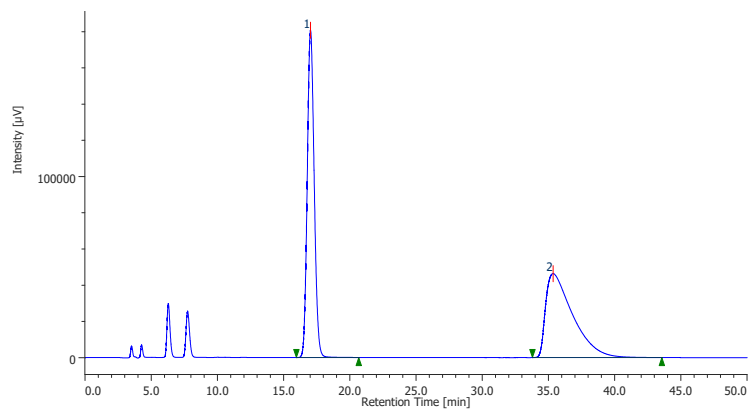
(2) Chromatogram of *trans*-**12x** (95% ee for (3*S*,4*S*))



	Retention time (min)	Peak area (%)
1	17.5	97.55
2	23.5	2.45

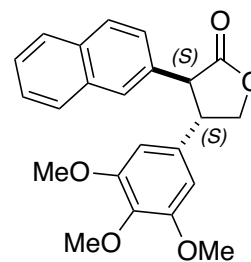
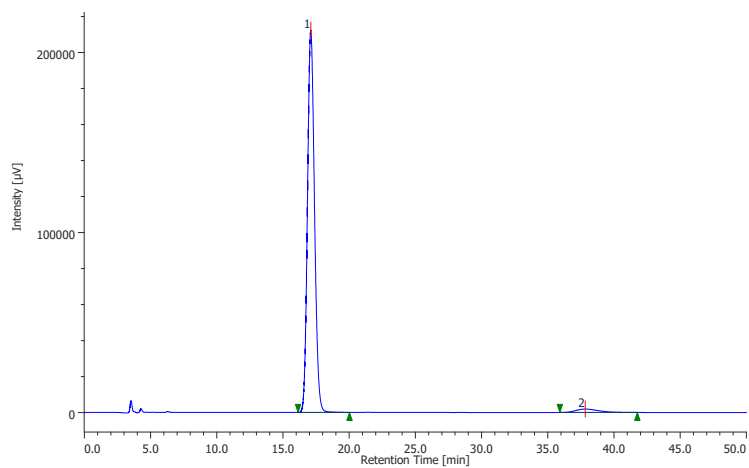
For γ -lactone *trans*-**12y**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHiRAL 5C (4.6 mm \times 250 mm), *n*-hexane/IPA = 2/3, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic *trans*-**12y**



	Retention time (min)	Peak area (%)
1	17.0	49.97
2	35.3	50.03

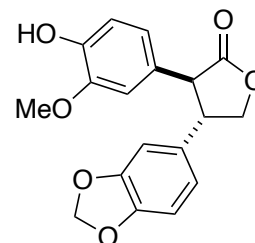
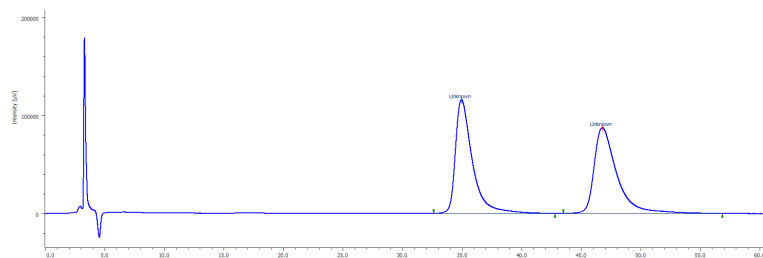
(2) Chromatogram of *trans*-**12y** (94% ee for (3*S*,4*S*))



	Retention time (min)	Peak area (%)
1	17.1	97.17
2	37.8	2.83

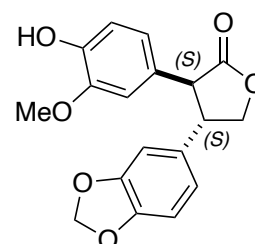
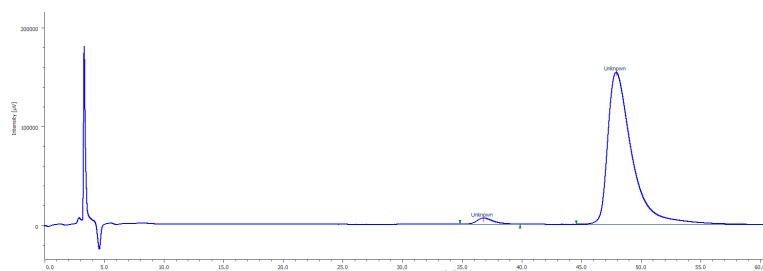
For cinnanomumolide ((3*S*,4*S*)-**13**), the enantiomeric excess was determined by HPLC analysis; HPLC (CHIRALPAK IC (4.6 mm × 250 mm), *n*-hexane/IPA = 3/2, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic cinnanomumolide (**13**)



	Retention time (min)	Peak area (%)
1	34.9	49.83
2	46.8	50.17

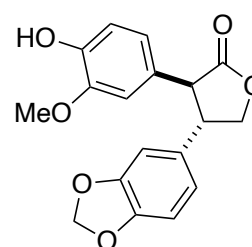
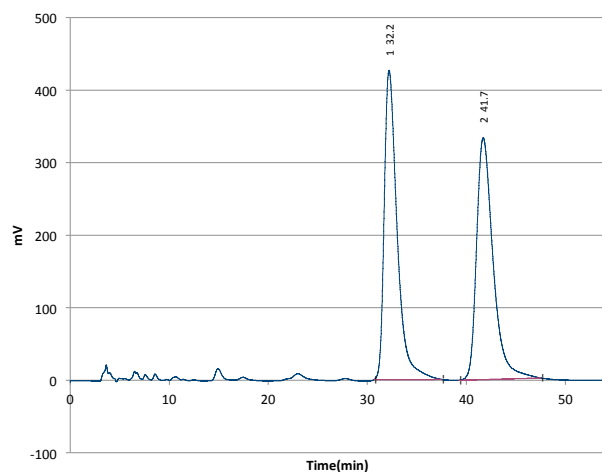
(2) Chromatogram of cinnanomumolide ((3*S*,4*S*)-**13**, 95% ee)



	Retention time (min)	Peak area (%)
1	36.8	2.70
2	47.9	97.30

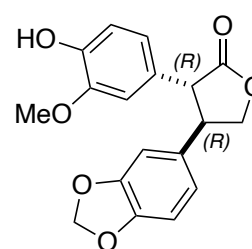
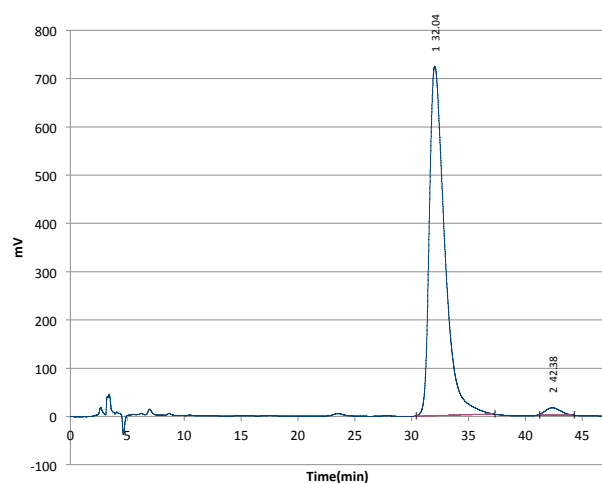
For cinnassin A₇ ((3*R*,4*R*)-*ent*-**13**), the enantiomeric excess was determined by HPLC analysis; HPLC (CHIRALPAK IC (4.6 mm × 250 mm), *n*-hexane/IPA = 3/2, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic cinnamomumolide (*ent*-**13**)



	Retention time (min)	Peak area (%)
1	32.2	49.95
2	41.7	50.05

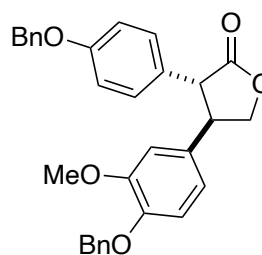
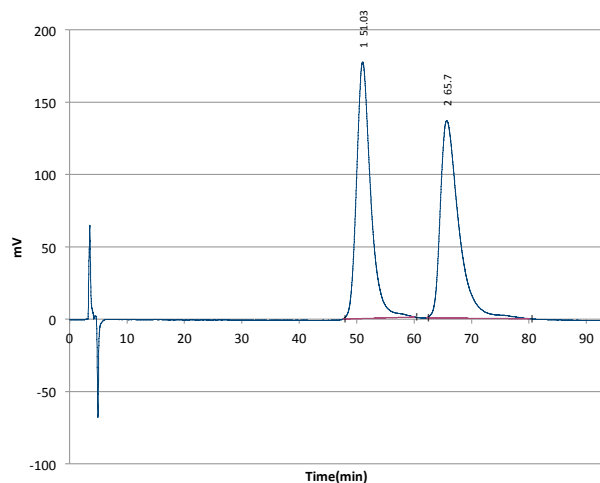
(2) Chromatogram of cinnassin A₇ ((3*R*,4*R*)-*ent*-**13**, 96% ee)



	Retention time (min)	Peak area (%)
1	32.0	98.03
2	42.4	1.97

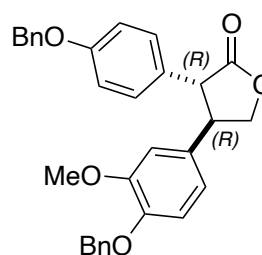
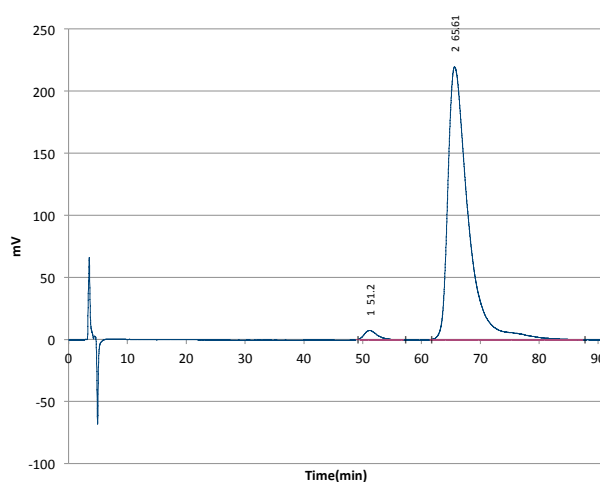
For γ -lactone *trans*-**12z**, the enantiomeric excess was determined by HPLC analysis; HPLC (CHIRALPAK IC (4.6 mm \times 250 mm), *n*-hexane/IPA = 3/2, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic *trans*-**12z**



	Retention time (min)	Peak area (%)
1	51.0	50.00
2	65.7	50.00

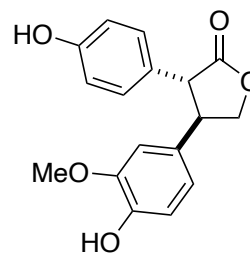
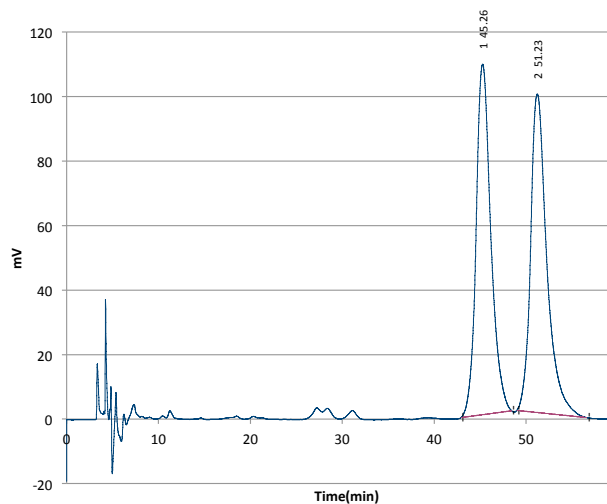
(2) Chromatogram of *trans*-**12z** (96% ee for (3*R*,4*R*))



	Retention time (min)	Peak area (%)
1	51.2	2.18
2	65.6	97.82

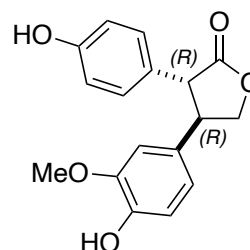
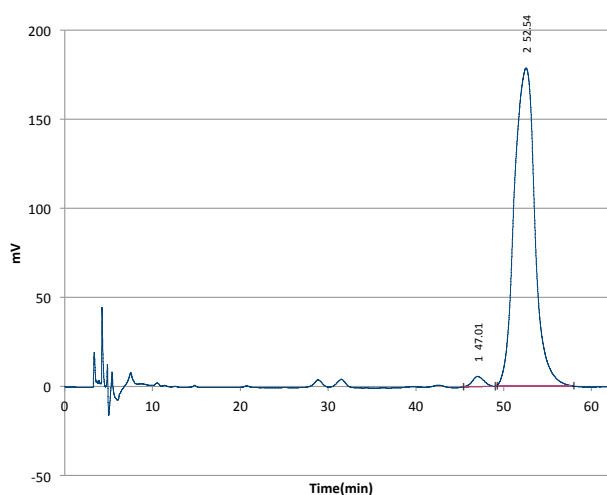
For cinnanomulactone ((3*R*,4*R*)-**14**), the enantiomeric excess was determined by HPLC analysis; HPLC (CHIRALPAK ID (4.6 mm × 250 mm), *n*-hexane/IPA = 17/3, flow rate = 1.0 mL/min, λ = 254 nm).

(1) Chromatogram of racemic cinnanomulactone (**14**)



	Retention time (min)	Peak area (%)
1	45.3	49.96
2	51.2	50.04

(2) Chromatogram of cinnanomulactone ((3*R*,4*R*)-**14**, 96% ee)



	Retention time (min)	Peak area (%)
1	47.0	1.78
2	52.5	98.22

Computational Details

Structure of Naphthothiophene-Type Complex (S)-10b

The structures of conformational isomers of (S)-10b were fully optimized by ONIOM (M06/6-31G(d,p)-LanL2DZ(Rh):HF/3-21G) calculations and characterized by frequency calculation, using the Gaussian 16 software package.⁴⁵ The ONIOM partitioning of the complex (S)-10b is shown in **Figure S18**. Gibbs free energies were also computed for the gas phase by single-point energy calculations at the same level.

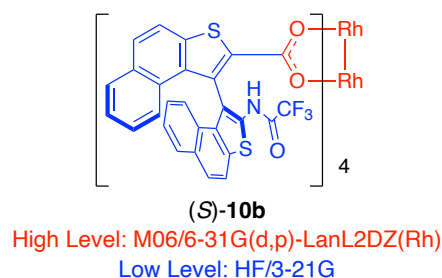


Figure S18. ONIOM Partitioning for (S)-10b.

Computational investigation was examined for estimation of the stabilities of all possible structures of complex (S)-10b. D_2 -symmetric structure (up-up-down-down ligand arrangement) was found to be more stable than the other possible structures, C_1 -symmetric (up-up-up-down), C_2 -symmetric (up-up-down-down), C_4 -symmetric (all-up) structures as shown in **Figure S19**. Although these calculations were performed with the complexes without coordination of the axial ligands such as EtOH at the rhodium atoms, the significant stability of D_2 -symmetric structure could support the D_2 -symmetric structure of complex (S)-10b.

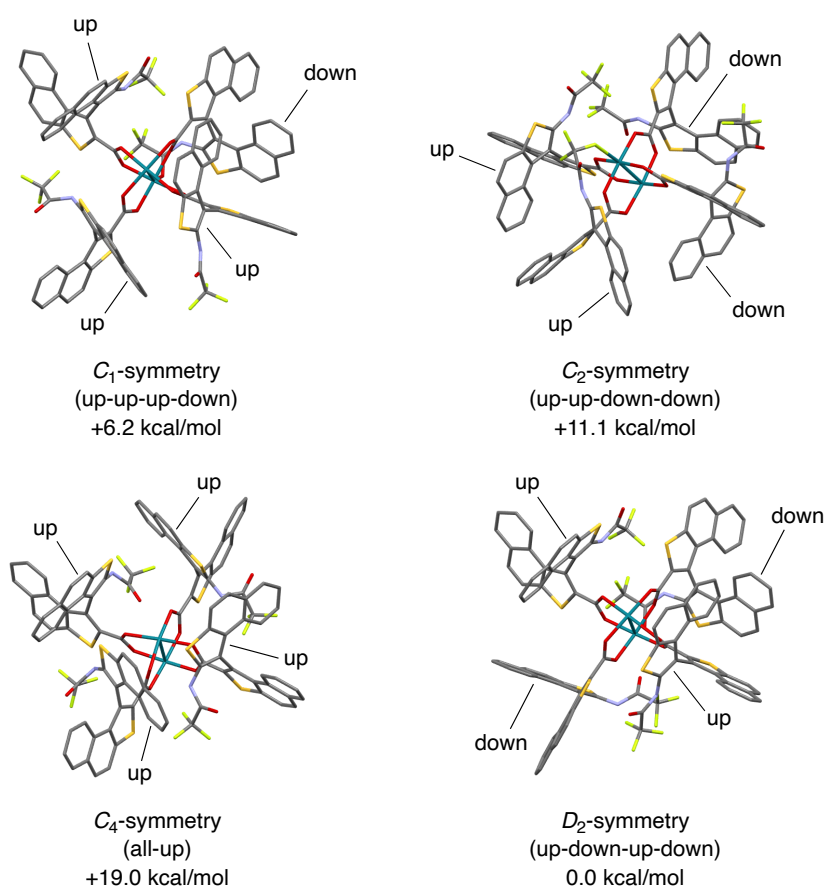
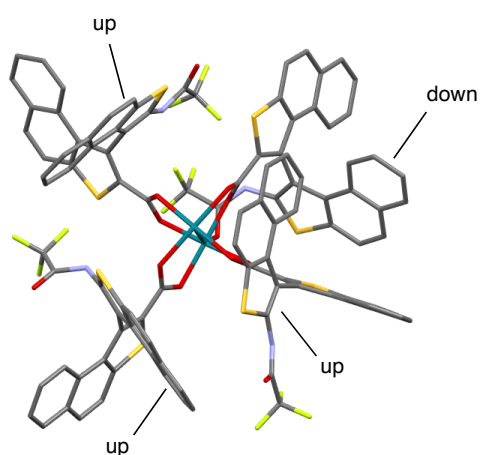


Figure S19. Energy Differences between Conformational Isomers of Complex (S)-10b.

XYZ Coordinates and Thermochemical Data (Energies in Hartree)



C₁-Symmetric (up-up-up-down) Structure

Electronic Energy = -9784.791997

Electronic and Zero-Point Energy = -9783.324901

Enthalpy = -9783.217441

Free Energy = -9783.475860

Rh	-0.42470800	0.15055600	-1.72735800
Rh	0.18470700	-0.29676600	0.53622900
O	-2.09874000	1.01607400	-0.98494300
C	-2.16043900	1.37301500	0.23314100
O	-1.35630300	1.01172900	1.13070000
C	-3.37333200	2.15798300	0.48710400
S	-4.25920800	1.85749800	2.01258000
C	-5.59510800	2.86505600	1.38989500
C	-6.81080800	3.05290900	2.07081600
H	-6.97514900	2.56991300	3.01139800
C	-7.75638400	3.82598800	1.49974700
H	-8.69779500	3.98072900	1.98857100
C	-7.53999100	4.44429100	0.23393200
C	-8.55365800	5.24200200	-0.34288700
H	-9.47223300	5.36884400	0.19604300
C	-8.37532500	5.83493500	-1.55230000
H	-9.14950200	6.43773800	-1.98261200
C	-7.16325400	5.65537600	-2.23995900
H	-7.01820800	6.12733800	-3.19106300
C	-6.16782500	4.89239100	-1.71028800

H	-5.25482900	4.78492800	-2.24450100
C	-6.32053600	4.25759900	-0.45464200
C	-5.32037700	3.42121300	0.16368300
C	-4.00379800	3.00774400	-0.34242900
C	-3.38367200	3.56541800	-1.57817300
C	-2.79448400	4.91533200	-1.66706700
C	-2.65194700	5.92890300	-0.65255600
C	-3.09503500	5.78827100	0.68510100
H	-3.57253300	4.88777700	0.98512400
C	-2.93948800	6.79360300	1.58960200
H	-3.29668600	6.66376000	2.59174600
C	-2.32164900	8.00242900	1.22349800
H	-2.20120300	8.78159600	1.94877500
C	-1.88281300	8.17006300	-0.05012200
H	-1.40846300	9.08507100	-0.34666600
C	-2.03749100	7.14879200	-1.01601300
C	-1.57814400	7.35662800	-2.34713900
H	-1.12516700	8.29754000	-2.59062700
C	-1.71352900	6.39775500	-3.28644700
H	-1.36948400	6.54531900	-4.28973700
C	-2.32645700	5.18593400	-2.92800900
S	-2.56611800	3.82984500	-4.07040500
C	-3.33317200	2.90199100	-2.73527100
N	-3.85540300	1.62835400	-2.99820600
H	-4.80994400	1.45500300	-2.74574200
C	-3.09294700	0.59919000	-3.36941900
O	-1.90348100	0.62462600	-3.64345600
C	-3.87557500	-0.70522600	-3.42690800
F	-5.11334200	-0.48242900	-3.91848900
F	-3.26254000	-1.61391200	-4.17803400
F	-4.04651400	-1.20208000	-2.17681600
O	0.51775100	1.96080700	-1.53938800
C	1.26651800	2.15128000	-0.52413400
O	1.48144000	1.31050800	0.39253800
C	1.84108300	3.48914400	-0.45583000
S	1.33393600	4.66349800	-1.70697100
C	2.28631200	5.91302900	-0.86408400
C	2.41194800	7.24069400	-1.31225700
H	1.92476900	7.54511300	-2.21543000

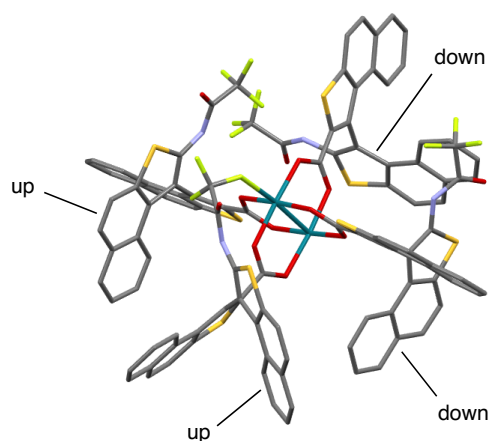
C	3.15748200	8.10079700	-0.58944600
H	3.28169800	9.11561300	-0.91304800
C	3.78417400	7.69779200	0.62660100
C	4.52359500	8.63344300	1.38376000
H	4.62194900	9.63317800	1.00756200
C	5.09340500	8.28129100	2.56627700
H	5.65240200	8.99643000	3.13553000
C	4.93583400	6.97118800	3.04882000
H	5.36781100	6.69748600	3.99040500
C	4.23657300	6.04401800	2.33723500
H	4.11856800	5.06237600	2.73014200
C	3.65073200	6.37102200	1.09139900
C	2.89668000	5.44735200	0.27776800
C	2.64630700	4.01939700	0.48326700
C	3.32637500	3.21539800	1.53282200
C	2.78431000	2.75139200	2.80756800
C	1.48550900	2.96987100	3.37624000
C	0.48976200	3.77802600	2.77853300
H	0.69700400	4.27116900	1.85613900
C	-0.72468100	3.94360100	3.36691600
H	-1.45856500	4.56230100	2.89388400
C	-1.02278300	3.31023400	4.58776500
H	-1.98936200	3.44004800	5.03171900
C	-0.08281500	2.54189500	5.19587900
H	-0.29264500	2.06096500	6.13157500
C	1.19452600	2.35957000	4.61581600
C	2.18368100	1.58170100	5.28249500
H	1.93240800	1.12859200	6.22117700
C	3.41749500	1.42573700	4.75482100
H	4.16923800	0.85234000	5.25777800
C	3.70114200	2.01883400	3.51409300
S	5.29261200	1.90032300	2.69110000
C	4.59917400	2.85179200	1.33176900
N	5.31958000	3.13824400	0.17474600
H	4.78171400	3.32450600	-0.64770900
C	6.66161100	3.18028800	0.08640000
O	7.45345000	2.96752900	0.97145400
C	7.15439200	3.56899100	-1.30174900
F	8.09441600	2.70994900	-1.73296100

F	6.15021100	3.58228500	-2.20225000
F	7.70531100	4.79424400	-1.27659000
O	1.33583700	-0.73132500	-2.30871700
C	1.95317700	-1.45178600	-1.46096700
O	1.61859900	-1.58643700	-0.24254400
C	3.06484100	-2.19445400	-2.04228300
S	3.24788200	-2.09055200	-3.82354200
C	4.62671700	-3.21588300	-3.70799000
C	5.38365400	-3.64093400	-4.81453300
H	5.14537500	-3.28051900	-5.79410200
C	6.40678800	-4.49486700	-4.60849500
H	7.00903700	-4.82717100	-5.43110800
C	6.70168600	-4.99760700	-3.30773100
C	7.74818200	-5.92978100	-3.13256800
H	8.32685800	-6.21679700	-3.98896000
C	8.01110400	-6.46199200	-1.91013000
H	8.80392300	-7.17180300	-1.78472200
C	7.22248000	-6.09129800	-0.80840000
H	7.40751400	-6.53409200	0.14941100
C	6.21438900	-5.18606400	-0.94353300
H	5.61282700	-4.94744700	-0.10061100
C	5.93332800	-4.59052500	-2.19479500
C	4.88362800	-3.62627500	-2.42080300
C	3.98753400	-2.98054100	-1.45776000
C	4.11589400	-3.13814800	0.01298600
C	5.17550200	-2.56188000	0.84733300
C	6.24402600	-1.67408900	0.48126200
C	6.40005900	-1.11341800	-0.80893300
H	5.70467400	-1.36283200	-1.57526400
C	7.41960500	-0.25465200	-1.08118500
H	7.51196500	0.17385900	-2.05834000
C	8.35365800	0.09053800	-0.08745700
H	9.13029000	0.79034200	-0.31274200
C	8.23304400	-0.43250600	1.15948800
H	8.92519100	-0.16014100	1.93165700
C	7.17547800	-1.31353200	1.47937600
C	7.03011500	-1.80498400	2.80784700
H	7.75515600	-1.51297000	3.54175200
C	5.99650600	-2.60425400	3.14694200

H	5.87468600	-2.96365400	4.14828100
C	5.07370900	-2.97172900	2.15297600
S	3.65029200	-4.02414100	2.44511100
C	3.25965400	-3.89602400	0.69208400
N	2.14301100	-4.53715800	0.14773900
H	1.31862400	-3.98492300	0.02183900
C	2.18574100	-5.83727900	-0.20173900
O	3.10780700	-6.59478500	-0.03077600
C	0.93400900	-6.31176500	-0.91898000
F	1.15591600	-6.44181700	-2.23611900
F	-0.08855500	-5.44258200	-0.75435700
F	0.54538200	-7.51038600	-0.44675100
O	-1.35783100	-1.69177000	-1.73075700
C	-1.63365600	-2.23352100	-0.61078400
O	-1.18960600	-1.85588300	0.50917200
C	-2.50187100	-3.40441700	-0.70712800
S	-2.61947000	-4.23726300	-2.28694700
C	-3.71484100	-5.42627700	-1.53338200
C	-4.28263100	-6.51359300	-2.22179600
H	-4.04443900	-6.67599300	-3.25285300
C	-5.12612200	-7.33029500	-1.55828100
H	-5.57654100	-8.16517500	-2.05799800
C	-5.43881600	-7.11442400	-0.18429900
C	-6.32112100	-7.99097400	0.48584700
H	-6.74852200	-8.80636800	-0.06458800
C	-6.62142200	-7.81119300	1.79895200
H	-7.29067500	-8.48073900	2.30074200
C	-6.04139000	-6.74245300	2.50321100
H	-6.26781300	-6.60685400	3.54174600
C	-5.18899600	-5.87956500	1.88442100
H	-4.75007800	-5.08708000	2.44109700
C	-4.86387900	-6.03138200	0.51618000
C	-3.97385200	-5.15855900	-0.20909300
C	-3.25726500	-3.96659300	0.25262200
C	-3.48146600	-3.32147400	1.57429900
C	-2.82528400	-3.62741000	2.84476400
C	-1.80168200	-4.59212700	3.12800100
C	-1.24154800	-5.45071900	2.15404400
H	-1.56616100	-5.37867000	1.14238900

C	-0.29088900	-6.36542000	2.48873300
H	0.10078300	-7.01788800	1.73781200
C	0.17037400	-6.46730200	3.81420100
H	0.92286500	-7.18953000	4.05959200
C	-0.34124400	-5.65070800	4.77128300
H	0.00227500	-5.71721900	5.78523600
C	-1.34071400	-4.69984900	4.45859100
C	-1.88522200	-3.86580400	5.47572000
H	-1.51180400	-3.96635400	6.47562100
C	-2.85663400	-2.97050700	5.19368200
H	-3.27393100	-2.34481900	5.95623000
C	-3.31827400	-2.86782000	3.87167600
S	-4.61508500	-1.74067100	3.35348600
C	-4.41161000	-2.36123100	1.67373500
N	-5.14933800	-1.86119500	0.60185700
H	-4.87776000	-2.18409400	-0.30727900
C	-6.18084400	-1.00250500	0.69971000
O	-6.64733900	-0.54566500	1.71514800
C	-6.72449400	-0.58827500	-0.66097100
F	-5.98955400	0.43067300	-1.17696000
F	-7.98710100	-0.17228400	-0.56408600
F	-6.65879300	-1.60480100	-1.54158100

C₂-Symmetric (up-up-down-down) Structure



Electronic Energy = -9784.793983

Electronic and Zero-Point Energy = -9783.324750

Enthalpy = -9783.221097

Free Energy = -9783.468044

Rh	0.05935000	0.44742500	-1.18149000
Rh	0.02248500	-0.43596300	1.03328600
O	1.42042100	-1.06417000	-1.69357600
C	1.74086200	-1.90293600	-0.81900200
O	1.35262300	-1.86464000	0.40050600
C	2.45200900	-3.15670300	-1.10942900
S	1.83857300	-4.09483300	-2.51273800
C	2.86637300	-5.46243700	-1.99342200
C	2.90368500	-6.69986200	-2.65884400
H	2.29775700	-6.85814200	-3.52689700
C	3.71065700	-7.66641200	-2.17694800
H	3.76594200	-8.62031100	-2.66340400
C	4.49362200	-7.45629200	-1.00566300
C	5.29871900	-8.50281200	-0.50139800
H	5.31714700	-9.43451000	-1.03266200
C	6.02873600	-8.33969400	0.63234300
H	6.63510400	-9.13857700	1.00946000
C	5.98062800	-7.11317600	1.31661700
H	6.54809600	-6.98531100	2.21653200
C	5.22131400	-6.08389400	0.85133100
H	5.20220700	-5.16686100	1.38711500
C	4.45671800	-6.21406200	-0.33281900

C	3.61532200	-5.17674300	-0.87963000
C	3.39304300	-3.79928000	-0.39937000
C	4.25749000	-3.17109000	0.64273000
C	5.68150900	-2.86398800	0.41846200
C	6.46056100	-2.93125300	-0.79236000
C	5.93282700	-3.25945300	-2.06603500
H	4.89416000	-3.45787800	-2.16781600
C	6.73028600	-3.32050100	-3.16669400
H	6.30300800	-3.58013200	-4.11465100
C	8.10624400	-3.04188900	-3.07435200
H	8.72232400	-3.09615500	-3.94949200
C	8.64114200	-2.69759800	-1.87484500
H	9.68557700	-2.46945200	-1.78891800
C	7.84024000	-2.62942800	-0.71030400
C	8.42402600	-2.24960700	0.53056300
H	9.47149200	-2.02369500	0.55705300
C	7.67462600	-2.16538500	1.64954000
H	8.10396300	-1.87142500	2.58567100
C	6.30793600	-2.47509000	1.57329800
S	5.21013300	-2.41813600	2.98975700
C	3.86890800	-2.94661200	1.90981300
N	2.57155000	-3.05751800	2.36984800
H	1.88933200	-3.02688100	1.62674800
C	2.15329200	-2.82937200	3.62497000
O	2.83029500	-2.67609800	4.61236900
C	0.63428800	-2.70750700	3.67650900
F	0.26322700	-1.44917100	3.24921000
F	0.04568900	-3.56882700	2.83162800
F	0.15875800	-2.86487000	4.90563300
O	-1.45556700	-0.85535100	-1.64048100
C	-1.93999800	-1.61420300	-0.73627500
O	-1.53209600	-1.66659300	0.45819200
C	-3.08029600	-2.39901200	-1.19901100
S	-3.77247600	-1.93903900	-2.78505500
C	-5.01830900	-3.19550200	-2.56215300
C	-6.06071800	-3.42937800	-3.47639800
H	-6.13401200	-2.83670800	-4.36479100
C	-6.95955200	-4.39515400	-3.19690600
H	-7.77009600	-4.59150800	-3.87063100

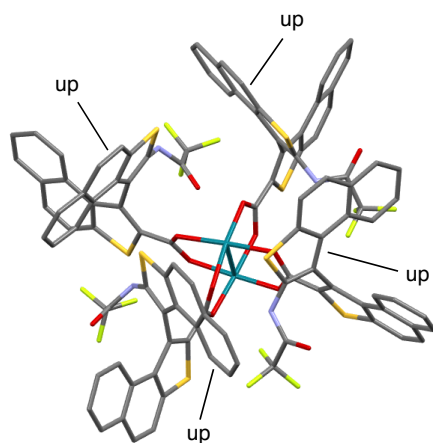
C	-6.86510100	-5.17279200	-2.00619900
C	-7.82487300	-6.17507900	-1.74118800
H	-8.61275600	-6.32933900	-2.45245800
C	-7.75601500	-6.92818200	-0.61223300
H	-8.48795800	-7.68612700	-0.41794000
C	-6.71299100	-6.71028600	0.30358700
H	-6.65289000	-7.30811200	1.19086500
C	-5.77355900	-5.75112800	0.07651100
H	-4.98594600	-5.61368400	0.77695200
C	-5.81814300	-4.94559600	-1.08550800
C	-4.86902600	-3.90266800	-1.39180100
C	-3.72403200	-3.42417500	-0.60987100
C	-3.30898000	-3.99475600	0.69715200
C	-2.54697500	-5.23112700	0.89184500
C	-2.00010100	-6.13031000	-0.08700500
C	-2.12111700	-5.94670600	-1.48592100
H	-2.64898100	-5.10081800	-1.85859600
C	-1.58280500	-6.83792700	-2.36104300
H	-1.69334200	-6.67848500	-3.41505300
C	-0.88553000	-7.96801400	-1.89554900
H	-0.46837400	-8.66317500	-2.59649700
C	-0.74663900	-8.17125300	-0.56011000
H	-0.21378300	-9.02578900	-0.19112400
C	-1.29632500	-7.26468100	0.37624700
C	-1.14051900	-7.49345400	1.77243200
H	-0.59966900	-8.36192700	2.09248100
C	-1.65745200	-6.63517300	2.67824500
H	-1.53904400	-6.80002500	3.72999800
C	-2.35996400	-5.50988500	2.22003800
S	-3.06802300	-4.26913400	3.30585900
C	-3.63752200	-3.38758000	1.84334400
N	-4.36733700	-2.21148000	1.93136300
H	-4.76519500	-1.87529800	1.07534800
C	-4.52026900	-1.47703400	3.05049700
O	-4.09893600	-1.73905800	4.14978500
C	-5.36667700	-0.24207900	2.79818600
F	-4.91859200	0.41146100	1.68930900
F	-6.64233800	-0.59276900	2.54757800
F	-5.34158900	0.59461600	3.83039600

O	-1.36371500	1.80680600	-0.59776100
C	-1.76192200	1.80171700	0.59998600
O	-1.32117100	1.03031400	1.51722900
C	-2.79867200	2.71378000	1.07133200
S	-3.01177800	2.85140300	2.84290100
C	-4.34321900	4.00221500	2.55408100
C	-5.09774600	4.59879800	3.58000600
H	-4.87804200	4.37481800	4.60347800
C	-6.09732900	5.43875700	3.24234800
H	-6.69494600	5.90208000	4.00247100
C	-6.38515200	5.73845300	1.87868600
C	-7.43118400	6.63218300	1.55814000
H	-8.00041300	7.06202300	2.35920600
C	-7.71058000	6.94638800	0.26587100
H	-8.50466700	7.62607000	0.03047800
C	-6.94352900	6.38085500	-0.76659500
H	-7.15266600	6.63950900	-1.78521000
C	-5.93123200	5.51318900	-0.48959300
H	-5.35244400	5.11161000	-1.28585200
C	-5.62286200	5.15401700	0.84342700
C	-4.57233900	4.23829300	1.21789500
C	-3.65761800	3.47290900	0.36628000
C	-3.71763200	3.46097600	-1.11910400
C	-3.06738800	4.41562300	-2.01886100
C	-2.26441200	5.56209200	-1.70020100
C	-1.91156900	5.93944500	-0.38158400
H	-2.24277900	5.34517800	0.43812200
C	-1.15713000	7.04574000	-0.14642200
H	-0.87867400	7.30231000	0.85440400
C	-0.71396900	7.85208900	-1.21211300
H	-0.09797300	8.70207200	-1.00713800
C	-1.03817400	7.52010200	-2.48721600
H	-0.70069600	8.12169000	-3.30869800
C	-1.81065500	6.36887500	-2.76708100
C	-2.12532000	6.02538600	-4.11169000
H	-1.75787900	6.65252300	-4.89983600
C	-2.87425400	4.93745500	-4.39431000
H	-3.11803600	4.67657300	-5.40415600
C	-3.34734000	4.15063000	-3.33283100

S	-4.41348400	2.72440500	-3.55266700
C	-4.45777800	2.54654800	-1.75881500
N	-5.22576200	1.56343100	-1.13930300
H	-5.16293800	1.51304100	-0.13950200
C	-6.07411500	0.73592800	-1.78118700
O	-6.26145800	0.67126800	-2.97089800
C	-6.82146800	-0.17186600	-0.82139700
F	-7.81255400	-0.81494500	-1.43054700
F	-7.31209300	0.53423700	0.21371700
F	-5.97370200	-1.09796300	-0.29637700
O	1.60102700	1.70276400	-0.55939900
C	2.08113100	1.53990400	0.59308900
O	1.60198700	0.75695000	1.48519000
C	3.30224100	2.20034600	1.04327200
S	4.01181800	1.62655000	2.58519200
C	5.37254900	2.75127200	2.33209800
C	6.44139300	2.90572000	3.23357000
H	6.46697000	2.32828700	4.13473800
C	7.41177600	3.79499400	2.93969100
H	8.23367500	3.94147300	3.61260400
C	7.38422100	4.55130300	1.73101100
C	8.43250100	5.45129200	1.43671000
H	9.22598700	5.56387200	2.14964200
C	8.44267600	6.15593500	0.27460000
H	9.24152500	6.83615200	0.05761100
C	7.40172300	5.97983200	-0.65257300
H	7.41847200	6.52061900	-1.57744100
C	6.37326000	5.12521400	-0.39427700
H	5.60496800	4.99578500	-1.11843300
C	6.32169100	4.39219900	0.81468100
C	5.26796100	3.47004500	1.16330000
C	4.03903800	3.14793500	0.43574400
C	3.57459900	3.90364700	-0.75650300
C	3.76315600	3.56942200	-2.16496700
C	4.42316600	2.43769300	-2.74771700
C	5.05288900	1.41921100	-1.99303100
H	5.04903800	1.47754600	-0.92845500
C	5.67065800	0.37346800	-2.60448300
H	6.14055800	-0.38780000	-2.01834000

C	5.69567900	0.28043600	-4.00922300
H	6.18309000	-0.55336500	-4.47116100
C	5.10679500	1.24427200	-4.76215800
H	5.12289800	1.18663300	-5.83331900
C	4.46116000	2.34752000	-4.15616400
C	3.86589900	3.36316700	-4.95666000
H	3.90633200	3.26403900	-6.02346200
C	3.26986700	4.43547600	-4.39073400
H	2.82849700	5.20635600	-4.98895300
C	3.23099700	4.52474800	-2.99025100
S	2.49401300	5.89657200	-2.09670700
C	2.93626900	5.06557700	-0.56490300
N	2.62558500	5.58326800	0.68964300
H	2.71083600	4.94989200	1.45957100
C	2.24231200	6.84520900	0.94285200
O	2.09878900	7.73665600	0.14002000
C	1.97205800	7.10432100	2.41998600
F	2.16057100	5.99638100	3.16444100
F	0.70271200	7.51728100	2.60003700
F	2.78197000	8.06780300	2.88305000

C₄-Symmetric (all-up) Structure



Electronic Energy = -9784.777226

Electronic and Zero-Point Energy = -9783.309628

Enthalpy = -9783.202935

Free Energy = -9783.455473

Rh	0.02056800	-0.06948500	-2.62776100
Rh	0.08448100	-0.01498500	-0.25669500
O	-1.72926800	0.96397200	-2.50586600
C	-2.26745700	1.18846300	-1.37189100
O	-1.76681700	0.85067800	-0.25736200
C	-3.49858000	1.96787600	-1.47754000
S	-4.19517900	2.14221500	-3.11529500
C	-5.47595600	3.16633700	-2.41966900
C	-6.53721300	3.70882700	-3.16710200
H	-6.61522100	3.49527500	-4.21332400
C	-7.44235300	4.48590400	-2.53891300
H	-8.26832300	4.90303300	-3.08080300
C	-7.31483000	4.79631900	-1.15343200
C	-8.24899100	5.65450200	-0.53164700
H	-9.06470600	6.03312500	-1.11649200
C	-8.11358700	6.00443600	0.77444100
H	-8.82387800	6.65882600	1.23880100
C	-7.02132700	5.51901300	1.51325800
H	-6.89652500	5.81926100	2.53423100
C	-6.11071400	4.68319300	0.94331300
H	-5.27483700	4.35275300	1.51049900
C	-6.23960600	4.27345700	-0.40308500

C	-5.31990000	3.38612300	-1.07129200
C	-4.17975100	2.63773600	-0.53004700
C	-3.74878200	2.65819200	0.89388500
C	-4.42499200	2.04160200	2.03918600
C	-5.63480100	1.26887200	2.07665700
C	-6.37160900	0.91063400	0.92422100
H	-6.02906500	1.22247200	-0.03319600
C	-7.51316600	0.17482400	1.01976200
H	-8.04649900	-0.08791100	0.12943100
C	-7.99130600	-0.24656100	2.27446900
H	-8.89631300	-0.81738100	2.33565800
C	-7.30053200	0.07328800	3.40007300
H	-7.64902900	-0.24718800	4.36261500
C	-6.10635800	0.82840400	3.33240700
C	-5.37415600	1.12649800	4.51672100
H	-5.75665000	0.77970600	5.45653800
C	-4.21910200	1.82365900	4.46220000
H	-3.66013500	2.04281500	5.34903200
C	-3.75840700	2.27915900	3.21464500
S	-2.26297200	3.24272600	2.98679300
C	-2.63164800	3.30458900	1.22708100
N	-1.79090200	3.95919700	0.32113800
H	-0.93286500	3.50878200	0.06350500
C	-2.16851800	5.13406100	-0.23662800
O	-3.07940500	5.83478300	0.12118100
C	-1.40197000	5.46805500	-1.50171500
F	-0.22622600	4.80355200	-1.55514400
F	-2.11944800	5.09708800	-2.57790100
F	-1.15368800	6.78160600	-1.60393600
O	1.09061400	1.69212400	-2.61382900
C	1.33379600	2.26672400	-1.51134800
O	0.84529500	1.90034700	-0.38800200
C	2.21185400	3.42274900	-1.58891600
S	2.48849000	4.14082300	-3.20408900
C	3.53169800	5.36570700	-2.43211600
C	4.15667800	6.41173800	-3.13418400
H	3.99932700	6.51567600	-4.18797800
C	4.94371200	7.26853700	-2.45252800
H	5.42651400	8.08080500	-2.95929300

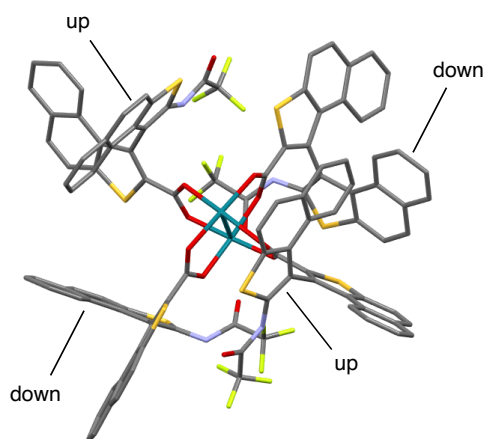
C	5.17154100	7.11101900	-1.05442700
C	6.02973700	8.00285000	-0.37334600
H	6.47932100	8.80401800	-0.92710100
C	6.28850000	7.84758100	0.95151900
H	6.94214300	8.52647700	1.46149800
C	5.70200800	6.78026000	1.65247800
H	5.91952600	6.64628100	2.69309600
C	4.86630800	5.90895700	1.02388700
H	4.44503400	5.10036900	1.57028200
C	4.55956100	6.05359000	-0.34771900
C	3.68047800	5.17471700	-1.07812700
C	2.87519600	4.04749300	-0.59920400
C	2.86216300	3.53530500	0.79812000
C	2.20519600	4.12511600	1.96681800
C	1.40621700	5.31431400	2.05869400
C	1.08817600	6.13489000	0.95047300
H	1.44947200	5.86937400	-0.01560100
C	0.31548100	7.24564800	1.09869700
H	0.06760000	7.83508800	0.24122500
C	-0.18378900	7.60823200	2.36377700
H	-0.79439000	8.48281900	2.46204800
C	0.09851500	6.83832500	3.44586400
H	-0.28537600	7.09638300	4.41350100
C	0.89110300	5.67280100	3.32349100
C	1.15398900	4.85812400	4.46121900
H	0.75017900	5.15700400	5.40835800
C	1.88367100	3.72688700	4.35397100
H	2.07263700	3.10433500	5.20449300
C	2.40150300	3.37164200	3.09702000
S	3.38179800	1.90047700	2.79363700
C	3.49209900	2.38988400	1.06836100
N	4.09519700	1.56236500	0.11372800
H	3.59525500	0.72377700	-0.11954400
C	5.16774300	1.97376700	-0.60346800
O	5.90510900	2.88411800	-0.33204000
C	5.35536600	1.20093700	-1.90519900
F	6.18827800	0.14549000	-1.77412600
F	4.16617500	0.72087100	-2.33820400
F	5.86328800	1.99963600	-2.84722500

O	1.79136500	-1.14129200	-2.60575300
C	2.40072400	-1.28977000	-1.50863300
O	2.03066900	-0.76024300	-0.40324500
C	3.60532100	-2.10651100	-1.54964300
S	4.31744700	-2.43081600	-3.15935800
C	5.56564900	-3.42172700	-2.36241300
C	6.62042700	-4.04616000	-3.05217500
H	6.71742400	-3.91437100	-4.11009400
C	7.49400300	-4.79840900	-2.35360400
H	8.31413700	-5.27842800	-2.85021100
C	7.34057700	-4.99830400	-0.95061300
C	8.24187900	-5.83396500	-0.25455200
H	9.05067800	-6.28063700	-0.79947900
C	8.08494700	-6.07724300	1.07314200
H	8.77085000	-6.71431300	1.59456200
C	7.00474400	-5.49911700	1.76050800
H	6.86630800	-5.70813500	2.80228900
C	6.12552400	-4.68268300	1.11741300
H	5.30553500	-4.27106500	1.65332400
C	6.27465600	-4.38706500	-0.25591500
C	5.38623600	-3.53009300	-1.00313200
C	4.25599500	-2.71867200	-0.53918700
C	3.77355200	-2.65897400	0.86967700
C	4.41762600	-2.01416400	2.01979300
C	5.63940900	-1.26255200	2.07969500
C	6.43001000	-0.96959200	0.94682500
H	6.12514700	-1.32203100	-0.00827300
C	7.56666600	-0.23027700	1.05517500
H	8.13443000	-0.00585500	0.17529400
C	7.99104300	0.25053000	2.30761300
H	8.88804800	0.83198000	2.37766300
C	7.25233400	-0.01367400	3.41656700
H	7.55801000	0.35624800	4.37580600
C	6.05716500	-0.76543200	3.33303700
C	5.26900500	-1.00173100	4.49477700
H	5.61279300	-0.61544500	5.43401200
C	4.10528900	-1.68263200	4.41886100
H	3.50132600	-1.85011400	5.28716800
C	3.69133400	-2.18101700	3.17156100

S	2.17816600	-3.10644800	2.91476300
C	2.61838600	-3.25191200	1.17836600
N	1.76692300	-3.87159200	0.25701900
H	0.91446200	-3.39093900	0.03006200
C	2.14328400	-4.99691600	-0.39254300
O	3.05551000	-5.72413600	-0.09773700
C	1.32025300	-5.28015800	-1.64313200
F	2.08863700	-5.82131100	-2.59166400
F	0.78049300	-4.13597100	-2.12019600
F	0.30096300	-6.13736300	-1.40825500
O	-1.03367100	-1.81832000	-2.52531500
C	-1.24859800	-2.35359700	-1.39964800
O	-0.71164800	-1.97018700	-0.30468300
C	-2.08485500	-3.55718700	-1.46412200
S	-2.27636900	-4.32676100	-3.07074400
C	-3.35598400	-5.53459700	-2.32548200
C	-3.97452900	-6.58053900	-3.03440900
H	-3.79077400	-6.69636500	-4.08270000
C	-4.79996200	-7.41463000	-2.36979800
H	-5.29079600	-8.21613200	-2.88577100
C	-5.03937700	-7.26131100	-0.97262900
C	-5.90229800	-8.15513300	-0.29988100
H	-6.37417300	-8.93430100	-0.86620500
C	-6.12901600	-8.03775100	1.03498500
H	-6.78343200	-8.72087800	1.53800900
C	-5.48948100	-7.01783700	1.76006200
H	-5.65348200	-6.93535000	2.81589700
C	-4.65513000	-6.13872400	1.13928900
H	-4.16661800	-5.38800900	1.71343400
C	-4.40874200	-6.22388500	-0.25147300
C	-3.54566800	-5.32815300	-0.97982700
C	-2.80168700	-4.16168900	-0.50106200
C	-2.96814000	-3.57120500	0.85387300
C	-2.23116800	-3.89053100	2.07733100
C	-1.26874400	-4.93048500	2.30390400
C	-0.82810300	-5.81816100	1.29751200
H	-1.18997900	-5.70486000	0.30349400
C	0.05279400	-6.81649900	1.57961100
H	0.37853500	-7.46751800	0.79487200

C	0.54873400	-6.98653200	2.88495900
H	1.24734900	-7.77235500	3.08922200
C	0.14549900	-6.14710400	3.87427000
H	0.51983000	-6.26231700	4.87268000
C	-0.77194000	-5.10301700	3.61361300
C	-1.20323700	-4.23951100	4.66092600
H	-0.79472200	-4.38203400	5.64195100
C	-2.12085600	-3.27455300	4.43620500
H	-2.46195300	-2.63605000	5.22512500
C	-2.64657800	-3.13012000	3.14025300
S	-3.96014100	-1.98954000	2.70988000
C	-3.92812000	-2.66344700	1.03915100
N	-4.92658100	-2.30345800	0.11840900
H	-5.85303400	-2.63182100	0.30352100
C	-4.72904800	-1.55621800	-0.97566500
O	-3.69415400	-1.04591300	-1.33230100
C	-5.97929300	-1.39825500	-1.83565900
F	-6.32647200	-0.10252600	-1.95054000
F	-7.03566700	-2.05418100	-1.30500600
F	-5.76186500	-1.87775000	-3.06668900

***D*₂-Symmetric (up-down-up-down) Structure**



Electronic Energy = -9784.804892

Electronic and Zero-Point Energy = -9783.338010

Enthalpy = -9783.231383

Free Energy = -9783.485739

Rh	0.00017600	-0.00006200	-1.13325500
Rh	-0.00005900	0.00009100	1.25947300
O	-0.59130400	1.96231600	-1.00290300
C	-0.58860800	2.56430200	0.10986800
O	-0.34232900	2.03089900	1.23094800
C	-1.01282800	3.96060000	0.10278500
S	-1.90298300	4.55531400	1.53638300
C	-2.17949500	6.09451300	0.67418300
C	-2.94782900	7.15318800	1.19005600
H	-3.41229200	7.05644300	2.14951500
C	-3.09694600	8.26640100	0.44284900
H	-3.68451000	9.08680100	0.80496100
C	-2.49057700	8.38201900	-0.84190500
C	-2.66555500	9.55912700	-1.60396100
H	-3.25877500	10.35179100	-1.19133200
C	-2.09812900	9.68850000	-2.83183200
H	-2.23587900	10.58440000	-3.40319000
C	-1.32201600	8.63857900	-3.35235500
H	-0.86785700	8.74302400	-4.31734700
C	-1.13604000	7.49164500	-2.64291700
H	-0.53297000	6.71556900	-3.05042300
C	-1.71666000	7.32199900	-1.36366600

C	-1.57623700	6.13357000	-0.56056800
C	-0.89119800	4.87426200	-0.87287100
C	-0.09212500	4.62025600	-2.09988000
C	1.27531500	5.10024600	-2.33824400
C	2.13294600	5.88515700	-1.49005300
C	1.76438400	6.35574000	-0.20673100
H	0.79562700	6.13460800	0.17255700
C	2.62427900	7.09449300	0.54609400
H	2.31607600	7.44418800	1.51117400
C	3.90971700	7.40822400	0.06811700
H	4.57554200	7.99264600	0.67113700
C	4.29656500	6.96816600	-1.15741000
H	5.27422100	7.19741100	-1.53460900
C	3.42666400	6.19877600	-1.96412000
C	3.85560200	5.73832100	-3.24150800
H	4.84189300	5.99643300	-3.57377100
C	3.04548100	4.98950300	-4.01926900
H	3.36692100	4.62988200	-4.97529900
C	1.75677900	4.68127200	-3.55245500
S	0.58399500	3.67400300	-4.45928700
C	-0.57168800	3.87390800	-3.09678400
N	-1.83989300	3.28964200	-3.13618200
H	-2.61557800	3.84591400	-2.83253400
C	-2.01924400	1.96427900	-3.30689000
O	-1.18606200	1.14981700	-3.62263600
C	-3.45697800	1.54728800	-3.04742600
F	-4.31439800	2.47981400	-3.51422400
F	-3.74085800	0.37460900	-3.60633800
F	-3.68571300	1.45542000	-1.70897300
O	1.93742800	0.68580000	-1.04555600
C	2.54694300	0.64281800	0.07148300
O	2.03666400	0.29800800	1.17304200
C	3.94503700	1.05310600	0.01752300
S	4.50129400	1.97183400	-1.41159700
C	6.12153600	2.06143200	-0.66935400
C	7.22420500	2.69691400	-1.26889000
H	7.11128100	3.17385200	-2.22074400
C	8.40972600	2.68135700	-0.62641000
H	9.26908100	3.15159500	-1.06261600

C	8.55607100	2.04836100	0.64276400
C	9.80842100	2.05552500	1.29658500
H	10.63612400	2.53595300	0.81202200
C	9.96507000	1.47058300	2.51323700
H	10.91796000	1.48040800	3.00314500
C	8.86483900	0.85503400	3.13400300
H	8.98433500	0.40366100	4.09849700
C	7.64590600	0.82928100	2.52763100
H	6.82334600	0.37034700	3.02140800
C	7.45112000	1.41869900	1.25646600
C	6.19425100	1.42717500	0.54935600
C	4.90661500	0.84496100	0.93225900
C	4.68601300	0.02445400	2.15014600
C	4.35195100	0.52188900	3.48317300
C	4.11980100	1.87128700	3.91452300
C	4.16968700	2.99483100	3.05415100
H	4.39902300	2.85484200	2.02372100
C	3.92427200	4.24851200	3.52084000
H	3.95620700	5.07946000	2.84507800
C	3.62059900	4.45979900	4.87895000
H	3.42920800	5.45298100	5.23327100
C	3.56758400	3.40379600	5.73125600
H	3.33410900	3.55105100	6.76788200
C	3.81026100	2.08658300	5.27547900
C	3.73572200	0.98703400	6.17691300
H	3.49803800	1.18174600	7.20408600
C	3.95147600	-0.27729000	5.75185500
H	3.88921300	-1.10787600	6.42521400
C	4.25562600	-0.49211800	4.39814100
S	4.55176600	-2.11385000	3.68336700
C	4.79587900	-1.30822200	2.08887100
N	5.03505400	-2.02813200	0.92091800
H	5.00647200	-1.50343400	0.06766700
C	5.25916400	-3.35335800	0.85505500
O	5.33365800	-4.12131400	1.78354600
C	5.37792900	-3.84832100	-0.57966600
F	5.99864300	-2.93577400	-1.35271400
F	6.05002700	-4.99855500	-0.63413900
F	4.15006100	-4.05614500	-1.11788500

O	0.59167300	-1.96229400	-1.00226800
C	0.58866000	-2.56427800	0.11051600
O	0.34214900	-2.03083400	1.23149100
C	1.01286900	-3.96056800	0.10298900
S	1.90329500	-4.55579400	1.53619900
C	2.17976400	-6.09463300	0.67333500
C	2.94828900	-7.15344700	1.18864100
H	3.41294600	-7.05703300	2.14803800
C	3.09734400	-8.26635300	0.44096700
H	3.68505100	-9.08684600	0.80263600
C	2.49071600	-8.38151800	-0.84370600
C	2.66561800	-9.55831700	-1.60625300
H	3.25898200	-10.35109800	-1.19405700
C	2.09794300	-9.68725700	-2.83405700
H	2.23563800	-10.58292900	-3.40578800
C	1.32164300	-8.63719600	-3.35400900
H	0.86728200	-8.74130100	-4.31894300
C	1.13573300	-7.49054800	-2.64408700
H	0.53250800	-6.71436800	-3.05116700
C	1.71661200	-7.32135200	-1.36489800
C	1.57627600	-6.13324100	-0.56131400
C	0.89111400	-4.87385100	-0.87300800
C	0.09164300	-4.61955300	-2.09971300
C	-1.27582200	-5.09968700	-2.33773600
C	-2.13308900	-5.88489600	-1.48943500
C	-1.76408900	-6.35568100	-0.20631600
H	-0.79527100	-6.13446200	0.17275600
C	-2.62364100	-7.09475600	0.54659000
H	-2.31509600	-7.44460400	1.51150500
C	-3.90916100	-7.40860500	0.06892100
H	-4.57471100	-7.99328000	0.67199900
C	-4.29643600	-6.96834000	-1.15639900
H	-5.27416100	-7.19766600	-1.53336600
C	-3.42689100	-6.19864200	-1.96319300
C	-3.85627400	-5.73802500	-3.24037700
H	-4.84261400	-5.99625300	-3.57240500
C	-3.04650400	-4.98893900	-4.01823600
H	-3.36827100	-4.62920500	-4.97411300
C	-1.75771400	-4.68058300	-3.55173700

S	-0.58534100	-3.67305500	-4.45878500
C	0.57080500	-3.87305200	-3.09669200
N	1.83894300	-3.28861600	-3.13653600
H	2.61497200	-3.84510700	-2.83418500
C	2.01805000	-1.96314800	-3.30637000
O	1.18450000	-1.14845700	-3.62068200
C	3.45598000	-1.54621600	-3.04779600
F	3.73947900	-0.37340800	-3.60663600
F	4.31307400	-2.47863700	-3.51545100
F	3.68565800	-1.45470100	-1.70950500
O	-1.93715500	-0.68589500	-1.04588600
C	-2.54681100	-0.64277200	0.07106200
O	-2.03668300	-0.29780900	1.17265700
C	-3.94488100	-1.05312700	0.01718400
S	-4.50120100	-1.97174800	-1.41197100
C	-6.12137100	-2.06152100	-0.66960200
C	-7.22405000	-2.69700700	-1.26911700
H	-7.11117800	-3.17381600	-2.22104300
C	-8.40950700	-2.68163200	-0.62651800
H	-9.26886700	-3.15188800	-1.06269600
C	-8.55577500	-2.04881600	0.64275600
C	-9.80806500	-2.05615400	1.29669000
H	-10.63577700	-2.53658400	0.81214300
C	-9.96464900	-1.47136800	2.51342500
H	-10.91749400	-1.48132300	3.00341800
C	-8.86441100	-0.85580400	3.13416100
H	-8.98385700	-0.40454300	4.09871400
C	-7.64553300	-0.82989200	2.52768400
H	-6.82296600	-0.37093900	3.02143100
C	-7.45081400	-1.41915500	1.25643700
C	-6.19400400	-1.42745000	0.54920800
C	-4.90637200	-0.84519800	0.93207400
C	-4.68568000	-0.02502600	2.15017300
C	-4.35140900	-0.52289800	3.48300000
C	-4.11918700	-1.87243000	3.91389600
C	-4.16918700	-2.99571300	3.05318900
H	-4.39867200	-2.85541200	2.02283600
C	-3.92371200	-4.24953700	3.51946100
H	-3.95574100	-5.08027200	2.84344600

C	-3.61984600	-4.46124300	4.87746200
H	-3.42841300	-5.45453400	5.23145300
C	-3.56669800	-3.40550000	5.73008000
H	-3.33307000	-3.55306900	6.76662600
C	-3.80943800	-2.08814700	5.27474000
C	-3.73476000	-0.98888300	6.17650800
H	-3.49691600	-1.18391800	7.20358200
C	-3.95058300	0.27557100	5.75187700
H	-3.88822200	1.10594900	6.42548200
C	-4.25493900	0.49081800	4.39827600
S	-4.55122300	2.11277400	3.68408600
C	-4.79555800	1.30766600	2.08935900
N	-5.03488900	2.02799200	0.92169500
H	-5.00631500	1.50363400	0.06823700
C	-5.25906100	3.35324100	0.85638900
O	-5.33347400	4.12081800	1.78519700
C	-5.37807900	3.84876200	-0.57811100
F	-5.99914200	2.93660900	-1.35133900
F	-4.15028100	4.05653600	-1.11654400
F	-6.04994900	4.99914600	-0.63201500

NBO Analysis for Complex (S)-10b (Figure 25)

We performed NBO analysis for Complex (S)-10b to investigate intramolecular orbital interactions at the M06/6-31G+(d,p)-LanL2DZ(Rh) level, based on the crystal structure of (S)-10b with two EtOH molecules as axial ligands (CCDC 1837271), using the Gaussian 16 software package (threshold for printing: 0.50 kcal/mol).⁴⁵

(1) For ligand I

Second order perturbation theory analysis of Fock matrix in NBO basis

Donor NBO (i)	Acceptor NBO (j)	E(2) kcal/mol	E(j) – E(i) a.u.	F(i,j) a.u.
BD(1) N160–H161 (#209)	BD*(1) S158–C159 (#1478)	4.64	0.94	0.059
LP(1) O121 (#548)	BD*(1) S123–C124 (#1427)	0.68	0.81	0.021
LP(1) O163 (#556)	BD*(1) C157–S158 (#1477)	0.73	0.94	0.024
LP(2) O163 (#557)	BD*(1) C157–S158 (#1477)	2.34	0.49	0.031

(2) For ligand II

Second order perturbation theory analysis of Fock matrix in NBO basis

Donor NBO (i)	Acceptor NBO (j)	E(2) kcal/mol	E(j) – E(i) a.u.	F(i,j) a.u.
BD(1) N111–H112 (#142)	BD*(1) S109–C110 (#1411)	2.82	0.96	0.047
LP(2) O114 (#534)	BD*(1) C108–S109 (#1410)	0.58	0.48	0.015

(1) For ligand III

Second order perturbation theory analysis of Fock matrix in NBO basis

Donor NBO (i)	Acceptor NBO (j)	E(2) kcal/mol	E(j) – E(i) a.u.	F(i,j) a.u.
BD(1) N209–H210 (#276)	BD*(1) S207–C208 (#1545)	4.28	0.96	0.057
LP(1) O168 (#567)	BD*(1) S172–C173 (#1494)	0.71	0.80	0.022
LP(2) O170 (#572)	BD*(1) C171–S172 (#1491)	0.57	0.63	0.018
LP(1) O212 (#579)	BD*(1) C206–S207 (#1544)	0.72	0.91	0.023
LP(2) O212 (#580)	BD*(1) C206–S207 (#1544)	2.42	0.47	0.031

(1) For ligand IV

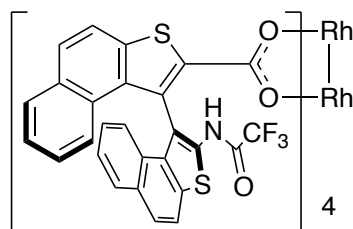
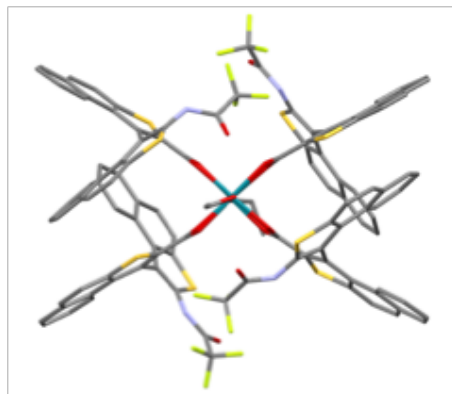
Second order perturbation theory analysis of Fock matrix in NBO basis

Donor NBO (i)	Acceptor NBO (j)	E(2) kcal/mol	E(j) – E(i) a.u.	F(i,j) a.u.
BD(1) N62–H63 (#75)	BD*(1) S60–C61 (#1343)	4.06	0.95	0.055
LP(2) O21 (#499)	BD*(1) C24–S25 (#1290)	0.54	0.63	0.018
LP(1) O23 (#502)	BD*(1) S25–C26 (#1293)	0.66	0.78	0.020
LP(2) O65 (#511)	BD*(1) C59–S60 (#1344)	1.22	0.49	0.022

Optimized Structure of Complex (S)-10b and Naphthofuran-Type Complex (S)-52 (Figure 26)

The structures of naphthothiophene-type complex (S)-10b and naphthofuran-type complex (S)-52 with coordination of two EtOH molecules as the axial ligands at the rhodium atoms were optimized by M06/6-31G(d,p)-LanL2DZ(Rh) calculations, using the Gaussian 16 software package.⁴⁵

XYZ Coordinates of Naphthothiophene-Type Complex (S)-10b



Rh	0.05361200	0.01393000	-1.24054800
Rh	0.03460200	0.05319500	1.21309900
O	0.02903400	-0.07792600	-3.48805500
H	-0.21547100	0.83210700	-3.76966700
C	1.31518900	-0.46291700	-4.06641200
H	1.50085000	-1.47470600	-3.69772700
H	2.09803300	0.20115300	-3.66821100
C	1.23596900	-0.42428800	-5.57400900
H	2.19951200	-0.71076700	-6.01447800
H	0.46986200	-1.12506200	-5.92235500
H	0.98709500	0.58618900	-5.92505900
O	0.25297700	0.04719300	3.47132900
H	0.97012600	-0.55503600	3.75272600
C	-0.93563400	-0.05094600	4.30548100
H	-1.69266200	0.52137700	3.75770000
H	-0.73795100	0.46450100	5.25682900
C	-1.36615500	-1.48675200	4.50878300
H	-2.30959100	-1.52604400	5.06775300
H	-1.51587500	-1.97145200	3.53723100
H	-0.61271300	-2.05731400	5.06987300
O	1.54301700	1.47091000	-1.17820800

C	1.93365000	1.90141000	-0.02460000
O	1.39972900	1.58959100	1.10548900
C	3.06365500	2.82367000	0.04439500
S	3.40032800	3.53936100	1.65128300
C	4.83479800	4.34015600	0.95203700
C	5.71282900	5.14574400	1.70452400
H	5.52852200	5.31078300	2.76226600
C	6.78747800	5.70489700	1.06865100
H	7.49324900	6.32281900	1.61898400
C	6.99940600	5.52132600	-0.32945400
C	8.09387300	6.15785300	-0.96139700
H	8.76814000	6.75204300	-0.34817700
C	8.29821400	6.04366300	-2.31820800
H	9.14017000	6.53910400	-2.79227100
C	7.39468100	5.29112900	-3.09165500
H	7.53571100	5.21600400	-4.16593300
C	6.32341000	4.64956600	-2.50268300
H	5.64066500	4.09483800	-3.13395500
C	6.09845500	4.72203700	-1.10607500
C	5.00433200	4.07761200	-0.41610900
C	3.98846600	3.16861700	-0.91636500
C	3.93077300	2.66027500	-2.30388700
C	4.86908500	1.76204400	-2.94595600
C	5.93670300	0.99237700	-2.36758500
C	6.18253800	0.90517400	-0.97462600
H	5.52920000	1.42758800	-0.28104200
C	7.21851500	0.13706600	-0.48194500
H	7.37832500	0.06306800	0.59183700
C	8.06827100	-0.56955800	-1.35664900
H	8.88451300	-1.16244300	-0.95459800
C	7.83393500	-0.53107800	-2.71245500
H	8.46437800	-1.09294500	-3.39943300
C	6.76155300	0.22247500	-3.24906600
C	6.48592200	0.18179200	-4.64633700
H	7.12988200	-0.42040800	-5.28293600
C	5.41918400	0.85616700	-5.18078300
H	5.18619300	0.79914100	-6.23986800
C	4.62976000	1.64044600	-4.31929600
S	3.18933000	2.57381400	-4.85955800

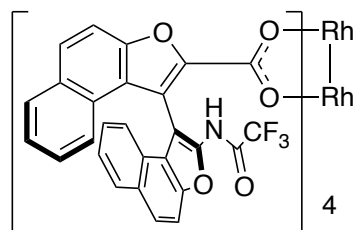
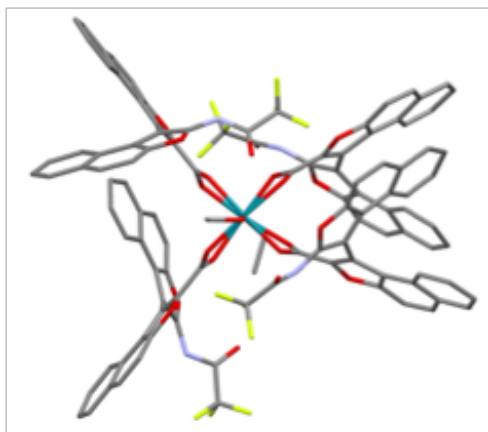
C	2.96422900	3.10647900	-3.15983100
N	1.87686700	3.90541500	-2.78569900
H	2.06588800	4.66727200	-2.13989100
C	0.58181700	3.56070200	-3.01893200
O	0.18748100	2.68526200	-3.79462600
C	-0.39191600	4.40154500	-2.19780700
F	-0.03987700	5.73530300	-2.27979700
F	-1.67179000	4.26705200	-2.61192500
F	-0.32729800	4.06104300	-0.85967000
O	1.59500100	-1.37543400	-1.14520500
C	2.14619400	-1.58509000	0.00351300
O	1.64880200	-1.23323900	1.13996400
C	3.44918800	-2.24333400	0.01177000
S	4.36603600	-2.38148700	-1.52149200
C	5.70094200	-3.14675800	-0.60576800
C	6.88265200	-3.63218300	-1.19970900
H	7.02509500	-3.55253600	-2.27313200
C	7.83143200	-4.19871600	-0.39127800
H	8.75230800	-4.59108700	-0.81725200
C	7.65105300	-4.28845400	1.02122300
C	8.66284700	-4.85450200	1.83229600
H	9.56753400	-5.21977400	1.35069400
C	8.51230000	-4.94195200	3.19875700
H	9.29600500	-5.37803700	3.81102100
C	7.33441000	-4.45969300	3.80124800
H	7.21539600	-4.52217600	4.87893200
C	6.32645900	-3.90615400	3.03699900
H	5.43107400	-3.54176700	3.52807000
C	6.44860300	-3.80686400	1.63048200
C	5.44045700	-3.23943000	0.77004300
C	4.13706400	-2.71765300	1.10672800
C	3.47412700	-2.77574600	2.42875100
C	3.49989400	-1.78853100	3.48272900
C	4.22269900	-0.54794900	3.55325100
C	5.08190700	-0.07501800	2.52950000
H	5.20286900	-0.65227100	1.61704900
C	5.76861300	1.11337500	2.67340800
H	6.41721900	1.46930900	1.87454900
C	5.63193000	1.88865500	3.84290900

H	6.18499800	2.81912900	3.94037100
C	4.78893400	1.46749200	4.84461900
H	4.66056200	2.06028700	5.74768700
C	4.06643400	0.25448800	4.72985000
C	3.20405100	-0.16544100	5.78346000
H	3.10680000	0.47353500	6.65768700
C	2.50919200	-1.34599900	5.70545800
H	1.85263500	-1.67046200	6.50855700
C	2.66521300	-2.13822900	4.54988200
S	1.79892200	-3.69790900	4.28713600
C	2.62310700	-3.81472000	2.69489900
N	2.32240900	-4.82641800	1.78717200
H	2.72154000	-4.72580500	0.85652000
C	1.49977000	-5.88017400	2.02976300
O	0.91104500	-6.11659800	3.09109300
C	1.31527600	-6.82100400	0.84886500
F	2.11947000	-6.47748000	-0.22244900
F	1.63020300	-8.10181700	1.20487500
F	0.01686100	-6.81039300	0.42302100
O	-1.41649300	-1.40599500	-1.10792900
C	-1.87007000	-1.79832400	0.03213200
O	-1.35998100	-1.49004700	1.17781500
C	-3.03280500	-2.67944800	0.02407100
S	-3.53494300	-3.37291600	1.59842200
C	-4.91785900	-4.14516400	0.77168600
C	-5.87761300	-4.92767000	1.44369100
H	-5.79638300	-5.08841000	2.51485100
C	-6.89944100	-5.46998900	0.71238200
H	-7.66565300	-6.07031400	1.19763600
C	-6.97533200	-5.29384400	-0.70046700
C	-8.01776500	-5.91339900	-1.42989000
H	-8.75988500	-6.48906100	-0.88064100
C	-8.08805900	-5.80559700	-2.80070300
H	-8.89124200	-6.28714300	-3.35044600
C	-7.09852900	-5.07850300	-3.48905200
H	-7.13449300	-5.01002700	-4.57233800
C	-6.07521500	-4.45379200	-2.80480000
H	-5.32084200	-3.91752200	-3.36707900
C	-5.98870100	-4.51957800	-1.39293800

C	-4.95283900	-3.88903200	-0.60740200
C	-3.87666300	-3.00695800	-1.02294300
C	-3.67333100	-2.49738800	-2.39902600
C	-4.53879600	-1.60019400	-3.13811700
C	-5.71604100	-0.89245700	-2.71118400
C	-6.14009600	-0.80971900	-1.36232000
H	-5.53744200	-1.27889300	-0.58936800
C	-7.27711200	-0.10966000	-1.01046700
H	-7.56725800	-0.03198400	0.03511000
C	-8.06043200	0.52413200	-1.99603900
H	-8.96208900	1.05726400	-1.70870100
C	-7.65268500	0.49741800	-3.31033200
H	-8.22682500	1.01236100	-4.07881200
C	-6.46622100	-0.17328600	-3.69682500
C	-6.00429800	-0.09497700	-5.04170400
H	-6.59558700	0.46615800	-5.76157100
C	-4.82412500	-0.68213800	-5.41692200
H	-4.44532600	-0.59171500	-6.43072400
C	-4.11303700	-1.42756700	-4.45930700
S	-2.55525400	-2.25640500	-4.80920100
C	-2.58654000	-2.89401100	-3.13797600
N	-1.55542200	-3.67854800	-2.63920800
H	-1.69891400	-4.00581400	-1.68665200
C	-0.30365600	-3.75762000	-3.15590700
O	0.06323300	-3.34030400	-4.26052300
C	0.65594700	-4.53924800	-2.26897800
F	1.95040700	-4.22820400	-2.52647700
F	0.48423000	-5.88769000	-2.47608900
F	0.42402000	-4.31029600	-0.91753900
O	-1.47986400	1.39398100	-1.21089200
C	-2.07788500	1.62292700	-0.08537400
O	-1.61163000	1.32251000	1.07800400
C	-3.39204600	2.25421200	-0.16806100
S	-4.15772400	2.38144300	-1.78483300
C	-5.59868000	3.09098800	-1.00227800
C	-6.72958800	3.53074600	-1.71719500
H	-6.75867000	3.43793600	-2.79850300
C	-7.77678100	4.05985400	-1.01385000
H	-8.66740800	4.40844500	-1.53231200

C	-7.73722900	4.17345400	0.40736100
C	-8.84228600	4.72229500	1.09996900
H	-9.70816300	5.03799600	0.52153800
C	-8.82695700	4.85982600	2.47016600
H	-9.68108600	5.28266800	2.99071000
C	-7.69065200	4.45214200	3.19374100
H	-7.66970200	4.56333900	4.27391300
C	-6.59645300	3.91230400	2.54709100
H	-5.73767400	3.61518800	3.13616500
C	-6.58230300	3.74847600	1.14068800
C	-5.47980600	3.19000000	0.39282200
C	-4.20188300	2.69472600	0.85742100
C	-3.72335700	2.73960200	2.25628900
C	-4.04249900	1.82963300	3.33340200
C	-4.81095800	0.61293300	3.31132900
C	-5.39373900	0.06276700	2.14197000
H	-5.25255100	0.55565600	1.18372000
C	-6.13502300	-1.10100500	2.19892800
H	-6.56851700	-1.51786100	1.29173500
C	-6.32453900	-1.77824600	3.42006700
H	-6.91562700	-2.68975500	3.44475600
C	-5.75125500	-1.28292800	4.56809700
H	-5.87800200	-1.79739100	5.51860900
C	-4.98961700	-0.08901200	4.54818700
C	-4.40942800	0.40362600	5.75293600
H	-4.57178000	-0.15640400	6.67122900
C	-3.66080400	1.55187400	5.76099000
H	-3.20793300	1.92635400	6.67473200
C	-3.48529800	2.24234300	4.54818600
S	-2.47860600	3.72651500	4.39857200
C	-2.89227000	3.75482700	2.65025300
N	-2.36579600	4.71221700	1.78748500
H	-2.57061100	4.57967100	0.79928200
C	-1.57511800	5.75279100	2.15684000
O	-1.21156700	6.02180100	3.30777500
C	-1.09562400	6.61601400	0.99961300
F	-1.80758900	6.37174200	-0.16113400
F	0.22785500	6.37902000	0.73511600
F	-1.23184700	7.94038300	1.29455100

XYZ Coordinates of Naphthofuran-Type Complex (S)-52



Rh	0.39532900	-0.34464700	1.18364100
Rh	0.35940800	0.47188000	-1.12950100
O	0.56153400	-0.90478400	3.39845400
H	0.01871600	-1.70800900	3.56363500
C	1.95533800	-1.16919400	3.78092300
H	2.46301000	-0.21374400	3.63674600
H	2.38015900	-1.89954700	3.07786800
C	2.02065300	-1.65706400	5.20980500
H	3.06723400	-1.75640200	5.52447800
H	1.52251600	-0.94818200	5.88069800
H	1.53831600	-2.63805000	5.30625200
O	0.35775300	1.07346100	-3.32828500
H	1.26861100	1.22135500	-3.65684100
C	-0.54996700	2.18437400	-3.65319300
H	-1.47158300	1.92486500	-3.12188900
H	-0.74656700	2.15236500	-4.73272600
C	-0.00754900	3.51322000	-3.18821100
H	-0.76851100	4.29565500	-3.28031000
H	0.28749100	3.46004100	-2.13247000
H	0.85880000	3.84025700	-3.77433400
O	1.66556900	-1.84573600	0.52669000
C	2.11436100	-1.79517600	-0.68539400
O	1.89469200	-0.84883200	-1.52815100
C	2.91919800	-2.93272500	-1.11253600
C	3.89406500	-4.21040500	-2.63491400
C	4.30380900	-4.71190400	-3.87779900
H	4.00836900	-4.21267700	-4.79457000
C	5.05649600	-5.85888800	-3.84777300

H	5.40758800	-6.30483600	-4.77508000
C	5.39422000	-6.51351300	-2.62028700
C	6.16250400	-7.70197200	-2.63185300
H	6.49493100	-8.09514800	-3.59026600
C	6.48227500	-8.35346100	-1.46010700
H	7.07210800	-9.26486800	-1.48498800
C	6.04097400	-7.83761700	-0.22504500
H	6.29322400	-8.35535500	0.69565400
C	5.29148400	-6.67956700	-0.17569800
H	4.95664900	-6.29055100	0.78170000
C	4.95332800	-5.98941500	-1.36106500
C	4.18032100	-4.78634400	-1.39843100
C	3.53785800	-3.94726200	-0.40909900
C	3.53668600	-4.10662800	1.04391600
C	4.63280500	-3.98680100	1.98558000
C	6.02179700	-3.68090200	1.87490700
C	6.67824100	-3.43115300	0.64789100
H	6.10968800	-3.48553600	-0.27675000
C	8.02186400	-3.12132300	0.61629200
H	8.50795600	-2.92619700	-0.33593300
C	8.76758300	-3.05684700	1.81246100
H	9.82540000	-2.81394000	1.77609800
C	8.15357200	-3.30010500	3.02158200
H	8.72161500	-3.25016600	3.94814300
C	6.77347200	-3.61255300	3.09323900
C	6.14257900	-3.84296800	4.35436100
H	6.75360000	-3.78022000	5.25121700
C	4.80127800	-4.12738000	4.45369200
H	4.30196900	-4.29372700	5.40171000
C	4.09030500	-4.19033900	3.25036200
C	2.42925000	-4.36261600	1.80581200
N	1.12028900	-4.60773500	1.42671200
H	0.99568700	-4.99533100	0.49669900
C	0.00799300	-4.19698200	2.10117100
O	-0.02577600	-3.56110300	3.15614200
C	-1.26962600	-4.70273700	1.44029200
F	-1.31694200	-6.08225100	1.51730100
F	-2.38012700	-4.20922800	2.02221200
F	-1.26375200	-4.39608700	0.09223800

O	1.97387300	0.93212000	1.52510800
C	2.23284600	1.84349400	0.65302000
O	1.68584100	1.94566300	-0.51204200
C	3.23534000	2.84574900	0.98462200
C	4.51164200	4.01648600	2.36337400
C	5.08395900	4.52082500	3.53925100
H	4.82215200	4.10110800	4.50358800
C	5.96151000	5.56488500	3.38911100
H	6.43049800	6.01132800	4.26236800
C	6.29584700	6.09815400	2.10363900
C	7.21460000	7.16777600	1.98629700
H	7.64544500	7.58204600	2.89530300
C	7.56393800	7.67763100	0.75376200
H	8.26825700	8.50074400	0.68211300
C	7.01666000	7.11907600	-0.41811400
H	7.31547900	7.50362400	-1.38891000
C	6.11399400	6.07585000	-0.34130300
H	5.74127000	5.61397300	-1.25308900
C	5.71715200	5.55339400	0.91196300
C	4.76874200	4.49660200	1.07917500
C	3.93060400	3.73104000	0.19027400
C	3.79499700	3.81569200	-1.25982600
C	3.96848700	2.75508600	-2.22790500
C	4.47819900	1.42410700	-2.16737800
C	5.11061000	0.86865300	-1.03099000
H	5.21486800	1.46530000	-0.12975600
C	5.63347500	-0.40760800	-1.06969700
H	6.13383400	-0.81649700	-0.19478800
C	5.52778700	-1.18482700	-2.24132700
H	5.94209100	-2.19186100	-2.26440800
C	4.89849200	-0.67560200	-3.35585200
H	4.79132900	-1.28124200	-4.25360000
C	4.37676600	0.63959900	-3.36125300
C	3.79690200	1.18814000	-4.54836500
H	3.71145800	0.54383300	-5.41948800
C	3.37595600	2.49782200	-4.61457600
H	2.96835000	2.93895100	-5.51800400
C	3.50800300	3.25219100	-3.43950800
C	3.30097600	4.88315400	-1.95816300

N	3.02584600	6.18349400	-1.55550000
H	3.71522100	6.64509000	-0.96584700
C	1.87556900	6.85768100	-1.86534200
O	0.90927900	6.42660800	-2.48965600
C	1.89178200	8.31408800	-1.41024200
F	2.84112800	8.54228000	-0.43105800
F	2.19302400	9.13454800	-2.46713000
F	0.68101900	8.68621000	-0.91501700
O	-0.94913800	1.16424800	1.56790500
C	-1.71066200	1.58527900	0.60325400
O	-1.35767700	1.60091400	-0.63003000
C	-3.02940700	1.99880700	1.03522700
C	-4.87717300	3.20603900	0.92404300
C	-5.81314800	4.15870300	0.50351300
H	-5.63838500	4.74408700	-0.39189000
C	-6.94157200	4.27932200	1.27277200
H	-7.71272300	4.99634500	0.99987500
C	-7.14797000	3.48916400	2.44730000
C	-8.31669700	3.66415900	3.22628800
H	-9.05224600	4.39644300	2.89944900
C	-8.51904200	2.93536500	4.37808100
H	-9.41963400	3.08133000	4.96724400
C	-7.54875000	2.00417000	4.79831100
H	-7.70407300	1.43963000	5.71291600
C	-6.39993400	1.80379100	4.05994500
H	-5.65767500	1.08822100	4.39890800
C	-6.17285200	2.52510700	2.86621700
C	-5.00746700	2.38559600	2.04469300
C	-3.80409300	1.57894300	2.10667700
C	-3.52080400	0.49023600	3.05071900
C	-4.29496800	-0.72572500	3.27959500
C	-5.48119200	-1.30509300	2.73056000
C	-6.18927900	-0.77379000	1.62645500
H	-5.80657100	0.11834200	1.13664000
C	-7.34606300	-1.37128700	1.16909700
H	-7.86123100	-0.96796100	0.30006100
C	-7.85761700	-2.52056400	1.80717600
H	-8.77624400	-2.97343000	1.44434400
C	-7.17724500	-3.07604800	2.86667300

H	-7.55233700	-3.97320300	3.35588700
C	-5.97042100	-2.50647400	3.34493500
C	-5.26342800	-3.12361900	4.42015200
H	-5.66959400	-4.03865600	4.84395600
C	-4.09851500	-2.58898700	4.91156100
H	-3.53305200	-3.03865800	5.71945100
C	-3.66104900	-1.40336800	4.31605300
C	-2.47760600	0.42610300	3.95030500
N	-1.39737900	1.25948000	4.11896400
H	-1.07411800	1.64216000	3.22055400
C	-0.53675300	1.28628800	5.17062400
O	-0.62990000	0.72578300	6.26400500
C	0.66507900	2.19429200	4.91045200
F	1.83972400	1.55075500	5.19143600
F	0.60242500	3.29840400	5.72665500
F	0.73057500	2.64805400	3.61256100
O	-1.31836300	-1.50752800	0.71222300
C	-1.72310000	-1.47069400	-0.50727300
O	-1.00687100	-1.02256400	-1.49525500
C	-3.04535600	-1.91144300	-0.89730200
C	-4.85897900	-3.15673900	-0.68801300
C	-5.74283000	-4.12953400	-0.20661300
H	-5.51938700	-4.66582200	0.70879000
C	-6.88136800	-4.32788800	-0.94256000
H	-7.61764700	-5.06141900	-0.62161500
C	-7.14610600	-3.59396200	-2.14148200
C	-8.32730600	-3.84547600	-2.87927200
H	-9.02561400	-4.58873000	-2.49973400
C	-8.58866800	-3.17667700	-4.05551000
H	-9.49897100	-3.38080100	-4.61146200
C	-7.66450600	-2.23176400	-4.54259500
H	-7.86374200	-1.71426200	-5.47635800
C	-6.50465100	-1.95811400	-3.84569600
H	-5.80035800	-1.23367700	-4.23982100
C	-6.21829400	-2.61388900	-2.62730800
C	-5.03663100	-2.39716100	-1.84454800
C	-3.85121400	-1.56841800	-1.97459800
C	-3.61615800	-0.55835300	-3.01395300
C	-4.44134800	0.60018600	-3.33419000

C	-5.57420900	1.23935100	-2.74350000
C	-6.17367600	0.82359700	-1.53163700
H	-5.75334000	-0.02756900	-1.00176100
C	-7.26739800	1.48929300	-1.01821100
H	-7.69908400	1.17976300	-0.06841100
C	-7.82166900	2.59095900	-1.70423300
H	-8.68872300	3.09959500	-1.29198300
C	-7.24991600	3.02784000	-2.87736100
H	-7.66059600	3.88493000	-3.40751900
C	-6.11154500	2.38289700	-3.42308900
C	-5.51396300	2.87252500	-4.62306800
H	-5.95385200	3.74657800	-5.09655900
C	-4.40357600	2.27443100	-5.16793800
H	-3.92006600	2.63241600	-6.06983100
C	-3.90827100	1.15641900	-4.49188400
C	-2.62219000	-0.56394000	-3.97165400
N	-1.48049700	-1.32433600	-4.04920000
H	-1.18056900	-1.63762800	-3.11654300
C	-0.53940000	-1.32122500	-5.03388900
O	-0.59166000	-0.81642300	-6.15613100
C	0.73906000	-2.04943800	-4.60686400
F	0.59139400	-2.70567500	-3.40568100
F	1.78497800	-1.17020300	-4.50212100
F	1.10096800	-2.98906500	-5.54012400
O	3.12966200	-3.08270200	-2.47261200
O	-2.78672000	0.44460400	-4.89128300
O	-3.65824900	-2.85949200	-0.09645300
O	-3.67911300	2.97162100	0.29145700
O	3.13511600	4.58287900	-3.30073200
O	3.59602700	2.99224200	2.31649500
O	2.72638000	-4.44027300	3.14888300
O	-2.53084900	-0.71201200	4.72062300

引用文献

- 1) (a) Davies, H. M. L.; Beckwith, R. E. J. Catalytic Enantioselective C–H Activation by Means of Metal–Carbenoid-Induced C–H Insertion. *Chem. Rev.* **2003**, *103*, 2861–2904.
 (b) Slattery, C. N.; Ford, A.; Maguire, A. R. Catalytic Asymmetric C–H Insertion Reactions of α -Diazocarbonyl Compounds. *Tetrahedron* **2010**, *66*, 6681–6705.
 (c) Doyle, M. P.; Duffy, R.; Ratnikov, M.; Zhou, L. Catalytic Carbene Insertion into C–H Bonds. *Chem. Rev.* **2010**, *110*, 704–724.
 (d) Doyle, M. P.; Liu, Y.; Ratnikov, M. Catalytic, Asymmetric, Intramolecular Carbon–Hydrogen Insertion. *Org. React.* **2013**, *80*, 1–132.
 (e) Ford, A.; Miel, H.; Ring, A.; Slattery, C. N.; Maguire, A. R.; McKervy, M. A. Modern Organic Synthesis with α -Diazocarbonyl Compounds. *Chem. Rev.* **2015**, *115*, 9981–10080.
- 2) Davies, H. M. L.; Bruzinski, P. R.; Lake, D. H.; Kong, N.; Fall, M. J. Asymmetric Cyclopropanations by Rhodium(II) *N*-(Arylsulfonyl)prolinate Catalyzed Decomposition of Vinyldiazomethanes in the Presence of Alkenes. Practical Enantioselective Synthesis of the Four Stereoisomers of 2-Phenylcyclopropan-1-amino Acid. *J. Am. Chem. Soc.* **1996**, *118*, 6897–6907.
- 3) (a) Davies, H. M. L.; Morton, D. Guiding Principles for Site Selective and Stereoselective Intermolecular C–H Functionalization by Donor/Acceptor Rhodium Carbenes. *Chem. Soc. Rev.* **2011**, *40*, 1857–1869.
 (b) Fu, J.; Ren, Z.; Bacsá, J.; Musaev, D. G.; Davies, H. M. L. Desymmetrization of Cyclohexanes by Site- and Stereoselective C–H Functionalization. *Nature* **2018**, *564*, 395–399.
- 4) Watanabe, N.; Ogawa, T.; Ohtake, Y.; Ikegami, S.; Hashimoto, S. Dirhodium(II) Tetrakis[*N*-phthaloyl-(*S*)-*tert*-leucinate]: A Notable Catalyst for Enantiotopically Selective Aromatic Substitution Reactions of α -Diazocarbonyl Compounds. *Synlett* **1996**, 85–86.
- 5) DeAngelis, A.; Dmitrenko, O.; Yap, G. P. A.; Fox, J. M. Chiral Crown Conformation of Rh₂(*S*-PTTL)₄: Enantioselective Cyclopropanation with α -Alkyl- α -diazoesters. *J. Am. Chem. Soc.* **2009**, *131*, 7230–7231.
- 6) (a) Lindsay, V. N. G.; Lin, W.; Charette, A. B. Experimental Evidence for the All-Up Reactive Conformation of Chiral Rhodium(II) Carboxylate Catalysts: Enantioselective Synthesis of *cis*-Cyclopropane α -Amino Acids. *J. Am. Chem. Soc.* **2009**, *131*, 16383–16385.
 (b) Werlé, C.; Goddard, R.; Philipps, P.; Farès, C.; Fürstner, A. Stabilization of a Chiral Dirhodium Carbene by Encapsulation and a Discussion of the Stereochemical Implications. *Angew. Chem. Int. Ed.* **2016**, *55*, 10760–10765. *Angew. Chem.* **2016**, *128*, 10918–10923.
- 7) Yamawaki, M.; Tsutsui, H.; Kitagaki, S.; Anada, M.; Hashimoto, S. Dirhodium(II) Tetrakis[*N*-tetrachlorophthaloyl-(*S*)-*tert*-leucinate]: A New Chiral Rh(II) Catalyst for Enantioselective Amidation of C–H Bonds. *Tetrahedron Lett.* **2002**, *43*, 9561–9564.
- 8) Borowiak, T.; Wolska, I.; Brycki, B.; Zieliński, A.; Kowalczyk, I. Spectroscopic Properties of *N*-*n*-Butyltetrachlorophthalimide and Supramolecular Interactions in Its Crystals. *J. Mol. Struct.* **2007**, *833*, 197–202.
- 9) (a) Reddy, R. P.; Davies, H. M. L. Dirhodium Tetracarboxylates Derived from Adamantylglycine as Chiral

- Catalysts for Enantioselective C–H Aminations. *Org. Lett.* **2006**, *8*, 5013–5016.
- (b) Shimada, N.; Hanari, T.; Kurosaki, Y.; Takeda, K.; Anada, M.; Nambu, H.; Shiro, M.; Hashimoto, S. Catalytic Asymmetric Synthesis of the *endo*-6-Aryl-8-oxabicyclo[3.2.1]oct-3-en-2-one Natural Product from *Ligusticum chuanxing* via 1,3-Dipolar Cycloaddition of a Formyl-Derived Carbonyl Ylide Using Rh₂(S-TCPTTL)₄. *J. Org. Chem.* **2010**, *75*, 6039–6042.
- (c) Shimada, N.; Oohara, T.; Krishnamurthi, J.; Nambu, H.; Hashimoto, S. Catalytic Enantioselective Intermolecular Cycloaddition of Diazodiketoester-Derived Carbonyl Ylides with Indoles Using Chiral Dirhodium(II) Carboxylates. *Org. Lett.* **2011**, *13*, 6284–6287.
- (d) Lindsay, V. N. G.; Nicolas, C.; Charette, A. B. Asymmetric Rh(II)-Catalyzed Cyclopropanation of Alkenes with Diaceptor Diazo Compounds: *p*-Methoxyphenyl Ketone as a General Stereoselectivity Controlling Group. *J. Am. Chem. Soc.* **2011**, *133*, 8972–8981.
- (e) Wang, H.; Guptill, D. M.; Varela-Alvarez, A.; Musaev, D. G.; Davies, H. M. L. Rhodium-Catalyzed Enantioselective Cyclopropanation of Electron-Deficient Alkenes. *Chem. Sci.* **2013**, *4*, 2844–2850.
- (f) Fu, L.; Wang, H.; Davies, H. M. L. Role of *Ortho*-Substituents on Rhodium-Catalyzed Asymmetric Synthesis of β -Lactones by Intramolecular C–H Insertions of Aryldiazoacetates. *Org. Lett.* **2014**, *16*, 3036–3039.
- (g) Yamaguchi, A. D.; Chepiga, K. M.; Yamaguchi, J.; Itami, K.; Davies, H. M. L. Concise Syntheses of Dictyodendrins A and F by a Sequential C–H Functionalization Strategy. *J. Am. Chem. Soc.* **2015**, *137*, 644–647.
- (h) Liao, K.; Pickel, T. C.; Boyarskikh, V.; Bacsá, J.; Musaev, D. G.; Davies, H. M. L. Site-Selective and Stereoselective Functionalization of Non-Activated C–H Bonds. *Nature* **2017**, *551*, 609–613.
- (i) Garlets, Z. J.; Wertz, B. D.; Liu, W.; Voight, E. A.; Davies, H. M. L. Regio- and Stereoselective Rhodium(II)-Catalyzed C–H Functionalization of Cyclobutanes. *Chem* **2020**, *6*, 304–313.
- (j) Garlets, Z. J.; Sanders, J. N.; Malik, H.; Gampe, C.; Houk, K. N.; Davies, H. M. L. Enantioselective C–H Functionalization of Bicyclo[1.1.1]pentanes. *Nat. Catal.* **2020**, *3*, 351–357.
- 10) (a) Qin, C.; Boyarskikh, V.; Hansen, J. H.; Hardcastle, K. I.; Musaev, D. G.; Davies, H. M. L. D₂-Symmetric Dirhodium Catalyst Derived from a 1,2,2-Triarylcyclopropanecarboxylate Ligand: Design, Synthesis and Application. *J. Am. Chem. Soc.* **2011**, *133*, 19198–19204.
- (b) Qin, C.; Davies, H. M. L. Rh₂(*R*-TPCP)₄-Catalyzed Enantioselective [3+2]-Cycloaddition between Nitrones and Vinyldiazoacetates. *J. Am. Chem. Soc.* **2013**, *135*, 14516–14519.
- (c) Qin, C.; Davies, H. M. L. Role of Sterically Demanding Chiral Dirhodium Catalysts in Site-Selective C–H Functionalization of Activated Primary C–H Bonds. *J. Am. Chem. Soc.* **2014**, *136*, 9792–9796.
- (d) Liao, K.; Negretti, S.; Musaev, D. G.; Bacsá, J.; Davies, H. M. L. Site-Selective and Stereoselective Functionalization of Unactivated C–H Bonds. *Nature* **2016**, *533*, 230–234.
- (e) Liao, K.; Yang, Y.-F.; Li, Y.; Sanders, J. N.; Houk, K. N.; Musaev, D. G.; Davies, H. M. L. Design of Catalysts for Site-Selective and Enantioselective Functionalization of Non-Activated Primary C–H Bonds. *Nat. Chem.* **2018**, *10*, 1048–1055.
- (f) Liu, W.; Ren, Z.; Bosse, A. T.; Liao, K.; Goldstein, E. L.; Bacsá, J.; Musaev, D. G.; Stoltz, B. M.; Davies, H. M. L. Catalyst-Controlled Selective Functionalization of Unactivated C–H Bonds in the Presence of

Electronically Activated C–H Bonds. *J. Am. Chem. Soc.* **2018**, *140*, 12247–12255.

- 11) Liao, K.; Liu, W.; Niemeyer, Z. L.; Ren, Z.; Bacsá, J.; Musaev, D. G.; Sigman, M. S.; Davies, H. M. L. Site-Selective Carbene-Induced C–H Functionalization Catalyzed by Dirhodium Tetrakis(triarylcyclopropanecarboxylate) Complexes. *ACS Catal.* **2018**, *8*, 678–682.
- 12) (a) Furuta, T.; Yamamoto, J.; Kitamura, Y.; Hashimoto, A.; Masu, H.; Azumaya, I.; Kan, T.; Kawabata, T. Synthesis of Axially Chiral Amino Acid and Amino Alcohols via Additive–Ligand-Free Pd-Catalyzed Domino Coupling Reaction and Subsequent Transformations of the Product Amidoaza[5]helicene. *J. Org. Chem.* **2010**, *75*, 7010–7013.
(b) Furuta, T.; Nikaído, M.; Yamamoto, J.; Kuribayashi, T.; Kawabata, T. Synthesis of Axially Chiral Amino Acid Derivatives via the Selective Monoesterification of 1,1'-Biaryl-2,2'-dicarboxylic Acids. *Synthesis* **2013**, *45*, 1312–1318.
- 13) Lu, W.-J.; Xu, P.; Murai, T.; Sasamori, T.; Tokitoh, N.; Kawabata, T.; Furuta, T. Asymmetric Intramolecular C–H Insertion Promoted by Dirhodium(II) Carboxylate Catalyst Bearing Axially Chiral Amino Acid Derivatives. *Synlett* **2017**, *28*, 679–683.
- 14) (a) Li, G.-P.; Sun, Y.-Z. Structure of the Bis(pyridine)adduct of Dirhodium(II) Tetrabenzoate. *Huaxue Xuebao* **1981**, *39*, 945–950.
(b) Pirrung, M. C.; Morehead Jr., A. T. Electronic Effects in Dirhodium(II) Carboxylates. Linear Free Energy Relationships in Catalyzed Decomposition of Diazo Compounds and CO and Isonitrile Complexation. *J. Am. Chem. Soc.* **1994**, *116*, 8991–9000.
- 15) (a) Cotton, F. A.; Thompson, J. L. Preparation and Structural Characterization of Three Tetracarboxylato Dirhodium (Rh–Rh) Compounds with Bulky Ligands. *Inorg. Chim. Acta* **1984**, *81*, 193–203.
(b) Hikichi, K.; Kitagaki, S.; Anada, M.; Nakamura, S.; Nakajima, M.; Shiro, M.; Hashimoto, S. Synthesis and Evaluation of Novel Dirhodium(II) Carboxylate Catalysts with Atropisomeric Biaryl Backbone. *Heterocycles* **2003**, *61*, 391–401.
- 16) (a) Pascoe, D. J.; Ling, K. B.; Cockcroft, S. L. The Origin of Chalcogen-Bonding Interactions. *J. Am. Chem. Soc.* **2017**, *139*, 15160–15167.
(b) Tsuzuki, S.; Sato, N. Origin of Attraction in Chalcogen–Nitrogen Interaction of 1,2,5-Chalcogenadiazole Dimers. *J. Phys. Chem. B* **2013**, *117*, 6849–6855.
(c) Nagao, Y.; Hirata, T.; Goto, S.; Sano, S.; Kakehi, A.; Iizuka, K.; Shiro, M. Intramolecular Nonbonded S...O Interaction Recognized in (Acylimino)thiadiazoline Derivatives as Angiotensin II Receptor Antagonists and Related Compounds. *J. Am. Chem. Soc.* **1998**, *120*, 3104–3110.
(d) Iwaoka, M.; Takemoto, S.; Tomoda, S. Statistical and Theoretical Investigation on the Directionality of S...O Interactions. Implication for Molecular Design and Protein Engineering. *J. Am. Chem. Soc.* **2002**, *124*, 10613–10620.
(e) Mukherjee, A. J.; Zade, S. S.; Singh, H. B.; Sunoj, R. B. Organoselenium Chemistry: Role of Intramolecular Interactions. *Chem. Rev.* **2010**, *110*, 4357–4416.
(f) Beno, B. R.; Yeung, K.-S.; Bartberger, M. D.; Pennington, L. D.; Meanwell, N. A. A Survey of the Role of Noncovalent Sulfur Interactions in Drug Design. *J. Med. Chem.* **2015**, *58*, 4383–4438.
(g) Huang, H.; Yang, L.; Facchetti, A.; Marks, T. J. Organic and Polymeric Semiconductors Enhanced by

- Noncovalent Conformational Locks. *Chem. Rev.* **2017**, *117*, 10291–10318.
- (h) Zhou, B.; Gabbaï, F. P. Redox-Controlled Chalcogen-Bonding at Tellurium: Impact on Lewis Acidity and Chloride Anion Transport Properties. *Chem. Sci.* **2020**, *11*, 7495–7500.
- 17) (a) Benz, S.; López-Andarias, J.; Mareda, J.; Sakai, N.; Matile, S. Catalysis with Chalcogen Bonds. *Angew. Chem. Int. Ed.* **2017**, *56*, 812–815. *Angew. Chem.* **2017**, *129*, 830–833.
- (b) Benz, S.; Mareda, J.; Besnard, C.; Sakai, N.; Matile, S. Catalysis with Chalcogen Bonds: Neutral Benzodiselenazole Scaffolds with High-Precision Selenium Donors of Variable Strength. *Chem. Sci.* **2017**, *8*, 8164–8169.
- (c) Wonner, P.; Vogel, L.; Düser, M.; Gomes, L.; Kniep, F.; Mallick, B.; Werz, D. B.; Huber, S. M. Carbon–Halogen Bond Activation by Selenium-Based Chalcogen Bonding. *Angew. Chem. Int. Ed.* **2017**, *56*, 12009–12012. *Angew. Chem.* **2017**, *129*, 12172–12176.
- (d) Wonner, P.; Vogel, L.; Kniep, F.; Huber, S. M. Catalytic Carbon–Chlorine Bond Activation by Selenium-Based Chalcogen Bond Donors. *Chem. Eur. J.* **2017**, *23*, 16972–16975.
- (e) Wang, W.; Zhu, H.; Liu, S.; Zhao, Z.; Zhang, L.; Hao, J.; Wang, Y. Chalcogen–Chalcogen Bonding Catalysis Enables Assembly of Discrete Molecules. *J. Am. Chem. Soc.* **2019**, *141*, 9175–9179.
- (f) Young, C. M.; Elmi, A.; Pascoe, D. J.; Morris, R. K.; McLaughlin, C.; Woods, A. M.; Frost, A. B.; de la Houpliere, A.; Ling, K. B.; Smith, T. K.; Slawin, A. M. Z.; Willoughby, P. H.; Cockroft, S. L.; Smith, A. D. The importance of 1,5-Oxygen•••Chalcogen Interactions in Enantioselective Isochalcogenourea Catalysis. *Angew. Chem. Int. Ed.* **2020**, *59*, 3705–3710. *Angew. Chem.* **2020**, *132*, 3734–3739.
- (g) Wang, W.; Zhu, H.; Feng, L.; Yu, Q.; Hao, J.; Zhu, R.; Wang, Y. Dual Chalcogen–Chalcogen Bonding Catalysis. *J. Am. Chem. Soc.* **2020**, *142*, 3117–3124.
- (h) He, X.; Wang, X.; Tse, Y.-L. S.; Ke, Z.; Yeung, Y.-Y. Bis-selenonium Cations as Bidentate Chalcogen Bond Donors in Catalysis. *ACS Catal.* **2021**, *11*, 12632–12642.
- 18) Mézlová, M.; Petříčková, H.; Maloň, P.; Kozmík, V.; Svoboda, J. Axially Chiral 3,3'-Bi(1-benzothiophene)-2,2'-dicarboxylic Acid and Its Derivatives. *Collect. Czech. Chem. Commun.* **2003**, *68*, 1020–1038.
- 19) Meca, L.; Řeha, D.; Havlas, Z. Racemization Barriers of 1,1'-Binaphthyl and 1,1'-Binaphthalene-2,2'-diol: A DFT Study. *J. Org. Chem.* **2003**, *68*, 5677–5680.
- 20) Murai, T.; Xing, Y.; Kuribayashi, T.; Lu, W.; Guo, J.-D.; Yella, R.; Hamada, S.; Sasamori, T.; Tokitoh, T.; Kawabata, T.; Furuta, T. Synthesis and Structural Properties of Axially Chiral Binaphthothiophene Dicarboxylic Acid. *Chem. Pharm. Bull.* **2018**, *66*, 1203–1206.
- 21) (a) Bundhun, A.; Ramasami, P.; Murray, J. S.; Politzer, P. Trends in σ -Hole Strengths and Interactions of F_3MX Molecules ($M = C, Si, Ge$ and $X = F, Cl, Br, I$). *J. Mol. Model.* **2013**, *19*, 2739–2746.
- (b) Mani, D.; Arunan, E. The $X-C\cdots Y$ ($X = O/F, Y = O/S/F/Cl/Br/N/P$) 'Carbon Bond' and Hydrophobic Interactions. *Phys. Chem. Chem. Phys.* **2013**, *15*, 14377–14383.
- (c) Grabowski, S. J. Tetrel Bond- σ -Hole Bond as a Preliminary Stage of the S_N2 Reaction. *Phys. Chem. Chem. Phys.* **2014**, *16*, 1824–1834.
- 22) Hamada, S.; Wang, S.; Murai, T.; Xing, Y.; Inoue, T.; Ueda, Y.; Sasamori, T.; Kawabata, T.; Furuta, T. Synthesis of Axially Chiral Binaphthothiophene δ -Amino Acid Derivatives Bearing Chalcogen Bonds.

- Heterocycles* **2020**, *101*, 328–338.
- 23) Murai, T.; Lu, W.; Kuribayashi, T.; Morisaki, K.; Ueda, Y.; Hamada, S.; Kobayashi, Y.; Sasamori, T.; Tokitoh, N.; Kawabata, T.; Furuta, T. Conformational Control in Dirhodium(II) Paddlewheel Catalysts Supported by Chalcogen-Bonding Interactions for Stereoselective Intramolecular C–H Insertion Reactions. *ACS Catal.* **2021**, *11*, 568–578.
 - 24) (a) Liu, C.; Zhong, S.-M.; Chen, R.-Y.; Wu, Y.; Zhu, X.-J. Two New Compounds from the Dried Tender Stems of *Cinnamomum cassia*. *J. Asian Nat. Prod. Res.* **2009**, *11*, 845–849.
 (b) Chen, J.-P.; Ding, C.-H.; Liu, W.; Hou, X.-L.; Dai, L.-X. Palladium-Catalyzed Regio-, Diastereo-, and Enantioselective Allylic Alkylation of Acylsilanes with Monosubstituted Allyl Substrates. *J. Am. Chem. Soc.* **2010**, *132*, 15493–15495.
 - 25) Liu, X.; Fu, J.; Yao, X.-J.; Yang, J.; Liu, L.; Xie, T.-G.; Jiang, P.-C.; Jiang, Z.-H.; Zhu, G.-Y. Phenolic Constituents Isolated from the Twigs of *Cinnamomum cassia* and Their Potential Neuroprotective Effects. *J. Nat. Prod.* **2018**, *81*, 1333–1342.
 - 26) Kim, G. J.; Lee, J. Y.; Choi, H. G.; Kim, S. Y.; Kim, E.; Shim, S. H.; Nam, J.-W.; Kim, S.-H.; Choi, H. Cinnamomulactone, a New Butyrolactone from the Twigs of *Cinnamomum cassia* and Its Inhibitory Activity of Matrix Metalloproteinases. *Arch. Pharm. Res.* **2017**, *40*, 304–310.
 - 27) (a) Birman, V. B.; Li, X. Benzotetramisole: A Remarkably Enantioselective Acyl Transfer Catalyst. *Org. Lett.* **2006**, *8*, 1351–1354.
 (b) Kobayashi, M.; Okamoto, S. Unexpected Reactivity of Annulated 3*H*-Benzothiazol-2-ylideneamines as an Acyl Transfer Catalyst. *Tetrahedron Lett.* **2006**, *47*, 4347–4350.
 (c) Merad, J.; Pons, J.-M.; Chuzel, O.; Bressy, C. Enantioselective Catalysis by Chiral Isothioureas. *Eur. J. Org. Chem.* **2016**, 5589–5610.
 - 28) (a) Wang, G.; Shi, Q.; Hu, W.; Chen, T.; Guo, Y.; Hu, Z.; Gong, M.; Guo, J.; Wei, D.; Fu, Z.; Huang, W. Organocatalytic Asymmetric *N*-Sulfonyl Amide C–N Bond Activation to Access Axially Chiral Biaryl Amino Acids. *Nat. Commun.* **2020**, *11*, 946.
 (b) Guo, D.; Peng, Q.; Zhang, B.; Wang, J. Atroposelective Dynamic Kinetic Resolution via *In Situ* Hemiaminals Catalyzed by *N*-Heterocyclic Carbene. *Org. Lett.* **2021**, *23*, 7765–7770.
 - 29) Hashimoto, T.; Kimura, H.; Nakatsu, H.; Maruoka, K. Synthetic Application and Structural Elucidation of Axially Chiral Dicarboxylic Acid: Asymmetric Mannich-type Reaction with Diazoacetate, (Diazomethyl)phosphonate, and (Diazomethyl)sulfone. *J. Org. Chem.* **2011**, *76*, 6030–6037.
 - 30) Paegle, E.; Belyakov, S.; Arsenyan, P. An Approach to the Selenobromination of Aryl(thienyl)alkynes: Access to 3-Bromobenzo[*b*]selenophenes and Selenophenothiophenes. *Eur. J. Org. Chem.* **2014**, *18*, 3831–3840.
 - 31) Lin, R.; Lee, K.-H.; Sung, H. H. Y.; Williams, I. D.; Lin, Z.; Jia, G. Rhenabenzenes and Unexpected Coupling Products from the Reactions of Rhenacyclobutadienes with Ethoxyethyne. *Organometallics* **2015**, *34*, 167–176.
 - 32) Murai, T.; Xing, Y.; Kurokawa, M.; Kuribayashi, T.; Nikaido, M.; Elboray, E. E.; Hamada, S.; Kobayashi, Y.; Sasamori, T.; Kawabata, T.; Furuta, T. One-Pot Preparation of (*NH*)-Phenanthridinones and Amide-Functionalized [7]Helicene-Like Molecules from Biaryl Dicarboxylic Acid. *ChemRxiv*. (DOI:

10.26434/chemrxiv-2021-0wzfl).

- 33) Tanaka, K.; Suzuki, H.; Osuga, H. Non-Photochemical Route to Chiral Disubstituted [7]Thiaheterohelicenes via Biaryl- and Carbonyl-Coupling Reactions. *J. Org. Chem.* **1997**, *62*, 4465–4470.
- 34) Mason, S. F.; Seal, R. H.; Roberts, D. R. Optical Activity in the Biaryl Series. *Tetrahedron* **1974**, *30*, 1671–1782.
- 35) (a) Bundhun, A.; Ramasami, P.; Murray, J. S.; Politzer, P. Trends in σ -Hole Strengths and Interactions of F_3MX Molecules ($M = C, Si, Ge$ and $X = F, Cl, Br, I$). *J. Mol. Model.* **2013**, *19*, 2739–2746.
(b) Mani, D.; Arunan, E. The $X-C\cdots Y$ ($X = O/F, Y = O/S/F/Cl/Br/N/P$) ‘Carbon Bond’ and Hydrophobic Interactions. *Phys. Chem. Chem. Phys.* **2013**, *15*, 14377–14383.
(c) Grabowskiab, S. J. Tetrel Bond- σ -Hole Bond as a Preliminary Stage of the S_N2 Reaction. *Phys. Chem. Chem. Phys.* **2014**, *16*, 1824–1834.
- 36) Xing, Y.; Nikaido, M.; Murai, T.; Hamada, S.; Kobayashi, Y.; Sasamori, T.; Kawabata, T.; Furuta, T. Concise Synthesis of an Amide-Functionalized [7]Helicene-Like Molecule via Intramolecular Amidation. *Heterocycles* **2021**, *103*, 544–553.
- 37) (a) Davies, H. M. L.; Grazini, M. V. A.; Aouad, E. Asymmetric Intramolecular C–H Insertions of Aryldiazoacetates. *Org. Lett.* **2001**, *3*, 1475–1477.
(b) Saito, H.; Oishi, H.; Kitagaki, S.; Nakamura, S.; Anada, M.; Hashimoto, S. Enantio- and Diastereoselective Synthesis of *cis*-2-Aryl-3-methoxycarbonyl-2,3-dihydrobenzofurans via the Rh(II)-Catalyzed C–H Insertion Process. *Org. Lett.* **2002**, *4*, 3887–3890.
(c) Koizumi, Y.; Kobayashi, H.; Wakimoto, T.; Furuta, T.; Fukuyama, T.; Kan, T. Total Synthesis of (–)-Serotobenine. *J. Am. Chem. Soc.* **2008**, *130*, 16854–16855.
(d) Natori, Y.; Tsutsui, H.; Sato, N.; Nakamura, S.; Nambu, H.; Shiro, M.; Hashimoto, S. Asymmetric Synthesis of Neolignans (–)-*epi*-Conocarpan and (+)-Conocarpan via Rh(II)-Catalyzed C–H Insertion Process and Revision of the Absolute Configuration of (–)-*epi*-Conocarpan. *J. Org. Chem.* **2009**, *74*, 4418–4421.
(e) Miyazawa, T.; Minami, K.; Ito, M.; Anada, M.; Matsunaga, S.; Hashimoto, S. Enantio- and Diastereoselective Desymmetrization of α -Alkyl- α -diazoesters by Dirhodium(II)-Catalyzed Intramolecular C–H Insertion. *Tetrahedron* **2016**, *72*, 3939–3947.
(f) Miyazawa, T.; Imai, K.; Ito, M.; Takeda, K.; Anada, M.; Matsunaga, S.; Hashimoto, S. Diastereo- and Enantioselective Construction of 6,7-Dioxabicyclo[2.2.1]heptane Derivatives by a Dirhodium(II)-Catalyzed Intramolecular C–H Insertion Reaction. *Heterocycles* **2017**, *95*, 1211–1229.
- 38) (a) Doyle, M. P.; May, E. J. Enantioselective β -Lactone Formation from Phenyl diazoacetates via Catalytic Carbon–Hydrogen Insertion. *Synlett* **2001**, *2001*, 967–969.
(b) Doyle, M. P.; Davies, S. B.; May, E. J. High Selectivity from Configurational Match/Mismatch in Carbon–Hydrogen Insertion Reactions of Steroidal Diazoacetates Catalyzed by Chiral Dirhodium(II) Carboxamides. *J. Org. Chem.* **2001**, *66*, 8112–8119.
(c) Villalobos, M. N.; Wood, J. L. Spirolactone Synthesis through a Rhodium(II)-Catalyzed Intramolecular C–H Insertion Reaction: Model Studies towards the Synthesis of Syringolides. *Tetrahedron Lett.* **2009**, *50*, 6450–6453.

- 39) Müller, P.; Allenbach, Y.; Robert, E. Rhodium(II)-Catalyzed Olefin Cyclopropanation with the Phenyliodonium Ylide Derived from Meldrum's Acid. *Tetrahedron: Asymmetry* **2003**, *14*, 779–785.
- 40) Doyle, M. P.; Bagheri, V.; Wandless, T. J.; Harn, N. K.; Brinker, D. A.; Eagle, C. T.; Loh, K. L. Exceptionally High Trans (Anti) Stereoselectivity in Catalytic Cyclopropanation Reactions. *J. Am. Chem. Soc.* **1990**, *112*, 1906–1912.
- 41) Davies, H. M. L.; Hansen, T.; Churchill, M. R. Catalytic Asymmetric C–H Activation of Alkanes and Tetrahydrofuran. *J. Am. Chem. Soc.* **2000**, *122*, 3063–3070.
- 42) Nakamura, E.; Yoshikai, N.; Yamanaka, M. Mechanism of C–H Bond Activation/C–C Bond Formation Reaction between Diazo Compound and Alkane Catalyzed by Dirhodium Tetracarboxylate. *J. Am. Chem. Soc.* **2002**, *124*, 7181–7192.
- 43) Rusek, M.; Kwaśna, K.; Budzianowski, A.; Katrusiak, A. Fluorine•••Fluorine Interactions in a High-Pressure Layered Phase of Perfluorobenzene. *J. Phys. Chem. C* **2020**, *124*, 99–106.
- 44) Werlé, C.; Goddard, R.; Philipps, P.; Farès, C.; Fürstner, A. Structure of Reactive Donor/Acceptor and Donor/Donor Rhodium Carbenes in the Solid State and Their Implications for Catalysis. *J. Am. Chem. Soc.* **2016**, *138*, 3797–3805.
- 45) Gaussian 16, Revision C.01, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; Li, X.; Caricato, M.; Marenich, A. V.; Bloino, J.; Janesko, B. G.; Gomperts, R.; Mennucci, B.; Hratchian, H. P.; Ortiz, J. V.; Izmaylov, A. F.; Sonnenberg, J. L.; Williams-Young, D.; Ding, F.; Lipparini, F.; Egidi, F.; Goings, J.; Peng, B.; Petrone, A.; Henderson, T.; Ranasinghe, D.; Zakrzewski, V. G.; Gao, J.; Rega, N.; Zheng, G.; Liang, W.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Throssell, K.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M. J.; Heyd, J. J.; Brothers, E. N.; Kudin, K. N.; Staroverov, V. N.; Keith, T. A.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A. P.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Millam, J. M.; Klene, M.; Adamo, C.; Cammi, R.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Farkas, O.; Foresman, J. B.; Fox, D. J. Gaussian, Inc., Wallingford CT, 2016.
- 46) Henkelman G.; Jónsson, H. Improved Tangent Estimate in the Nudged Elastic Band Method for Finding Minimum Energy Paths and Saddle Points. *J. Chem. Phys.* **2000**, *113*, 9978–9985.
- 47) Nordstrøm, L. U.; Vogt, H.; Madsen, R. Amide Synthesis from Alcohols and Amines by the Extrusion of Dihydrogen. *J. Am. Chem. Soc.* **2008**, *130*, 17672–17673.
- 48) Blum, J.; Zinger, B.; Milstein, D.; Buchman, O. Dimerization of Terminal Epoxides by Homogeneous Transition Metal Complexes. A Novel Synthesis of Carboxylic Esters. *J. Org. Chem.* **1978**, *43*, 2961–2967.
- 49) Xiong, T.; Li, Y.; Mao, L.; Zhang, Q.; Zhang, Q. Palladium-Catalyzed Allylic C–H Amination of Alkenes with *N*-Fluorodibenzene-sulfonimide: Water Plays an Important Role. *Chem. Commun.* **2012**, *48*, 2246–2248.
- 50) Berova, N. D.; Kurtev, B. J. Absolute Configurations of Some 1,2-Diphenylethane Derivatives. *Tetrahedron* **1969**, *25*, 2301–2311.
- 51) Domingo, L. R.; Gil, S.; Parra, M.; Segura, J. Unusual Regioselectivity in the Opening of Epoxides by Carboxylic Acid Enediolates. *Molecules* **2008**, *13*, 1303–1311.

論文目録

主論文

- (1) Synthesis of Axially Chiral Binaphthothiophene δ -Amino Acid Derivatives Bearing Chalcogen Atoms
Shohei Hamada, Shuo Wang, Takuya Murai, Yongning Xing, Takumi Inoue, Yoshihiro Ueda, Takahiro Sasamori, Takeo Kawabata, Takumi Furuta
Heterocycles **2020**, *101*, 328–338.
- (2) Conformational Control in Dirhodium(II) Paddlewheel Catalysts Supported by Chalcogen-Bonding Interactions for Stereoselective Intramolecular C–H Insertion Reactions
Takuya Murai, Wenjie Lu, Toshifumi Kuribayashi, Kazuhiro Morisaki, Yoshihiro Ueda, Shohei Hamada, Yusuke Kobayashi, Takahiro Sasamori, Norihiro Tokitoh, Takeo Kawabata, Takumi Furuta
ACS Catal. **2021**, *11*, 568–578.

参考論文

- (1) Synthesis and Structural Properties of Axially Chiral Binaphthothiophene Dicarboxylic Acid
Takuya Murai, Yongning Xing, Toshifumi Kuribayashi, Wenjie Lu, Jing-Dong Guo, Ramesh Yella, Shohei Hamada, Takahiro Sasamori, Norihiro Tokitoh, Takeo Kawabata, Takumi Furuta
Chem. Pharm. Bull. **2018**, *66*, 1203–1206.

謝辞

本論文の終わりに臨み、本研究を行うに際し終始御懇篤な御指導、御鞭撻を賜りました京都薬科大学大学院薬学研究科 古田 巧 教授に衷心より感謝の意を表します。

本研究の大部分において直接御指導賜りました京都大学化学研究所 川端 猛夫 教授（現、国際医療福祉大学福岡薬学部 教授、京都大学 名誉教授）に深く感謝致します。

本研究の遂行にあたり、有益な御助言、御指導を賜りました京都薬科大学大学院薬学研究科 小林 祐輔 准教授、浜田 翔平 助教に厚く御礼申し上げます。また、筆者が京都大学に在籍していた際、実験の御指導、御助言を賜りました京都大学化学研究所 上田 善弘 助教、森崎 一宏 助教（現、北海道大学大学院薬学研究院 助教）、吉田 圭佑 特定助教（名城大学薬学部 助教）、今吉 亜由美 助教 京都府立大学大学院生命環境科学研究科に心より感謝申し上げます。

筑波大学数理物質系化学域 笹森 貴裕 教授、並びに京都大学化学研究所 時任 宣博 教授におかれましては、本研究の遂行に不可欠な X 線結晶構造解析に御協力賜りました事に、感謝申し上げます。

また、副査として本論文の審査を引き受けて頂きました京都薬科大学大学院薬学研究科 安井 裕之 教授、大石 真也 教授に深く感謝致します。

本研究において質量分析を行って頂きました京都薬科大学共同利用機器センター 長谷川 功紀 准教授（現、福島県立医科大学保健科学部 教授）、服部 恭尚 講師、安東 友繁 助教（現、日本ウォータース株式会社 研究員）、及び京都大学化学研究所技術職員 藤橋 明子 氏に深く感謝致します。

本研究に関して多大なる御助言、御指導を頂きました 陸 文傑 博士、新井 健太 博士、榎藤 匠 洋 博士、芝山 啓允 博士、並びに関連する研究テーマに取り組む共同研究者として、本研究に多大なる御協力および有益な知見をご提供頂きました 栗林 俊文 修士、王 燦 修士、邢 永寧 博士、井上 拓美 氏に深く感謝致します。

4 年間の充実した研究生活を共に過ごして頂きました京都大学化学研究所 精密有機合成化学分野 川端研究室の卒業生並びに在学生の皆様心より感謝致します。また、研究室立ち上げの時期に携わらせて頂き、研究者としてだけでなく、指導者としての成長の機会を与えてくれた京都薬科大学 薬化学分野 古田研究室の在学生の皆様心より感謝致します。

6年間の研究生活を事務方として支援して頂きました京都薬科大学 薬化学分野 秘書 千藤 えりか 氏、及び京都大学化学研究所 精密有機合成化学分野 秘書 井上 香織 氏（旧姓、橋本）に感謝致します。山あり谷ありの研究生活でしたが、逐一悩みを聞いて頂き、助かりました。

末筆ながら、京都大学入学以来、9 年間に渡っての学業生活を容認し、経済的にも精神的にも支え続け、終始温かく見守って頂きました両親、姉に心より感謝の意を表します。