Axially Chiral Cyclic Diphosphine Ligand-Enabled Palladium-Catalyzed Intramolecular Asymmetric Hydroarylation

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HIGHLIGHTS
Novel axially chiral cyclic diphosphine ligands
Excellent enantioselectivity
Wide substrate scope
Synthesis of a new kind of chiral N-heterocycles

DATA AND SOFTWARE AVAILABILITY
1842685
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novel axially chiral ligand
excellent enantioselectivity
broad substrate scope
wide functional group tolerance
scale reaction without loss of ee
Axially Chiral Cyclic Diphosphine Ligand-Enabled Palladium-Catalyzed Intramolecular Asymmetric Hydroarylation

Can Liu,1,2 Xianjin Zhu,2 Pengxiang Zhang,2 Haijun Yang,2 Changjin Zhu,1 and Hua Fu1,2,3,*

SUMMARY
In transition metal-catalyzed asymmetric synthesis, enantioselectivity strongly depends on the structures of chiral ligands, so the development of new chiral ligands is crucial. Here, an efficient and highly enantioselective palladium-catalyzed intramolecular hydroarylation has been developed, and a new kind of N-heterocycles, 1H-pyrazolo[5,1-a]isoindol-2(8H)-ones containing a quaternary stereocenter, was prepared in high yields and excellent enantiomeric excess values. The reaction was effectively catalyzed by palladium-diphosphine complexes with numerous functional group tolerance, in which the newly developed axially chiral cyclic diphosphine ligands played key roles in the reactivity and enantioselectivity of the substrates. We believe that the cyclic diphosphine ligands with adjustable dihedral angles will find wide application in asymmetric synthesis.

INTRODUCTION
Nitrogen-containing compounds widely occur in biologically active molecules including natural products (Ruiz-Sanchis et al., 2011), agrochemicals, and pharmaceuticals (Leeson and Springthorpe, 2007). In particular, over 90% of pharmaceuticals contain at least one nitrogen atom in their structures, so the development of efficient approaches to N-heterocycles is of paramount importance (Carey et al., 2006; Duggers et al., 2005). Compounds containing a [1,8-diazabicyclo[3.3.0]octane skeleton exhibit diverse biological activities. For example, they are used as the androgen receptor modulator (Ulrich et al., 2014), angiotensin II receptor antagonist (Levin et al., 1994), and DNA topoisomerase inhibitor (Figure 1) (Katayama et al., 1999). However, 1H-pyrazolo[5,1-a]isoindol-2(8H)-ones as their derivatives have been ignored (Ivanovich et al., 2016). To the best of our knowledge, enantioselective synthesis of this kind of compounds containing a quaternary stereocenter has not been reported thus far.

Since the pioneering work by Cacchi and co-workers (Cacchi and Arcadi, 1983; Amorese et al., 1989; Cacchi, 1990; Arcadi et al., 1996), the palladium-catalyzed hydroarylation or reductive Heck reaction of aryl halides (pseudoarohalides) with alkynes has attracted much attention (Trost and Toste, 1999; Lee and Cha, 2001; Ichikawa et al., 2004; Dounay et al., 2008; Diethelm and Carreira, 2013; Schmidt and Hoffmann, 1991; Gottumukkala et al., 2011; Chen et al., 2012; Gao and Cook, 2012; Raoufmoghaddam et al., 2015). However, the development of highly enantioselective hydroarylation is still a great challenge, and only some examples of the enantioselective protocols have been reported till now (Minatti et al., 2007; Manathan et al., 2017; Liu and Zhou, 2013; Yue et al., 2015; Shen et al., 2015; Kong et al., 2017). It is well known that the enantioselectivity highly depends on structures of chiral ligands in the transition-metal-catalyzed asymmetric synthesis, so the development of new chiral ligands is crucial (Tang and Zhang, 2003; Noyori and Ohkuma, 2001). In this regard, the axially chiral diphosphine ligands have been proved to be highly efficient in various enantioselective transformations (Qiu et al., 2006; Zhang et al., 2000; Sun et al., 2008; Wu et al., 2005; Pai et al., 2000; Jeulin et al., 2004a, 2004b; Genêt, 2003; Benincori et al., 2000; Tietze et al., 2000; Hatano et al., 2001; Graff et al., 2015). Recently, we have developed a kind of novel axially chiral cyclo-[1,1’-biphenyl]-2,2’-diols (CYCNOL) with adjustable dihedral angles (Zhang et al., 2016), and the chiral cyclic phosphoramide ligands derived from CYCNOL have been successfully applied in iridium-catalyzed enantioselective arylation of unactivated racemic secondary allylic alcohols (Tian et al., 2017) and synthesis of dihydromidazooquinazolinones (Peng et al., 2017). Inspired by the ligands we developed (Zhang et al., 2016; Tian et al., 2017; Peng et al., 2017), we herein report a palladium-catalyzed intramolecular enantioselective hydroarylation by elaborate tuning of newly developed axially chiral cyclic diphosphine ligands derived from CYCNOL.
RESULTS AND DISCUSSION

Synthesis of Ligands

Racemic CYCNOL, Rac-CYC-8-NOL, Rac-CYC-9-NOL, and Rac-CYC-10-NOL, were prepared according to our previous procedures (Zhang et al., 2016). Subsequently, synthesis (following Zhou’s protocol [Xie et al., 2003]) and resolution of our axially chiral cyclic diphosphine ligands were performed (Figure 2) (see Supplemental Information for details).

Crystal Structures of Ligands

Single crystals of the axially chiral cyclic diphosphine ligands ((S)-CYC-8-BIPHP ((S)-E), (S)-CYC-9-BIPHP ((S)-F), and (S)-CYC-10-BIPHP ((S)-G) from mixed hexane and dichloromethane solvent were prepared, and their structures were unambiguously confirmed by X-ray diffraction analysis (see Supplemental Information, Data S1, S2, and S3 for details). According to the data from X-ray diffraction analysis, dihedral angles of the diphosphine ligands showed remarkable difference with a variety of ring sizes (Figure 3). It is known to all that the reactivity and enantioselectivity of substrates in the transition metal asymmetric
Optimization Study

At first, palladium-catalyzed enantioselective hydroarylation of 1-(2-iodobenzyl)-5-methyl-2-phenyl-1H-pyrazol-3(2H)-one (1a) leading to (S)-3a-methyl-1-phenyl-3,3a-dihydro-1H-pyrazolo[5,1-a]isoindol-2(8H)-one (2a) was used as the model to optimize conditions including catalysts, ligands, tertiary amines, acids, solvents, and temperature. As shown in Table 1, seven ligands including four common diphosphine ligands, (S)-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP), (R)-5,5'-bis(di(3,5-di-t-butyl-4-methoxyphenyl)phosphino)-4,4'-bi-1,3-benzodioxole (DTBM-SEGPHOS), (S)-MeO-BIPN, and (S)-7,7'-bis(diphenylphosphino)-2,2',3,3'-tetrahydro-1,1'-spirobiindane (SDP), and our three cyclic diphosphine ligands, (S)-E, (S)-F, and (S)-G, were screened using Pd(trifluoroacetic acid [TFA])\(_2\) as the catalysts and N,N-dimethylbenzylamine/TFA as the hydride donors in N,N-dimethylacetamide (DMA) under a nitrogen atmosphere at 150°C for 24 hr (entries 1–7). We were pleased to find that the three cyclic diphosphine ligands, (S)-E, (S)-F, and (S)-G, all provided high yields with excellent enantiomeric excess (ee) values (entries 5–7), in which (S)-F was optimal (entry 6).

Compared with the four common ligands, the advantage of our cyclo-[1,1'-biphenyl]diphosphine ligands, (S)-E, (S)-F, and (S)-G, is attributed to their combination of conformational rigidity and flexibility because they own the rigid biphenyl and the flexible full-carbon 6,6'-tethers. Meanwhile, the three cyclo-diphosphine ligands had little influence on the yields and ee values because of this factor. Single crystal of product 2a in entry 6 from mixed hexane and dichloromethane solvent was prepared, and its absolute configuration was determined to be S-form based on its single-crystal X-ray analysis (Table 1) (see Supplemental Information and Data S4 for details). Racemic 2a was obtained in 37% yield in the absence of ligand (entry 8). When other three tertiary amines, triethylamine, diisopropylethylamine, and proton sponge, were used instead of N,N-dimethylbenzylamine, lower ee values were observed (entries 9–11). Only a small amount of product 2a was found in the absence of amine (entry 12). Use of HOAc or HCOOH or absence of acid led to lower yields (entries 13–15). Two more palladium catalysts, Pd(db)\(_2\) and Pd(OAc)\(_2\), were tested (entries 16 and 17), and they were inferior to Pd(TFA)\(_2\) (compare entries 6, 16, and 17). The effect of solvents was surveyed, and DMA proved to be a suitable solvent (compare entries 6, 18, and 19). When ligand (S)-F was increased from 7.5 mol % to 10 mol % (entry 20), the same yield and ee value were observed (compare entries 6 and 20). We attempted variation of temperature (entries 21 and 22), and the results showed that 150°C was a suitable temperature (compare entries 6, 21, and 22). According to the aforementioned results, we think that Pd(TFA)\(_2\) as the catalyst; (S)-E, (S)-F, and (S)-G as the ligands; N,N-dimethylbenzylamine/TFA as the hydride donor; and DMA as the solvent are suitable in the present palladium-catalyzed intramolecular enantioselective hydroarylation.

**Figure 3.** Crystal Structures and Dihedral Angles of Axially Chiral Cyclic Diphosphine Ligands (S)-E, (S)-F, and (S)-G.
Table 1. Optimization of Conditions

| Entry | Ligand      | Amine      | Acid   | Yield of 2a (%)<sup>a</sup> | ee of 2a (%)<sup>b</sup> |
|-------|-------------|------------|--------|----------------------------|--------------------------|
| 1     | (S)-A       | BnNMe<sub>2</sub> | TFA    | 68                         | 23                       |
| 2     | (R)-B       | BnNMe<sub>2</sub> | TFA    | 31                         | −59                      |
| 3     | (S)-C       | BnNMe<sub>2</sub> | TFA    | 63                         | 28                       |
| 4     | (S)-D       | BnNMe<sub>2</sub> | TFA    | 73                         | −2                       |
| 5     | (S)-E       | BnNMe<sub>2</sub> | TFA    | 70                         | 96                       |
| 6     | (S)-F       | BnNMe<sub>2</sub> | TFA    | 76                         | 97                       |
| 7     | (S)-G       | BnNMe<sub>2</sub> | TFA    | 73                         | 96                       |
| 8     | –           | BnNMe<sub>2</sub> | TFA    | 37                         | 0                        |
| 9     | (S)-F       | NEt<sub>3</sub>  | TFA    | 76                         | 93                       |
| 10    | (S)-F       | DIPEA      | TFA    | 75                         | 92                       |

<sup>a</sup> Yield of 2a post purification

<sup>b</sup> ee of 2a as determined by HPLC
Entry | Ligand | Amine | Acid | Yield of 2a (%)<sup>a</sup> | ee of 2a (%)<sup>b</sup>
--- | --- | --- | --- | --- | ---
11 | (S)-F | PS | TFA | 57 | 88
12 | (S)-F | – | TFA | 8 | 94
13 | (S)-F | BnNMe<sub>2</sub> | HOAc | 48 | 95
14 | (S)-F | BnNMe<sub>2</sub> | HCOOH | 37 | 96
15 | (S)-F | BnNMe<sub>2</sub> | – | 35 | 96
16<sup>c</sup> | (S)-F | BnNMe<sub>2</sub> | TFA | 51 | 95
17<sup>d</sup> | (S)-F | BnNMe<sub>2</sub> | TFA | 63 | 96
18<sup>e</sup> | (S)-F | BnNMe<sub>2</sub> | TFA | 62 | 96
19<sup>f</sup> | (S)-F | BnNMe<sub>2</sub> | TFA | 56 | 95
20<sup>g</sup> | (S)-F | BnNMe<sub>2</sub> | TFA | 76 | 97

Table 1. Continued (Continued on next page)
1a

Pd(TFA)$_2$, ligand, amine, acid
solvent, N$_2$, 150 °C, 24 h

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Scope of the Investigation
After obtaining the optimized conditions, the substrate scope for the palladium-catalyzed intramolecular enantioselective hydroarylation of 1 was surveyed using (S)-F as the ligand. As shown in Figure 4, we first attempted variation of substituents R1 in 1; various alkyl groups including methyl, ethyl, propyl, isopropyl, cyclopropyl, cyclopentyl, phenethyl, and phenpropyl were feasible, and the reaction provided high reactivity (76%–83% yields) and excellent enantioselectivity (97%–99% ee) (see 2a-h). When substituents R1 in 1 were different substituted benzyls, their enantioselectivity was also excellent (98%–99% ee) (see 2i-m).

Subsequently, variation of substituents R2 in 1 was investigated (see 2n-ad). For substituents R2 with different substituted phenyls, the influence of electronic effect including electron-donating (see 2n-t), slight electron-withdrawing (see 2u-w), and strong electron-withdrawing groups (see 2x-z) on the phenyl rings was slight, and high reactivity (74%–84% yields) and excellent enantioselectivity (97%–99% ee) of the substrates were observed. When substituents R2 were benzyl (see 2aa and 2ab) and cyclohexyl (see 2ac and 2ad), the reaction also afforded high yields and excellent ee values. Variation of substituents R3 on the phenyl rings was investigated, and excellent results were obtained (see 2ae-ah).

Next, influence of the cyclic diphosphine ligands, (S)-E, (S)-F, and (S)-G, with different dihedral angles was investigated (Figure 4), and we found that the different substrates exhibited slight difference in reactivity and enantioselectivity with variation of the ligands. For all the tested substrates, (S)-F containing

Figure 4. Substrate Scope for Palladium-Catalyzed Asymmetric Cyclization of 1
Reaction conditions: under nitrogen atmosphere, 1-(2-iodobenzyl)-5-alkyl-2-alkyl-1H-pyrazol-3(2H)-one (1) (0.2 mmol, 1.0 equiv), Pd(TFA)2 (10 μmol, 5 mol%), (S)-F (15 μmol, 7.5 mol%), BnNMe2 (1.0 mmol, 5 equiv), TFA (0.4 mmol, 2 equiv), DMA (4.0 mL), temperature (150°C), time (24 hr) in a sealed tube. Isolated yield was obtained, and the ee values were determined by high-performance liquid chromatography analysis. Absolute configurations of products 2 were determined by comparing structure of (S)-2a (absolute configuration of (S)-2a was assigned by X-ray diffraction analysis). Bn, benzyl. See Transparent Methods for experimental details.

Figure 5. Applications of the Method
(A) Scale synthesis of (S)-2i.
(B) Palladium-catalyzed asymmetric cyclization of 1-(2-bromobenzyl)-5-methyl-2-phenyl-1H-pyrazol-3(2H)-one (3).
(C) Reduction of (S)-2i.
nine-membered ring was a suitable ligand. For synthesis of 2b and 2y, (S) G containing ten-membered ring showed slightly higher enantioselectivity than (S) E, which contained an eight-membered ring and (S) F. The present reaction showed tolerance of various functional groups including C-F, C-Cl, and C-Br bonds and ether, CF₂, nitro, cyano, ester, and amide groups. It is worthwhile to note that substrates 1 have unactivated 2-iodobenzy unit. In fact, it was usually difficult for the reaction of the substrates with this unit in previous report, and an effective solution was the use of substituted 2-halobenzoyls with high reactivity as the alternatives of 2-iodobenzy unit (Shen et al., 2015). In addition, no erosion of ee values was observed at such high temperature (150°C). The results showed that our catalyst system was highly efficient in the present reaction.

**Applications of the Method**

A scale synthesis of (S)-2i was performed as example. As shown in Figure 5A, reaction of 1i (2.15 mmol, 1.0 g) under standard conditions provided (S)-2i in 82% yield with 98% ee without loss of yield and enantioselectivity. We attempted the reaction of aryl bromide 3 under the conditions (Figure 5B), and (S)-2a was obtained in 38% yield with 97% ee. Furthermore, reduction of (S)-2i with LiAlH₄ provided (S)-4 in 95% yield with 98% ee without loss of ee (Figure 5C).

**Mechanism of the Reaction**

According to the experiments mentioned above and previous references (Raoufmoghaddam et al., 2015; Minatti et al., 2007), a reaction pathway of this palladium-catalyzed intramolecular enantioselective hydroarylation is proposed in Figure 6. Oxidative addition of the aryl iodide 1 to the in situ-formed Pd(0) diphosphine complex leads to the Pd(II) intermediate I, and then anion exchange of I with the salt (BnNHMe₂⁺ O₂CCF₃) provides II. Carbopalladation of the double bond in II yields the π-oxa-allyl palladium species III. A hydride transfer from the CH₂ of benzyl in BnNHMe₂ to palladium gives the Pd(II) hydride complex IV leaving the iminium ion V. Reductive elimination of the Pd(II) hydride complex IV finally affords the target product (2) with regeneration of Pd(0)L*.

**Extension of the Method**

Furthermore, the palladium-catalyzed intramolecular asymmetric hydroarylation of o-iodobenzyol derivatives (5) was attempted under conditions similar to those in (Figures 4 and 7), and we found that o-iodobenzyol derivatives (5) exhibited higher reactivity and lower enantioselectivity than o-iodobenzy derivatives (1). Unfortunately, the factors that lead to lower enantioselectivity of 6 than 2 are unknown for us.
Limitations of Study
It should be pointed out that there are limitations to the present method including requirement of higher temperature and maladjustment of other common ligands.

Conclusions
In summary, we have developed an efficient and highly enantioselective palladium-catalyzed intramolecular hydroarylation, in which the reactivity and enantioselectivity of the substrates were tuned by our newly developed axially chiral cyclic diphosphine ligands and the new kind of N-heterocycles, 1H-pyrazolo[5,1-a]isoindol-2(8H)-ones containing a quaternary stereocenter, were prepared in high yields and excellent ee values with numerous functional group tolerance. We believe that our axially chiral cyclic diphosphine ligands with the adjustable dihedral angles will find wide application in asymmetric synthesis.

METHODS
All methods can be found in the accompanying Transparent Methods supplemental file.

DATA AND SOFTWARE AVAILABILITY
Crystallographic data have been deposited in the Cambridge Crystallographic Data Center under accessions numbers CCDC: 1842685, 1822026, 1842686, and 1822025.

SUPPLEMENTAL INFORMATION
Supplemental Information includes Transparent Methods, 312 figures, 1 Scheme, 4 tables, and 4 data files and can be found with this article online at https://doi.org/10.1016/j.isci.2018.11.018.

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AUTHOR CONTRIBUTIONS
C.L. and H.F. conceived and design this subject; C.L. and X.Z. conducted the experimental work; C.L., X.Z., P.Z., H.Y., C.Z., and H.F. analyzed the results; C.L. and H.F. co-wrote the manuscript.

DECLARATION OF INTERESTS
There are no competing interests.
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iScience 10, 11–22, December 21, 2018
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Supplemental Information

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Axially Chiral Cyclic Diphosphine Ligand-Enabled Palladium-Catalyzed
Intramolecular Asymmetric Hydroarylation

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**Transparent Methods**

1. **General Procedures**

All reactions were carried out under a nitrogen atmosphere in dry solvents. The reactions were monitored by thin layer chromatography (TLC), and the products were isolated by silica gel column chromatography. Melting points were recorded on a Beijing Tech X-4 melting point apparatus. High-resolution mass spectra (HRMS) were recorded on LCMS-IT/TOF (SHIMADZU, Japan) with an electrospray ionization source. $^1$H, $^{13}$C, $^{19}$F and $^{31}$P NMR spectra were recorded on JNM-ECA 300, JEOL ECS-400 or JNM-ECA 600 spectrometers. Chemical shifts were reported in ppm down field from internal Me$_4$Si, external CFCl$_3$ and external H$_3$PO$_4$, respectively. The following abbreviations (or combinations thereof) were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext = sextet, h = heptet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets, td = triplet of doublets, br = broad. Chiral HPLC analysis was achieved using an Agilent 1100 Infinity series normal phase HPLC unit and Agilent Chemstation software. Daicel Chiralpak columns (250 × 4.6 mm) were used as specified in the text. Solvents were used of HPLC grade (Sigma Aldrich); all eluent systems were isocratic. Optical rotations were recorded using a WZZ-2S Polarimeter. Single crystal X-ray data were collected on a Bruker APEXII X-ray diffractometer equipped with a CMOS PHOTON 100 detector with a Cu Kα X-ray source (Kα = 1.54178 Å). Data were indexed, integrated and scaled using DENZO and SCALEPACK from the HKL program suite (Otwinowski and Minor, 1997). Structures of (S)-2a, (S)-C, (S)-D and (S)-E were solved through direct method (SHELXS-97) and refined by full-matrix least-squares (SHELXL-2014) on $F^2$. Anisotropic thermal parameters were used for the non-hydrogen atoms and isotropic parameters for the hydrogen atoms. The data obtained were deposited at the Cambridge Crystallographic Data Centre.
2. Synthesis and Characterization Data of Ligands (R)-E, (S)-E, (R)-F, (S)-F, (R)-G and (S)-G
Synthesis of diphosphine ligands were performed according to the previous procedures (Xie et al., 2003).

(1) Synthesis of compounds Rac-M-1

(a) Synthesis of Rac-5,6,7,8-tetrahydrodibenzo[a,c][8]annulene-1,12-diyl bis(trifluoromethanesulfonate) (Rac-M-1E)

**Typical procedure:** To a solution of Rac-CYC-8-NOL (see the reference for their synthesis) (Zhang et al., 2016) (3.0 g, 12.5 mmol) in 60 mL of CH₂Cl₂ was added pyridine (4.0 mL, 50 mmol), and followed by dropwise addition of triflic anhydride (5.2 mL, 27.7 mmol) at 0 °C. The mixture was stirred at room temperature for 6 h. After removal of the solvent, the residue was diluted with EtOAc (60 mL) and then washed with 5% aqueous HCl, saturated NaHCO₃, and brine (once for each). The organic layer was dried over anhydrous sodium sulfate, concentrated under reduced pressure, and passed through a silica gel plug (eluted with CH₂Cl₂) to give Rac-M-1E (6.0 g, 95%) as a white solid, mp = 72-73°C. ¹H NMR (400 MHz, CDCl₃) δ 7.48 (t, J = 8.0 Hz, 2H), 7.37 (d, J = 7.1 Hz, 2H), 7.23 (d, J = 7.6 Hz, 2H), 2.83 (dd, J = 13.7, 8.4 Hz, 2H), 2.25-2.15 (m, 2H), 2.15-2.02 (m, 2H), 1.53-1.39 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 147.83, 146.99, 130.92, 129.78, 127.06, 118.97, 118.45 (q, J = 320.2 Hz), 32.55, 29.30; ¹⁹F NMR (565 MHz, CDCl₃) δ -74.99; MS (EI): Calcd for C₁₈H₁₄F₆O₆S₂, M⁺ m/z 504. Found M⁺ m/z 504.

(b) Synthesis of Rac-6,7,8,9-tetrahydro-5H-dibenzo[a,c][9]annulene-1,13-diyl bis(trifluoromethanesulfonate) (Rac-M-1F)

Rac-M-1F was synthesized by the same procedure as that for Rac-M-1E as white solid. Yield 94%. mp = 73-74°C. ¹H NMR (400 MHz, CDCl₃) δ 7.48 (t, J = 8.0 Hz, 2H), 7.37 (d, J = 7.7 Hz, 2H), 7.25 (d, J = 8.1 Hz, 2H), 2.81 (ddd, J = 14.4, 7.0, 3.5 Hz, 2H), 2.08 (ddd, J = 14.2, 10.9, 3.1 Hz, 2H), 1.93-1.79 (m, 2H), 1.61-1.50 (m, 2H), 1.47-1.35 (m, 2H); ¹³C NMR (75 MHz, CDCl₃) δ...
147.10, 146.89, 130.50, 129.55, 128.23, 118.86, 118.41 (q, $J = 319.5$ Hz), 33.50, 28.81, 28.63; $^{19}$F NMR (565 MHz, CDCl$_3$) $\delta$ -75.17; MS (EI): Calcd for C$_{19}$H$_{16}$F$_6$O$_6$S$_2$, M$^+$ $m/z$ 518. Found M$^+$ $m/z$ 518.

(c) **Synthesis of Rac-5,6,7,8,9,10-hexahydrodibenzo[ace][10]annulene-1,14-diyl bis(trifluoromethanesulfonate) (Rac-M-1G)**

Rac-M-1G was synthesized by the same procedure as that for Rac-M-1E as a white solid. Yield 94%. mp = 74-75°C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.47 (t, $J = 8.0$ Hz, 2H), 7.39 (d, $J = 7.7$ Hz, 2H), 7.26 (d, $J = 8.1$ Hz, 2H), 2.67 (dt, $J = 14.1$, 3.9 Hz, 2H), 2.41 (td, $J = 13.6$, 4.2 Hz, 2H), 1.85-1.70 (m, 2H), 1.56-1.46 (m, 2H), 1.40-1.27 (m, 3H), 0.93-0.66 (m, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 147.54, 145.49, 130.45, 128.79, 128.46, 118.42, 118.33 (q, $J = 319.5$ Hz), 28.96, 28.80, 21.02; $^{19}$F NMR (565 MHz, CDCl$_3$) $\delta$ -75.54; MS (EI): Calcd for C$_{19}$H$_{16}$F$_6$O$_6$S$_2$, M$^+$ $m/z$ 518. Found M$^+$ $m/z$ 518.
(2) Synthesis of compounds Rac-M-2

(a) Synthesis of Rac-12-(diphenylphosphoryl)-5,6,7,8-tetrahydrodibenzo[a,c][8]-annulen-1-yl trifluoromethanesulfonate (Rac-M-2E)

**Typical procedure:** To a mixture of Rac-M-1E (5.0 g, 9.92 mmol), diphenylphosphine oxide (4.0 g, 19.84 mmol), palladium acetate (112 mg, 0.5 mmol) and 1,4-bis(diphenylphosphino)butane (dppb, 213 mg, 0.5 mmol) was added 30 mL of degassed DMSO and diisopropylethylamine (6.56 mL, 39.7 mmol), and the mixture was heated with stirring at 100 °C for 10 h. After cooling to room temperature, the reaction mixture was diluted with EtOAc, washed twice with water, dried over anhydrous MgSO₄ and concentrated under reduced pressure. The residue was chromatographed on a silica gel column eluted with petroleum ether/EtOAc (4:1 in volume) to give (S)-12-(diphenylphosphoryl)-5,6,7,8-tetrahydrodibenzo[a,c][8]-annulen-1-yl trifluoromethanesulfonate Rac-M-2E (4.9 g, 89%) as a white solid, mp = 203-205°C. ¹H NMR (400 MHz, CDCl₃) δ 7.72 (dd, J₁ = 11.7, J₂ = 7.4 Hz, 2H), 7.53-7.33 (m, 8H), 7.32-7.17 (m, 4H), 7.03 (d, J₁ = 8.0 Hz, 2H), 2.69 (dd, J₁ = 13.6, J₂ = 7.9 Hz, 1H), 2.37 (dd, J₁ = 13.2, J₂ = 7.5 Hz, 1H), 2.27-2.15 (m, 1H), 2.09-1.96 (m, 1H), 1.96-1.78 (m, 2H), 1.38-1.26 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 147.77, 146.69, 146.60, 146.21, 136.85, 136.78, 134.22, 133.14, 132.24, 132.15, 132.11, 131.77, 131.69, 131.59, 131.56, 131.49, 131.26, 131.24, 131.19, 131.15, 130.77, 130.01, 128.58, 128.44, 128.36, 128.24, 128.17, 128.05, 118.31 (q, J = 320.2 Hz), 118.23, , 32.36, 32.05, 29.73, 29.67; ¹⁹F NMR (283 MHz, CDCl₃) δ -74.49; ³¹P NMR (122 MHz, CDCl₃) δ 28.09; HRMS (ESI⁺): Calcd for [C₂₀H₁₅F₃O₄PS]⁺ m/z 557.1163. Found 557.1169.

(b) Synthesis of Rac-13-(diphenylphosphoryl)-6,7,8,9-tetrahydro-5H-dibenzo[a,c][9]-annulen-1-yl trifluoromethanesulfonate (Rac-M-2F)
Rac-M-2F was synthesized by the same procedure as that for Rac-M-2E as white solid, mp = 206-207°C, yield 88%. ¹H NMR (400 MHz, CDCl₃) δ 7.63-7.52 (m, 4H), 7.43 (t, J = 7.7 Hz, 3H), 7.39-7.30 (m, 5H), 7.28-7.20 (m, 2H), 7.09 (d, J = 7.7 Hz, 1H), 6.90 (d, J = 8.2 Hz, 1H), 2.68 (dt, J₁ = 13.8, J₂ = 4.5 Hz, 1H), 2.50-2.38 (m, 1H), 2.12-1.98 (m, 1H), 1.97-1.85 (m, 1H), 1.79-1.59 (m, 2H), 1.56-1.40 (m, 1H), 1.39-1.23 (m, 2H), 1.19-1.04 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 147.29, 146.17, 144.77, 144.68, 138.03, 137.95, 133.51, 132.94, 132.86, 132.85, 132.48, 131.96, 131.90, 131.87, 131.80, 131.70, 131.42, 131.37, 131.34, 131.31, 130.84, 129.36, 128.54, 128.20, 128.08, 128.03, 127.97, 127.90, 118.10 (q, J = 319.8 Hz), 117.64, 34.15, 32.30, 29.65, 28.92, 27.77; ¹⁹F NMR (565 MHz, CDCl₃) δ -75.64; ³¹P NMR (243 MHz, CDCl₃) δ 27.27; HRMS (ESI⁺): Calcd for C₃₀H₂₇F₃O₄PS, [M+H]⁺ m/z 571.1320. Found 571.1317.

(c) **Synthesis of Rac-14-(diphenylphosphoryl)-5,6,7,8,9,10-hexahydrodibenzo[a,e][10]-annulen-1-yl trifluoromethanesulfonate (Rac-M-2G)**

Rac-M-2G was synthesized by the same procedure as that for Rac-M-2E as a white solid. Yield 90%. mp = 204-205°C. ¹H NMR (400 MHz, CDCl₃) δ 7.79-7.70 (m, 2H), 7.54-7.33 (m, 8H), 7.29-7.17 (m, 5H), 6.61 (d, J = 7.8 Hz, 1H), 2.60 (t, J = 13.6 Hz, 2H), 2.46-2.32 (m, 2H), 1.70 (q, J = 12.7 Hz, 2H), 1.49-1.38 (m, 2H), 1.31-1.20 (m, 2H), 0.73-0.55 (m, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 147.50, 146.44, 143.68, 143.56, 138.82, 138.72, 133.50, 132.93, 132.90, 132.24, 132.12, 131.84, 131.67, 131.58, 131.55, 131.52, 131.15, 131.10, 130.97, 129.56, 128.42, 128.27, 128.06, 127.90, 127.71, 118.07 (q, J = 319.5 Hz), 116.55, 29.95, 29.08, 28.62, 28.54, 21.15, 20.55; ¹⁹F NMR (283 MHz, CDCl₃) δ -75.05; ³¹P NMR (122 MHz, CDCl₃) δ 27.11; HRMS (ESI⁺): Calcd for C₃₁H₂₆F₃O₄PS, [M+H]⁺ m/z 585.1476. Found 585.1516.
(3) Synthesis of compounds Rac-M-3 (Wu et al., 2004)

**Typical procedure:** In a 250 mL pressure tube Rac-M-2E (2.78 g, 5.0 mmol) and triphenylphosphine (2.62 g, 10.0 mmol) were dissolved in 100 mL of mixed solvent of degassed THF and toluene (1:1) under nitrogen atmosphere. To the solution was added trichlorosilane (10.1 mL, 100.0 mmol) at room temperature, and the mixture was stirred at 100 °C for 4 h. After cooling to ambient temperature, the mixture was diluted with diethyl ether. To the solution was added ice (250 g) and 20% NaOH solution (250 mL). The mixture was transferred to a separating funnel and shaken for 10 min. The organic layer was separated and washed successively with saturated NaHCO₃, brine and water. The solution was then dried over anhydrous Na₂SO₄ and the solvent removed under reduced pressure. The residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc 50:1) to afford Rac-M-3E (2.2 g, 82%) as a white solid, mp = 76-78°C. 

**1H NMR** (400 MHz, CDCl₃) δ 7.37-7.23 (m, 8H), 7.23-7.18 (m, 2H), 7.18-7.12 (m, 2H), 7.05 (d, J = 7.7 Hz, 1H), 7.02-6.94 (m, 3H), 2.68 (dd, J = 13.5, 7.8 Hz, 1H), 2.23-2.06 (m, 2H), 2.02-1.93 (m, 1H), 1.92-1.81 (m, 1H), 1.59 (t, J = 12.3 Hz, 1H), 1.41-1.19 (m, 2H); **13C NMR** (100 MHz, CDCl₃) δ 147.38, 146.48, 145.13, 145.08, 138.08, 137.95, 137.79, 137.49, 137.49, 137.19, 137.07, 136.10, 135.99, 134.62, 134.40, 133.33, 133.16, 132.48, 132.40, 130.84, 130.27, 129.79, 129.77, 129.35, 129.01, 128.85, 128.64, 128.52, 128.49, 128.25, 128.16, 120.10, 118.81, 116.91, 32.42, 31.92, 29.87, 29.72; **19F NMR** (565 MHz, CDCl₃) δ −75.18; **31P NMR** (243 MHz, CDCl₃) δ −9.79; **HRMS** (ESI⁺): Calcd for C₉₈H₁₂₃F₃O₃PS, [M+H]⁺ m/z 541.1214. Found 544.1207.

(b) Synthesis of Rac-13-(diphenylphosphanyl)-6,7,8,9-tetrahydro-5H-dibenzo[a,e][9]-annulen-1-yl trifluoromethanesulfonate (Rac-M-3F)
**Rac-M-3F** was synthesized by the same procedure as that for **Rac-M-3E** as a white solid. Yield 84%. mp = 96-97°C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.37 (t, $J = 8.0$ Hz, 1H), 7.33-7.18 (m, 11H), 7.15-7.08 (m, 3H), 7.08-7.02 (m, 1H), 2.80-2.66 (m, 1H), 2.09-1.90 (m, 2H), 1.81-1.66 (m, 1H), 1.64-1.17 (m, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 146.78, 146.49, 143.52, 143.46, 139.67, 139.34, 137.88, 137.77, 137.31, 137.19, 135.95, 135.84, 134.84, 134.63, 133.84, 133.76, 133.27, 133.08, 131.41, 130.27, 129.38, 128.96, 128.91, 128.45, 128.39, 128.32, 128.21, 123.18, 119.92, 118.61, 116.81, 113.63, 33.48, 32.85, 29.47, 29.10, 28.24; $^{19}$F NMR (565 MHz, CDCl$_3$) $\delta$ -75.44; $^{31}$P NMR (243 MHz, CDCl$_3$) $\delta$ -12.45; HRMS (ESI$^+$): Calcd for C$_{30}$H$_{27}$F$_3$O$_3$PS, [M+H]$^+$ m/z 555.1371. Found 555.1357.

(c) **Synthesis of Rac-14-(diphenylphosphanyl)-5,6,7,8,9,10-hexahydrodibenzo[a,c][10]-annulen-1-yl trifluoromethanesulfonate (Rac-M-3G)**

**Rac-M-3G** was synthesized by the same procedure as that for **Rac-M-3E** as a white solid. Yield 86%. mp = 115-116°C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.39-7.18 (m, 12H), 7.12-7.03 (m, 3H), 7.01 (ddd, $J = 7.2$, 3.4, 1.5 Hz, 1H), 2.61 (dt, $J = 13.9$, 3.4 Hz, 1H), 2.36 (td, $J = 13.6$, 4.0 Hz, 1H), 2.19 (td, $J = 13.7$, 3.9 Hz, 1H), 2.04-1.91 (m, 1H), 1.81-1.57 (m, 2H), 1.53-1.40 (m, 1H), 1.37-1.20 (m, 3H), 0.81-0.58 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 147.64, 145.30, 141.85, 141.80, 140.59, 140.28, 138.31, 138.21, 136.82, 136.71, 136.55, 136.43, 134.50, 134.36, 134.28, 133.75, 133.56, 131.82, 129.73, 129.38, 128.80, 128.43, 128.21, 119.80, 117.87, 116.62, 29.00, 28.83, 28.48, 21.08, 20.96; $^{19}$F NMR (565 MHz, CDCl$_3$) $\delta$ -75.69; $^{31}$P NMR (243 MHz, CDCl$_3$) $\delta$ -13.29; HRMS (ESI$^+$): Calcd for C$_{31}$H$_{29}$F$_3$O$_3$PS, [M+H]$^+$ m/z 569.1527. Found 569.1522.
(4) Synthesis of compounds Rac-M-4

(a) Synthesis of Rac-(12-(diphenylphosphanyl)-5,6,7,8-tetrahydrodibenzo[a,c][8]-annulen-1-yl) diphenylphosphine oxide (Rac-M-4E)

**Typical procedure:** To a mixture of Rac-M-3E (1.35 g, 2.5 mmol), diphenylphosphine oxide (1.0 g, 4.95 mmol), palladium acetate (28 mg, 0.125 mmol) and 1,4-bis(diphenylphosphino)butane (dppb, 53 mg, 0.125 mmol) was added 15 mL of degassed DMSO and diisopropylethylamine (1.64 mL, 1.28 g, 9.93 mmol), and the mixture was heated with stirring at 100 °C for 10 h. After cooling to room temperature, the reaction mixture was diluted with EtOAc, washed twice with water, dried over anhydrous MgSO₄ and concentrated under reduced pressure. The residue was chromatographed on a silica gel column eluted with petroleum ether/EtOAc (4:1 in volume) to give Rac-M-4E (2.15 g, 86%) as a white solid, mp = 248-249°C. ¹H NMR (600 MHz, CDCl₃) δ 8.01-7.87 (m, 2H), 7.54 (t, J = 6.9 Hz, 2H), 7.49 (t, J = 7.3 Hz, 1H), 7.47-7.41 (m, 2H), 7.37-7.25 (m, 8H), 7.22-7.15 (m, 3H), 7.16-7.11 (m, 3H), 7.05 (t, J = 7.5 Hz, 1H), 7.02-6.96 (m, 3H), 6.59 (d, J = 7.5 Hz, 1H), 1.91 (dd, J = 13.2, 7.5 Hz, 1H), 1.73-1.62 (m, 4H), 1.17 (t, J = 11.6 Hz, 1H), 1.12-1.01 (m, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 146.06, 145.98, 145.92, 143.22, 143.19, 142.86, 142.80, 142.75, 141.20, 141.12, 141.03, 141.00, 140.82, 139.38, 139.27, 136.92, 136.82, 135.99, 135.83, 134.40, 133.83, 133.71, 133.42, 133.31, 133.15, 132.61, 132.56, 131.74, 131.65, 131.30, 130.95, 130.89, 130.52, 129.48, 128.64, 128.59, 128.53, 128.29, 128.21, 128.15, 128.12, 127.96, 127.91, 127.87, 127.79, 127.70, 127.61, 127.30, 33.04, 30.88, 30.08, 29.93; ³¹P NMR (243 MHz, CDCl₃) δ 25.30, -11.16; HRMS (ESI⁺): Calcd for C₅₀H₃₅OP₂, [M+H]⁺ m/z 593.2163. Found 593.2169.

(b) Synthesis of Rac-(13-(diphenylphosphanyl)-6,7,8,9-tetrahydro-5H-dibenzo[a,c][9]-annulen-1-yl) diphenylphosphine oxide (Rac-M-4F)
Rac-M-4F was synthesized by the same procedure as that for Rac-M-4E as a white solid. Yield 85%. mp = 227-229°C. 1H NMR (400 MHz, CDCl3) δ 7.83 (dd, J = 11.3, 7.4 Hz, 2H), 7.49 (dd, J = 11.4, 7.6 Hz, 2H), 7.44-7.29 (m, 6H), 7.27-7.06 (m, 15H), 6.79 (d, J = 7.0 Hz, 1H), 1.95-1.76 (m, 1H), 1.55-1.26 (m, 4H), 1.24-0.98 (m, 4H), 0.97-0.80 (m, 1H); 13C NMR (100 MHz, CDCl3) δ 144.50, 144.41, 144.31, 144.23, 144.15, 142.91, 142.87, 142.59, 142.55, 141.62, 141.57, 139.96, 139.86, 139.72, 139.57, 136.29, 136.14, 135.78, 135.55, 134.62, 133.59, 133.43, 132.94, 132.77, 132.42, 132.24, 132.15, 132.12, 131.67, 131.58, 131.32, 131.20, 131.08, 130.74, 130.36, 130.06, 129.08, 128.65, 128.10, 127.97, 127.95, 127.87, 127.83, 127.71, 126.96, 126.79, 33.91, 30.99, 29.50, 29.26, 27.85; 31P NMR (243 MHz, CDCl3) δ 26.51, -12.45; HRMS (ESI+): Calcd for C41H37OP2, [M+H]+ m/z 607.2320. Found 607.2309.

(c) Synthesis of Rac-(14-(diphenylphosphanyl)-5,6,7,8,9,10-hexahydrodibenzo[a,e][10]-annulen-1-yl)diphenylphosphine oxide (Rac-M-4G)

Rac-M-4G was synthesized by the same procedure as that for Rac-M-4E as a white solid. Yield 87%. mp = 259-260°C. 1H NMR (400 MHz, CDCl3) δ 7.60 (q, J = 10.1 Hz, 4H), 7.45-7.14 (m, 21H), 7.10-7.03 (m, 2H), 1.96-1.71 (m, 2H), 1.59-1.39 (m, 3H), 1.21-1.01 (m, 5H), 0.71-0.36 (m, 2H); 13C NMR (100 MHz, CDCl3) δ 145.93, 145.85, 145.77, 144.97, 144.94, 144.65, 144.62, 143.96, 143.93, 143.86, 143.83, 140.10, 140.05, 139.92, 139.37, 139.28, 136.67, 136.54, 135.61, 135.38, 135.30, 134.26, 133.77, 133.01, 132.84, 132.76, 132.25, 132.16, 131.92, 131.82, 131.68, 131.62, 131.21, 131.20, 130.26, 128.81, 128.24, 128.21, 128.13, 128.04, 127.96, 127.91, 127.10, 126.79, 126.65, 28.96, 28.66, 28.41, 27.52, 21.07, 20.80; 31P NMR (122 MHz, CDCl3) δ 29.53, -14.53; HRMS (ESI+): Calcd for C42H39OP2, [M+H]+ m/z 621.2676. Found 621.2470.
(5) Separation of Rac-M-4 to provide (R)-M-4 and (S)-M-4

Rac-M-4 were separated to afford the (R)-M-4 and (S)-M-4 with the help of Daicel Chiral Technologies (China) Co., Ltd.

HPLC analysis for (R)-M-4E: Daicel Chiralpak IF; hexane/EtOH: 90:10; flow: 1.0 mL/min; \( \lambda = 220 \) nm. 99% ee (\( t_R \) (major) = 9.7 min, \( t_R \) (minor) = 12.4 min).

HPLC analysis for (S)-M-4E: Daicel Chiralpak IF; hexane/EtOH: 90:10; flow: 1.0 mL/min; \( \lambda = 220 \) nm. 99% ee (\( t_R \) (minor) = 9.8 min, \( t_R \) (major) = 12.4 min).

HPLC analysis for (R)-M-4F: Daicel Chiralpak IF; hexane/EtOH: 90:10; flow: 1.0 mL/min; \( \lambda = 220 \) nm. 99% ee (\( t_R \) (major) = 9.4 min, \( t_R \) (minor) = 12.2 min).

HPLC analysis for (S)-M-4F: Daicel Chiralpak IF; hexane/EtOH: 90:10; flow: 1.0 mL/min; \( \lambda = 220 \) nm. 99% ee (\( t_R \) (minor) = 9.3 min, \( t_R \) (major) = 12.2 min).

HPLC analysis for (R)-M-4G: Daicel Chiralpak IF; hexane/EtOH: 90:10; flow: 1.0 mL/min; \( \lambda = 220 \) nm. 98% ee (\( t_R \) (major) = 8.2 min, \( t_R \) (minor) = 11.2 min).

HPLC analysis for (S)-M-4G: Daicel Chiralpak IF; hexane/EtOH: 90:10; flow: 1.0 mL/min; \( \lambda = 220 \) nm. 98% ee (\( t_R \) (minor) = 8.3 min, \( t_R \) (major) = 11.3 min).
(6) Synthesis of ligands (R)-E, (S)-E, (R)-F, (S)-F, (R)-G and (S)-G

(a) Synthesis of \((S)-1,12\text{-bis(diphenylphosphanyl)}\)-5,6,7,8-tetrahydrodibenzo[\(a,c\)][8]-annulene ((S)-E)

**Typical procedure:** In a 250 mL pressure tube, \((S)\)-M-4E (0.592 g, 1.0 mmol) and triphenylphosphine (0.52 g, 2.0 mmol) were dissolved in the 20 mL of mixed solvent of degassed THF and toluene (1:1) under nitrogen atmosphere. To the solution was added trichlorosilane (2.02 mL, 20.0 mmol) at room temperature, and the mixture was stirred at 100 °C for 4 h. After cooling to ambient temperature, the mixture was diluted with diethyl ether. To the solution was added ice (50 g) and 20% NaOH solution (50 mL). The mixture was transferred to a separating funnel and shook for 10 min. The organic layer was separated and washed successively with saturated NaHCO\(_3\), brine and water. The solution was then dried over anhydrous Na\(_2\)SO\(_4\) and the solvent removed under reduced pressure. The residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc 50:1) to afford (S)-E (0.484 g, 84%) as a white solid, mp = 275-277°C. \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 7.50-7.43 (m, 4H), 7.34-7.27 (m, 6H), 7.24-7.20 (m, 2H), 7.19-7.14 (m, 6H), 7.11-7.05 (m, 4H), 6.97 (d, \(J = 7.5\) Hz, 2H), 6.92 (d, \(J = 7.6\) Hz, 2H), 1.87 (dd, \(J = 13.3, 7.8\) Hz, 2H), 1.77-1.66 (m, 2H), 1.49-1.39 (m, 2H), 1.20-1.08 (m, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 144.68, 144.65, 144.62, 142.47, 142.31, 142.15, 139.03, 138.95, 138.95, 138.87, 138.46, 136.52, 136.47, 136.42, 135.40, 135.28, 135.17, 133.32, 133.22, 133.12, 130.38, 129.42, 128.65, 128.36, 128.01, 127.98, 127.94, 127.86, 31.82, 30.16; \(^{31}\)P NMR (243 MHz, CDCl\(_3\)) \(\delta\) -9.37; HRMS (ESI\(^+\)): Calcd for C\(_{40}\)H\(_{35}\)P\(_2\), [M+H]\(^+\) \(m/z\) 577.2214. Found 577.2215. (R)-E was prepared by using the similar procedures.

(b) Synthesis of \((S)-1,13\text{-bis(diphenylphosphanyl)}\)-6,7,8,9-tetrahydro-\(5H\)-dibenzo-\([a,c]\)[9]annulene ((S)-F)
(S)-F was synthesized by the same procedure as that for (S)-E as a white solid. Yield 87%. mp = 225-226°C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.35-7.18 (m, 23H), 7.04 (d, \(J = 7.5\) Hz, 2H), 6.97 (d, \(J = 7.6\) Hz, 2H), 1.75-1.63 (m, 2H), 1.51-1.38 (m, 2H), 1.34-1.23 (m, 2H), 1.23-1.11 (m, 2H), 1.11-0.99 (m, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 144.83, 144.66, 144.48, 143.35, 143.31, 143.28, 139.26, 139.19, 139.12, 138.14, 136.12, 136.06, 136.01, 135.63, 135.51, 135.40, 133.00, 132.90, 132.80, 131.21, 129.54, 128.84, 128.26, 128.18, 128.15, 128.11, 127.92, 127.67, 32.72, 29.56, 28.11; \(^{31}\)P NMR (121 MHz, CDCl\(_3\)) \(\delta\) -12.45; HRMS (ESI\(^+\)) Calcd for C\(_{41}\)H\(_{37}\)P\(_2\), [M+H]\(^+\) \(m/z\) 591.2370. Found 591.2361. (R)-F was prepared by using the similar procedures.

(c) Synthesis of (S)-1,14-bis(diphenylphosphanyl)-5,6,7,8,9,10-hexahydrodibenzo-[a,e][10]annulene ((S)-G)

(S)-G was synthesized by the same procedure as that for (S)-E as a white solid. Yield 80%. mp = 247-249°C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.35-7.26 (m, 12H), 7.23-7.16 (m, 6H), 7.14-7.06 (m, 6H), 7.06-7.00 (m, 2H), 1.84 (td, \(J = 13.6, 3.6\) Hz, 2H), 1.56-1.49 (m, 2H), 1.43-1.32 (m, 2H), 1.20-1.08 (m, 4H), 0.71-0.49 (m, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 147.04, 146.99, 146.80, 146.60, 146.55, 142.06, 142.02, 141.98, 139.36, 139.28, 139.22, 138.28, 136.65, 136.58, 136.52, 135.55, 135.42, 135.30, 135.19, 135.06, 133.24, 133.10, 133.00, 132.90, 132.77, 132.30, 129.16, 128.85, 128.28, 128.19, 127.88, 127.62, 28.96, 28.43, 21.09; \(^{31}\)P NMR (121 MHz, CDCl\(_3\)) \(\delta\) -14.16; HRMS (ESI\(^+\)) Calcd for C\(_{42}\)H\(_{39}\)P\(_2\), [M+H]\(^+\) \(m/z\) 605.2527. Found 605.2524. (R)-G was prepared by using the similar procedures.
3. Synthesis and Characterization Data of Substrates

As shown in Scheme S1, compounds S4 were synthesized from the corresponding carboxylic acid as starting materials according to the literature procedure (Svenstrup et al., 1999). Compounds S5 were synthesized by the corresponding substituted toluene (Roberts et al., 2015). Compounds S6 were synthesized from the corresponding substituted hydrazine hydrochloride and the corresponding S4 (Sheng et al., 2015). Compounds S6 were performed from the corresponding S5 and the corresponding S4 according to the previous procedure (Yang et al., 2013).

Scheme S1. Synthetic routes of compounds 1a-ah and 3. Reagents and conditions: (a) SOCl₂, overnight; (b) Pyridine, CH₂Cl₂, 0 °C to rt, 2 h; (c) Abs. EtOH, reflux, 2.5 h; (d) AcONa, AcOH, reflux, 5–10 h; (e) NBS, CCl₄, (PhCO)₂, reflux; (f) CH₃CN, 120 °C, 24 h.

1-(2-Iodobenzyl)-5-methyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (1a): Pale yellow solid, mp = 173-174 °C; Eluent: EtOAc; ¹H NMR (400 MHz, CDCl₃) δ 7.74 (d, J = 7.9 Hz, 1H), 7.41 (t, J = 7.7 Hz, 2H), 7.33-7.25 (m, 4H), 6.95 (t, J = 7.5 Hz, 1H), 6.82 (d, J = 7.8 Hz, 1H), 5.47 (s, 1H), 4.73 (s, 2H), 2.19 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 166.53, 154.01, 139.57, 137.58, 134.49, 129.54, 129.41, 128.96, 127.76, 126.43, 125.86, 97.92, 96.60, 54.46, 12.87; HRMS (ESI⁺): Calcd for C₁₇H₁₆IN₂O, [M+H]⁺ m/z 391.0307. Found 391.0305.
5-Ethyl-1-(2-iodobenzyl)-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (2a): Pale yellow solid, mp = 120-121 °C; Eluent: EtOAc; 1H NMR (400 MHz, CDCl₃) δ 7.72 (d, J = 8.0 Hz, 1H), 7.41 (t, J = 7.7 Hz, 2H), 7.32-7.23 (m, 4H), 6.93 (t, J = 7.6 Hz, 1H), 6.80 (d, J = 7.8 Hz, 1H), 5.49 (s, 1H), 4.73 (s, 2H), 2.46 (q, J = 7.5 Hz, 2H), 1.26 (t, J = 7.5 Hz, 3H); 13C NMR (100 MHz, CDCl₃) δ 166.66, 159.89, 139.55, 137.76, 134.46, 129.50, 129.40, 128.93, 128.60, 128.90, 127.73, 126.47, 125.86, 96.24, 54.43, 20.06, 11.61; HRMS (ESI⁺): Calcd for C₁₈H₁₈IN₂O, [M+H]⁺ m/z 405.0454. Found 405.04546.

1-(2-Iodobenzyl)-2-phenyl-5-propyl-1,2-dihydro-3H-pyrazol-3-one (1c): Pale yellow solid, mp = 108-109 °C; Eluent: EtOAc; 1H NMR (400 MHz, CDCl₃) δ 7.72 (d, J = 7.9 Hz, 1H), 7.41 (t, J = 7.8 Hz, 2H), 7.32-7.23 (m, 4H), 6.93 (t, J = 7.6 Hz, 1H), 6.81 (d, J = 7.1 Hz, 1H), 5.48 (s, 1H), 4.73 (s, 2H), 2.41 (t, J = 7.6 Hz, 2H), 1.70 (sext, J = 7.4 Hz, 2H), 1.01 (t, J = 7.4 Hz, 3H); 13C NMR (100 MHz, CDCl₃) δ 166.65, 158.43, 139.54, 137.76, 134.47, 129.50, 128.93, 127.73, 126.47, 125.86, 96.24, 54.43, 20.06, 13.76; HRMS (ESI⁺): Calcd for C₁₉H₂₀IN₂O, [M+H]⁺ m/z 419.0620. Found 419.0612.

1-(2-Iodobenzyl)-5-isopropyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (1d): Pale yellow solid, mp = 164-165 °C; Eluent: EtOAc; 1H NMR (400 MHz, CDCl₃) δ 7.71 (d, J = 7.9 Hz, 1H), 7.40 (t, J = 7.7 Hz, 2H), 7.32-7.22 (m, 4H), 6.91 (t, J = 7.7 Hz, 1H), 6.77 (d, J = 7.8 Hz, 1H), 5.48 (s, 1H), 4.76 (s, 2H), 2.68 (hept, J = 6.8 Hz, 1H), 1.26 (d, J = 6.8 Hz, 6H); 13C NMR (100 MHz, CDCl₃) δ 166.55, 164.65, 139.47, 137.93, 134.34, 129.44, 129.33, 128.83, 127.67, 126.38, 125.86, 96.57,
5-Cyclopropyl-1-(2-iodobenzyl)-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (1e): Pale yellow solid, mp = 135-136 °C; Eluent: EtOAc; 1H NMR (400 MHz, CDCl₃) δ 7.73 (d, J = 7.9 Hz, 1H), 7.43-7.37 (m, 2H), 7.32-7.23 (m, 4H), 6.96-6.87 (m, 2H), 5.17 (s, 1H), 4.88 (s, 2H), 1.66-1.53 (m, 1H), 0.99-0.93 (m, 2H), 0.71-0.66 (m, 2H); 13C NMR (100 MHz, CDCl₃) δ 166.70, 161.17, 139.48, 137.96, 134.60, 129.42, 129.34, 128.79, 127.52, 126.88, 125.55, 97.03, 93.30, 55.15, 8.27, 7.70; HRMS (ESI⁺): Calcd for C₁₉H₂₀IN₂O, [M+H]⁺ m/z 419.0620. Found 419.0613.

5-Cyclopentyl-1-(2-iodobenzyl)-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (1f): Pale yellow solid, mp = 166-167 °C; Eluent: EtOAc; 1H NMR (400 MHz, CDCl₃) δ 7.72 (d, J = 7.9 Hz, 1H), 7.41 (t, J = 7.6 Hz, 2H), 7.33-7.21 (m, 4H), 6.93 (t, J = 7.5 Hz, 1H), 6.80 (d, J = 7.7 Hz, 1H), 5.48 (s, 1H), 4.78 (s, 2H), 2.76 (quint, J = 7.8 Hz, 1H), 2.05-1.91 (m, 2H), 1.83-1.59 (m, 6H); 13C NMR (150 MHz, CDCl₃) δ 166.74, 163.03, 139.48, 138.06, 134.39, 129.44, 129.37, 128.87, 127.72, 126.59, 125.93, 96.57, 95.01, 54.55, 36.98, 32.67, 25.26; HRMS (ESI⁺): Calcd for C₂₁H₂₂IN₂O, [M+H]⁺ m/z 445.0777. Found 445.0769.

1-(2-Iodobenzyl)-5-phenethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (1g): Pale yellow solid, mp = 200-201 °C; Eluent: EtOAc; 1H NMR (400 MHz, CDCl₃) δ 7.71 (d, J = 7.9 Hz, 1H), 7.41 (t, J = 7.5 Hz, 2H), 7.36-7.15 (m, 9H), 6.93 (t, J = 7.6 Hz, 1H), 6.67 (d, J = 7.6 Hz, 1H), 5.69 (s, 1H), 4.66 (s, 2H), 2.98 (t, J = 7.4 Hz, 2H), 2.80 (t, J = 7.5 Hz, 2H); 13C NMR (100 MHz, CDCl₃) δ 165.34, 156.61, 139.67, 139.50, 137.28, 133.50, 129.73, 129.61, 129.05, 128.77, 128.59, 128.52,
126.81, 126.44, 96.46, 96.37, 54.41, 33.90, 28.47; HRMS (ESI\(^+\)): Calcd for C\(_{24}\)H\(_{22}\)IN\(_2\)O, [M+H]\(^+\) \(m/z\) 481.0777. Found 481.0771.

1-(2-Iodobenzyl)-2-phenyl-5-(3-phenylpropyl)-1,2-dihydro-3\(H\)-pyrazol-3-one (1h): Pale yellow solid, mp = 172-173 °C; Eluent: EtOAc; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.73 (d, \(J = 7.9\) Hz, 1H), 7.49 (t, \(J = 7.4\) Hz, 1H), 7.40 (t, \(J = 7.7\) Hz, 2H), 7.33-7.16 (m, 6H), 7.08 (d, \(J = 7.2\) Hz, 2H), 7.00 (t, \(J = 7.6\) Hz, 1H), 6.68 (s, 1H), 6.41 (d, \(J = 7.7\) Hz, 1H), 5.06 (s, 2H), 2.71-2.60 (m, 4H), 1.99 (quint, \(J = 7.6\) Hz, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 158.85, 154.01, 140.16, 140.14, 135.17, 131.97, 130.47, 130.27, 129.47, 129.22, 128.71, 128.45, 128.41, 126.20, 96.19, 92.39, 54.68, 34.95, 28.41, 25.95; HRMS (ESI\(^+\)): Calcd for C\(_{25}\)H\(_{24}\)IN\(_2\)O, [M+H]\(^+\) \(m/z\) 495.0933. Found 495.0931.

5-Benzyl-1-(2-iodobenzyl)-2-phenyl-1,2-dihydro-3\(H\)-pyrazol-3-one (1i): Pale yellow solid, mp = 133-134 °C; Eluent: EtOAc; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.72 (d, \(J = 8.7\) Hz, 1H), 7.39 (t, \(J = 7.7\) Hz, 2H), 7.34-7.23 (m, 7H), 7.19 (d, \(J = 6.9\) Hz, 2H), 6.93 (t, \(J = 7.1\) Hz, 1H), 6.84-6.80 (m, 1H), 5.41 (s, 1H), 4.69 (s, 2H), 3.76 (s, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 166.27, 156.81, 139.58, 137.75, 135.30, 134.29, 129.53, 129.43, 128.94, 128.91, 128.78, 127.86, 127.37, 126.45, 125.90, 98.91, 96.51, 54.51, 33.30; HRMS (ESI\(^+\)): Calcd for C\(_{23}\)H\(_{21}\)IN\(_2\)O, [M+H]\(^+\) \(m/z\) 467.0620. Found 467.0615.

1-(2-Iodobenzyl)-2-phenyl-5-(2,4,6-trimethylbenzyl)-1,2-dihydro-3\(H\)-pyrazol-3-one (1j): Pale yellow solid, mp = 194-195 °C; Eluent: EtOAc; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.83-7.75 (m, 1H), 7.44 (t, \(J = 7.8\) Hz, 2H), 7.38-7.28 (m, 4H), 7.03-6.94 (m, 2H), 6.84 (s, 2H), 4.89 (s, 1H), 4.85 (s,
5-([1,1'-Biphenyl]-4-ylmethyl)-1-(2-iodobenzyl)-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (1k):
Pale yellow solid, mp = 184-185 °C; Eluent: EtOAc; ¹H NMR (400 MHz, CDCl₃) δ 7.71 (d, J = 7.9 Hz, 1H), 7.56 (d, J = 7.6 Hz, 2H), 7.52 (d, J = 8.1 Hz, 2H), 7.46-7.22 (m, 12H), 6.92 (t, J = 7.5 Hz, 1H), 6.83 (d, J = 7.7 Hz, 1H), 5.49 (s, 1H), 4.70 (s, 2H), 3.80 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 166.26, 156.60, 140.51, 140.28, 139.55, 137.78, 134.28, 129.51, 129.47, 128.94, 128.87, 127.89, 127.59, 127.47, 127.06, 126.48, 125.91, 98.99, 96.53, 54.54, 32.99; HRMS (ESI⁺): Calcd for C₂₉H₂₆IN₂O, [M+H]⁺ m/z 509.1090. Found 509.1078.

1-(2-Iodobenzyl)-5-(naphthalen-1-ylmethyl)-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (II):
Pale yellow solid, mp = 205-206 °C; Eluent: EtOAc; ¹H NMR (400 MHz, CDCl₃) δ 7.83 (d, J = 8.0 Hz, 1H), 7.77 (d, J = 8.2 Hz, 1H), 7.73 (d, J = 7.8 Hz, 1H), 7.63 (d, J = 8.3 Hz, 1H), 7.46 (t, J = 7.3 Hz, 1H), 7.43-7.36 (m, 4H), 7.33-7.23 (m, 5H), 6.99-6.91 (m, 2H), 5.16 (s, 1H), 4.79 (s, 2H), 4.15 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 166.23, 157.00, 139.66, 137.80, 134.31, 133.86, 131.64, 131.11, 129.60, 129.42, 129.00, 128.85, 128.39, 127.73, 127.41, 126.60, 126.47, 125.96, 125.71, 125.48, 123.43, 99.58, 96.82, 54.73, 30.95; HRMS (ESI⁺): Calcd for C₂₇H₂₄IN₂O, [M+H]⁺ m/z 517.0777. Found 517.0774.
1-(2-Iodobenzyl)-5-(naphthalen-2-ylmethyl)-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (1m): Pale yellow solid, mp = 196-197 °C; Eluent: EtOAc; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.86-7.74 (m, 3H), 7.69 (d, $J = 7.9$ Hz, 1H), 7.64 (s, 1H), 7.53-7.44 (m, 2H), 7.39 (t, $J = 7.6$ Hz, 2H), 7.33-7.20 (m, 5H), 6.89 (t, $J = 7.6$ Hz, 1H), 6.83 (d, $J = 7.7$ Hz, 1H), 5.52 (s, 1H), 4.69 (s, 2H), 3.92 (s, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 166.33, 156.49, 139.56, 137.87, 134.30, 133.45, 132.82, 132.58, 129.50, 128.98, 128.78, 127.92, 127.76, 127.72, 127.61, 126.67, 126.50, 126.44, 126.14, 125.93, 99.13, 96.48, 54.50, 33.59; HRMS (ESI$^+$): Calcd for C$_{27}$H$_{22}$IN$_2$O, [M+H]$^+$ m/z 517.0777. Found 517.0769.

5-Benzyl-1-(2-iodobenzyl)-2-(p-tolyl)-1,2-dihydro-3H-pyrazol-3-one (1n): Pale yellow solid, mp = 148-149 °C; Eluent: EtOAc; $^1$H NMR (600 MHz, CDCl$_3$) δ 7.73 (d, $J = 7.9$ Hz, 1H), 7.31 (t, $J = 7.3$ Hz, 2H), 7.28-7.24 (m, 2H), 7.21-7.17 (m, 4H), 7.12 (d, $J = 8.3$ Hz, 2H), 6.94 (t, $J = 8.2$ Hz, 1H), 6.80 (d, $J = 7.7$ Hz, 1H), 5.41 (s, 1H), 4.66 (s, 2H), 3.74 (s, 2H), 2.33 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 166.31, 155.99, 139.58, 138.28, 137.98, 135.39, 131.56, 130.14, 129.52, 129.00, 128.93, 128.83, 127.39, 126.46, 126.31, 98.61, 96.36, 54.31, 33.31, 21.22; HRMS (ESI$^+$): Calcd for C$_{24}$H$_{22}$IN$_2$O, [M+H]$^+$ m/z 481.0774. Found 481.0777.

5-Benzyl-1-(2-iodobenzyl)-2-(m-tolyl)-1,2-dihydro-3H-pyrazol-3-one (1o): Pale yellow solid, mp = 159-160 °C; Eluent: EtOAc; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.72 (d, $J = 7.9$ Hz, 1H), 7.34-7.23 (m, 5H), 7.19 (d, $J = 7.1$ Hz, 2H), 7.12-7.06 (m, 2H), 7.02 (d, $J = 7.9$ Hz, 1H), 6.93 (t, $J = 7.6$ Hz, 1H), 6.82 (d, $J = 7.7$ Hz, 1H), 5.40 (s, 1H), 4.67 (s, 2H), 3.75 (s, 2H), 2.32 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 166.24, 156.40, 139.51, 139.45, 137.87, 135.32, 134.12, 129.48, 129.17, 128.91, 128.87, 128.78, 127.33, 126.84, 126.48, 123.08, 98.77, 96.50, 54.43, 33.27, 21.38; HRMS (ESI$^+$): Calcd for C$_{24}$H$_{22}$IN$_2$O, [M+H]$^+$ m/z 481.0777. Found 481.0774.
5-Benzyl-1-(2-iodobenzyl)-2-(o-tolyl)-1,2-dihydro-3H-pyrazol-3-one (1p): Pale yellow solid, mp = 197-198 °C; Eluent: EtOAc; ¹H NMR (400 MHz, CDCl₃) δ 7.73 (d, J = 7.8 Hz, 1H), 7.35-7.20 (m, 8H), 7.19-7.11 (m, 1H), 7.01-6.91 (m, 2H), 6.76 (d, J = 7.6 Hz, 1H), 5.46 (s, 1H), 4.61 (d, J = 17.9 Hz, 1H), 4.45 (d, J = 17.9 Hz, 1H), 3.89-3.71 (m, 2H), 2.04 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 166.32, 154.89, 139.63, 137.93, 137.80, 135.50, 133.07, 131.56, 129.57, 128.96, 128.86, 128.68, 127.40, 126.90, 126.39, 97.84, 96.24, 53.88, 33.22, 17.57; HRMS (ESI⁺): Calcd for C₂₄H₂₂IN₂O, [M+H]⁺ m/z 481.0777. Found 481.0773.

5-Benzyl-2-(3,4-dimethylphenyl)-1-(2-iodobenzyl)-1,2-dihydro-3H-pyrazol-3-one (1q): Pale yellow solid, mp = 166-167 °C; Eluent: EtOAc; ¹H NMR (400 MHz, CDCl₃) δ 7.72 (d, J = 7.8 Hz, 1H), 7.33-7.22 (m, 4H), 7.18 (d, J = 7.1 Hz, 2H), 7.13 (d, J = 8.0 Hz, 1H), 7.02 (s, 1H), 6.96-6.91 (m, 2H), 6.81 (d, J = 7.7 Hz, 1H), 5.40 (s, 1H), 4.65 (s, 2H), 3.73 (s, 2H), 2.22 (s, 3H), 2.21 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 166.25, 155.60, 139.46, 138.05, 137.95, 137.08, 135.37, 131.65, 130.47, 129.42, 128.92, 128.85, 128.77, 127.71, 127.29, 126.44, 123.84, 98.44, 96.32, 54.18, 33.22, 19.87, 19.50; HRMS (ESI⁺): Calcd for C₂₅H₂₄IN₂O, [M+H]⁺ m/z 495.0933. Found 495.0925.

5-Benzyl-2-(3,5-dimethylphenyl)-1-(2-iodobenzyl)-1,2-dihydro-3H-pyrazol-3-one (1r): Pale yellow solid, mp = 200-201 °C; Eluent: EtOAc; ¹H NMR (400 MHz, CDCl₃) δ 7.73 (d, J = 7.9 Hz, 1H), 7.34-7.24 (m, 4H), 7.19 (d, J = 7.2 Hz, 2H), 6.97-6.91 (m, 2H), 6.85-6.80 (m, 3H), 5.39 (s, 1H), 4.67 (s, 2H), 3.74 (s, 2H), 2.27 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 166.31, 156.01, 139.53, 139.20, 138.04, 135.42, 133.98, 130.08, 129.50, 128.96, 128.91, 128.83, 127.35, 126.58,
124.17, 98.71, 96.52, 54.40, 33.30, 21.31; HRMS (ESI\(^+\)): Calcd for C\(_{25}\)H\(_{24}\)IN\(_2\)O, [M+H]\(^+\) \(m/z\) 495.0933. Found 495.0927.

1-(2-Iodobenzyl)-2-(4-methoxyphenyl)-5-methyl-1,2-dihydro-3\(H\)-pyrazol-3-one (Is): Pale yellow solid, mp = 105-106 °C; Eluent: EtOAc; \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 7.75 (d, \(J = 7.9\) Hz, 1H), 7.32-7.26 (m, 1H), 7.13 (d, \(J = 8.9\) Hz, 2H), 6.96 (t, \(J = 7.1\) Hz, 1H), 6.91 (d, \(J = 8.9\) Hz, 2H), 6.77 (d, \(J = 7.5\) Hz, 1H), 5.45 (s, 1H), 4.68 (s, 2H), 3.80 (s, 3H), 2.18 (s, 3H);
\(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 166.75, 159.63, 152.56, 139.64, 137.91, 129.60, 129.07, 128.48, 127.05, 126.46, 114.93, 97.30, 96.40, 55.65, 54.13, 12.79; HRMS (ESI\(^+\)): Calcd for C\(_{18}\)H\(_{18}\)IN\(_2\)O, [M+H]\(^+\) \(m/z\) 421.0413. Found 421.0406.

5-Benzyl-1-(2-iodobenzyl)-2-(4-methoxyphenyl)-1,2-dihydro-3\(H\)-pyrazol-3-one (1t): Pale yellow solid, mp = 120-121 °C; Eluent: EtOAc; \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 7.74 (d, \(J = 7.9\) Hz, 1H), 7.31 (t, \(J = 6.8\) Hz, 2H), 7.29-7.24 (m, 2H), 7.19 (d, \(J = 7.5\) Hz, 2H), 7.13 (d, \(J = 8.8\) Hz, 2H), 6.95 (t, \(J = 7.6\) Hz, 1H), 6.90 (d, \(J = 8.8\) Hz, 2H), 6.77 (d, \(J = 7.7\) Hz, 1H), 5.41 (s, 1H), 4.63 (s, 2H), 3.78 (s, 3H), 3.76 (s, 2H); \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 166.42, 159.68, 155.28, 139.61, 138.02, 135.44, 129.57, 129.02, 128.97, 128.84, 128.50, 127.42, 126.76, 126.48, 114.93, 98.24, 96.30, 55.64, 54.18, 33.32; HRMS (ESI\(^+\)): Calcd for C\(_{24}\)H\(_{22}\)IN\(_2\)O, [M+H]\(^+\) \(m/z\) 497.0726. Found 497.0719.

5-Benzyl-2-(4-fluorophenyl)-1-(2-iodobenzyl)-1,2-dihydro-3\(H\)-pyrazol-3-one (1u): Pale yellow solid, mp = 123-124 °C; Eluent: EtOAc; \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 7.74 (d, \(J = 7.9\) Hz, 1H), 7.33 (t, \(J = 7.3\) Hz, 2H), 7.29-7.25 (m, 2H), 7.22-7.18 (m, 4H), 7.08 (t, \(J = 8.6\) Hz, 2H), 6.96 (t, \(J = -S21-
8.2 Hz, 1H), 6.78 (d, \( J = 7.6 \) Hz, 1H), 5.41 (s, 1H), 4.66 (s, 2H), 3.79 (s, 2H); \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \( \delta \) 166.53, 162.06 (d, \( ^1\)J\(_{C-F} = 248.5 \) Hz), 156.98, 139.76, 137.60, 135.29, 130.40, 129.72, 129.04, 128.86, 128.22 (d, \( ^3\)J\(_{C-F} = 8.7 \) Hz), 127.53, 126.54, 116.54 (d, \( ^2\)J\(_{C-F} = 23.0 \) Hz), 98.81, 96.81, 54.65, 33.43; \(^{19}\)F NMR (283 MHz, CDCl\(_3\)) \( \delta \) -112.76; HRMS (ESI\(^+\)): Calcd for C\(_{23}\)H\(_{19}\)FIn\(_2\)O, [M+H]\(^+\) \( m/z \) 485.0526. Found 485.0520.

5-Benzyl-2-(4-chlorophenyl)-1-(2-iodobenzyl)-1,2-dihydro-3H-pyrazol-3-one (1v): Pale yellow solid, mp = 181-182 °C; Eluent: EtOAc; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.72 (d, \( J = 7.8 \) Hz, 1H), 7.35 (d, \( J = 7.6 \) Hz, 2H), 7.31-7.12 (m, 8H), 6.97 (t, \( J = 7.5 \) Hz, 1H), 6.39 (d, \( J = 7.1 \) Hz, 1H), 6.23 (s, 1H), 5.16 (s, 2H), 4.00 (s, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 158.80, 153.74, 140.13, 138.03, 135.10, 133.25, 130.47, 130.38, 130.05, 129.25, 129.21, 129.08, 128.15, 127.89, 126.69, 96.32, 93.54, 55.33, 33.54; HRMS (ESI\(^+\)): Calcd for C\(_{23}\)H\(_{19}\)ClIn\(_2\)O, [M+H]\(^+\) \( m/z \) 501.0231. Found 501.0229.

5-Benzyl-2-(4-bromophenyl)-1-(2-iodobenzyl)-1,2-dihydro-3H-pyrazol-3-one (1w): Pale yellow solid, mp = 152-153 °C; Eluent: EtOAc; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.75 (d, \( J = 7.9 \) Hz, 1H), 7.52 (d, \( J = 8.6 \) Hz, 2H), 7.36-7.24 (m, 5H), 7.19 (d, \( J = 7.0 \) Hz, 2H), 7.14 (d, \( J = 8.6 \) Hz, 2H), 6.96 (t, \( J = 7.1 \) Hz, 1H), 6.80 (d, \( J = 7.7 \) Hz, 1H), 5.40 (s, 1H), 4.68 (s, 2H), 3.78 (s, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 166.40, 158.00, 139.81, 137.50, 135.21, 133.58, 132.64, 129.77, 129.07, 128.89, 127.57, 127.13, 126.56, 121.48, 99.37, 96.80, 54.92, 33.51; HRMS (ESI\(^+\)): Calcd for C\(_{23}\)H\(_{19}\)BrIn\(_2\)O, [M+H]\(^+\) \( m/z \) 544.9725. Found 544.9705.
5-Benzyl-1-(2-iodobenzyl)-2-(4-(trifluoromethyl)phenyl)-1,2-dihydro-3H-pyrazol-3-one (1x): Pale yellow solid, mp = 146-147 °C; Eluent: EtOAc; $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.75 (d, $J = 7.7$ Hz, 1H), 7.66 (d, $J = 8.4$ Hz, 2H), 7.42 (d, $J = 8.3$ Hz, 2H), 7.34 (t, $J = 7.3$ Hz, 2H), 7.31-7.24 (m, 2H), 7.20 (d, $J = 7.1$ Hz, 2H), 6.95 (t, $J = 7.6$ Hz, 1H), 6.85 (d, $J = 7.6$ Hz, 1H), 5.42 (s, 1H), 4.73 (s, 2H), 3.81 (s, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 166.40, 159.57, 139.81, 137.82, 137.15, 135.02, 129.78, 129.01, 128.97, 128.84, 128.86 (q, $^2J_{C,F} = 32.7$ Hz), 127.53, 126.67, 126.47 (q, $^3J_{C,F} = 3.5$ Hz), 124.66, 123.84 (q, $^1J_{C,F} = 270.7$ Hz), 99.86, 97.07, 55.40, 33.53; $^{19}$F NMR (283 MHz, CDCl$_3$) $\delta -62.29$; HRMS (ESI$^+$): Calcd for C$_{24}$H$_{19}$F$_3$IN$_2$O, [M+H]$^+$ m/z 535.0494. Found 535.0486.

![Chemical Structure 1x](image1.png)

5-Benzyl-1-(2-iodobenzyl)-2-(4-nitrophenyl)-1,2-dihydro-3H-pyrazol-3-one (1y): Pale yellow solid, mp = 131-132 °C; Eluent: EtOAc; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.25 (d, $J = 9.0$ Hz, 2H), 7.76 (d, $J = 8.8$ Hz, 1H), 7.48 (d, $J = 9.0$ Hz, 2H), 7.38-7.72 (m, 6H), 6.96 (t, $J = 7.6$ Hz, 1H), 6.88 (d, $J = 8.6$ Hz, 1H), 5.43 (s, 1H), 4.75 (s, 2H), 3.84 (s, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 166.43, 161.43, 145.47, 140.59, 140.02, 134.87, 130.03, 129.15, 129.05, 128.92, 127.72, 126.94, 124.84, 123.86, 100.64, 97.52, 56.19, 33.79; HRMS (ESI$^+$): Calcd for C$_{25}$H$_{19}$F$_3$IN$_2$O$_3$, [M+H]$^+$ m/z 512.0471. Found 512.0465.

![Chemical Structure 1y](image2.png)

4-(3-Benzyl-2-iodobenzyl)-5-oxo-2,5-dihydro-1H-pyrazol-1-ylbenzonitrile (1z): Pale yellow solid, mp = 157-158 °C; Eluent: EtOAc; $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.90 (d, $J = 8.9$ Hz, 2H), 7.62 (d, $J = 8.9$ Hz, 2H), 7.41-7.35 (m, 1H), 7.35-7.30 (m, 2H), 7.18 (d, $J = 8.1$ Hz, 1H), 7.16-7.12 (m, 2H), 7.11-7.05 (m, 3H), 4.68 (d, $J = 13.9$ Hz, 1H), 3.98 (d, $J = 13.8$ Hz, 1H), 3.21 (s, 2H), 3.12 (d, $J = 17.2$ Hz, 1H), 2.95 (d, $J = 17.2$ Hz, 1H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 170.72, 142.41, 141.68, 136.12, 135.09, 133.00, 130.36, 128.68, 128.35, 127.94, 127.03, 123.35, 122.50, 44.70, 38.65, 31.07, 27.34.
2-Benzyl-1-(2-iodobenzyl)-5-methyl-1,2-dihydro-3H-pyrazol-3-one (1aa): Pale yellow solid, mp = 147-148 °C; Eluent: EtOAc; 1H NMR (400 MHz, CDCl₃) δ 7.80 (d, J = 7.9 Hz, 1H), 7.30-7.20 (m, 4H), 7.16 (d, J = 7.7 Hz, 2H), 6.97 (t, J = 7.6 Hz, 1H), 6.46 (d, J = 7.7 Hz, 1H), 5.45 (s, 1H), 4.87 (s, 2H), 4.70 (s, 2H), 2.12 (s, 3H); 13C NMR (100 MHz, CDCl₃) δ 166.06, 150.48, 139.63, 137.41, 136.03, 129.72, 129.09, 128.79, 127.87, 127.25, 126.13, 95.97, 95.80, 53.72, 45.60, 12.20; HRMS (ESI⁺): Calcd for C₂₄H₁₉INO₃, [M+H]⁺ m/z 492.0573. Found 492.0570.

[Diagram of 1aa]

2,5-Dibenzyl-1-(2-iodobenzyl)-1,2-dihydro-3H-pyrazol-3-one (1ab): Pale yellow solid, mp = 156-157 °C; Eluent: EtOAc; 1H NMR (400 MHz, CDCl₃) δ 7.76 (d, J = 7.8 Hz, 1H), 7.27-7.07 (m, 11H), 6.94 (t, J = 7.6 Hz, 1H), 6.44 (d, J = 7.7 Hz, 1H), 5.40 (s, 1H), 4.88 (s, 2H), 4.64 (s, 2H), 3.72 (s, 2H); 13C NMR (100 MHz, CDCl₃) δ 165.98, 153.30, 139.51, 137.41, 135.91, 135.20, 129.61, 128.93, 128.82, 128.75, 128.61, 127.85, 127.28, 127.14, 126.20, 96.81, 95.71, 53.85, 45.63, 32.64; HRMS (ESI⁺): Calcd for C₂₄H₂₂INO₂, [M+H]⁺ m/z 481.0777. Found 481.0772.

2-Cyclohexyl-1-(2-iodobenzyl)-5-methyl-1,2-dihydro-3H-pyrazol-3-one (1ac): Pale yellow solid, mp = 177-178 °C; Eluent: EtOAc; 1H NMR (400 MHz, CDCl₃) δ 7.84 (d, J = 7.9 Hz, 1H), 7.28-7.22 (m, 1H), 6.99 (t, J = 8.3 Hz, 1H), 6.59 (d, J = 7.8 Hz, 1H), 5.35 (s, 1H), 4.86 (s, 2H), 4.03 (tt, J = 12.3, 3.5 Hz, 1H), 2.11 (s, 3H), 1.88-1.74 (m, 4H), 1.66-1.61 (m, 3H), 1.31-1.15 (m, 3H); 13C NMR (100 MHz, CDCl₃) δ 167.49, 152.18, 139.57, 137.99, 129.62, 129.05, 126.47, 97.83, 96.10, 56.02, 54.87, 30.77, 26.28, 25.35, 12.56; HRMS (ESI⁺): Calcd for C₁₇H₂₂INO₂, [M+H]⁺ m/z 397.0777. Found 397.0775.
5-Benzyl-2-cyclohexyl-1-(2-iodobenzyl)-1,2-dihydro-3H-pyrazol-3-one (1ad): Pale yellow solid, mp = 112-113 °C; Eluent: EtOAc; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.82 (d, $J = 7.8$ Hz, 1H), 7.31-7.20 (m, 4H), 7.15 (d, $J = 6.9$ Hz, 2H), 6.97 (t, $J = 7.6$ Hz, 1H), 6.59 (d, $J = 7.7$ Hz, 1H), 5.30 (s, 1H), 4.81 (s, 2H), 4.00 (tt, $J = 12.3$, 3.3 Hz, 1H), 3.70 (s, 2H), 1.87 (td, $J = 12.4$, 2.9 Hz, 2H), 1.81-1.72 (m, 2H), 1.68-1.58 (m, 3H), 1.31-1.13 (m, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 167.26, 154.80, 139.53, 138.06, 135.51, 129.59, 128.98, 128.71, 126.55, 98.90, 96.05, 56.16, 54.87, 33.06, 30.71, 26.27, 25.30; HRMS (ESI$^+$): Calcd for C$_{23}$H$_{26}$IN$_2$O, [M+H]$^+$ m/z 473.1090. Found 473.1079.

5-Benzyl-1-(5-fluoro-2-iodobenzyl)-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (1ae): Pale yellow solid, mp = 191-192 °C; Eluent: EtOAc; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.65 (dd, $J = 8.6$, 5.5 Hz, 1H), 7.40 (t, $J = 7.7$ Hz, 2H), 7.34-7.24 (m, 6H), 7.20 (d, $J = 7.3$ Hz, 2H), 6.70 (td, $J = 8.3$, 2.8 Hz, 1H), 6.59-6.53 (m, 1H), 5.46 (s, 1H), 4.64 (s, 2H), 3.78 (s, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 166.32, 163.33 (d, $^1$J$_{C,F} = 249.4$ Hz), 156.72, 140.72 (d, $^3$J$_{C,F} = 7.6$ Hz), 139.97 (d, $^3$J$_{C,F} = 6.9$ Hz), 135.15, 134.26, 129.53, 128.99, 128.75, 127.99, 127.48, 125.89, 117.05 (d, $^2$J$_{C,F} = 21.9$ Hz), 114.23 (d, $^2$J$_{C,F} = 24.1$ Hz), 99.36, 89.15 (d, $^4$J$_{C,F} = 2.7$ Hz), 54.32, 33.38; $^{19}$F NMR (283 MHz, CDCl$_3$) δ -111.16; HRMS (ESI$^+$): Calcd for C$_{22}$H$_{19}$FlN$_2$O, [M+H]$^+$ m/z 485.0526. Found 485.0520.

5-Benzyl-1-(5-chloro-2-iodobenzyl)-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (1af): Pale yellow solid, mp = 212-213 °C; Eluent: EtOAc; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.60 (d, $J = 8.4$ Hz, 1H), 7.43-7.38 (m, 2H), 7.33-7.29 (m, 3H), 7.27-7.19 (m, 6H), 6.91 (dd, $J = 8.3$, 2.0 Hz, 1H), 6.74 (s,
1H), 5.48 (s, 1H), 4.63 (s, 2H), 3.80 (s, 2H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\) 166.29, 156.49, 140.46, 139.36, 135.35, 135.04, 134.23, 133.88, 129.50, 128.97, 128.68, 128.04, 127.45, 126.82, 126.02, 99.19, 93.49, 54.28, 33.39; HRMS (ESI\textsuperscript{+}): Calcd for C\textsubscript{23}H\textsubscript{19}ClIN\textsubscript{2}O, [M+H]\textsuperscript{+} \(m/z\) 501.0231. Found 501.0224.

5-Benzyl-1-(4-fluoro-2-iodobenzyl)-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (1ag): Pale yellow solid, mp = 152-153 °C; Eluent: EtOAc; \textsuperscript{1}H NMR (600 MHz, CDCl\textsubscript{3}) \(\delta\) 7.42 (dd, \(J\) = 7.7, 2.4 Hz, 1H), 7.38 (t, \(J\) = 7.7 Hz, 2H), 7.33-7.22 (m, 6H), 7.19 (d, \(J\) = 7.3 Hz, 2H), 7.01-6.91 (m, 1H), 6.75 (dd, \(J\) = 8.5, 5.7 Hz, 1H), 5.42 (s, 1H), 4.65 (s, 2H), 3.77 (s, 2H); \textsuperscript{13}C NMR (150 MHz, CDCl\textsubscript{3}) \(\delta\) 166.13, 161.09 (d, \(\textsuperscript{1}J_{C-F} = 252.7\) Hz), 156.83, 135.04 (d, \(\textsuperscript{4}J_{C-F} = 2.5\) Hz), 129.28, 128.77, 128.59, 127.66, 127.24, 127.18, 126.31 (d, \(\textsuperscript{2}J_{C-F} = 24.0\) Hz), 125.60, 115.76 (d, \(\textsuperscript{2}J_{C-F} = 21.3\) Hz), 99.07, 95.79 (d, \(\textsuperscript{3}J_{C-F} = 7.6\) Hz), 53.70, 33.17; \textsuperscript{19}F NMR (283 MHz, CDCl\textsubscript{3}) \(\delta\) -112.13; HRMS (ESI\textsuperscript{+}): Calcd for C\textsubscript{23}H\textsubscript{19}FlN\textsubscript{2}O, [M+H]\textsuperscript{+} \(m/z\) 485.0526. Found 485.0520.

Methyl 4-((5-benzyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-1-yl)methyl)-3-iodo-benzoate (1ah): Pale yellow solid, Mp = 189-190 °C; Eluent: EtOAc; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 8.38 (d, \(J\) = 1.6 Hz, 1H), 7.90 (dd, \(J\) = 8.1, 1.6 Hz, 1H), 7.40 (t, \(J\) = 7.7 Hz, 2H), 7.33-7.29 (m, 3H), 7.28-7.23 (m, 3H), 7.19 (d, \(J\) = 6.9 Hz, 2H), 6.85 (d, \(J\) = 8.1 Hz, 1H), 5.47 (s, 1H), 4.70 (s, 2H), 3.91 (s, 3H), 3.77 (s, 2H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\) 166.30, 165.09, 156.66, 142.73, 140.58, 135.07, 134.13, 131.20, 129.90, 129.61, 129.04, 128.80, 128.13, 127.54, 126.26, 125.97, 99.28, 95.92, 54.49, 52.62, 33.40; HRMS (ESI\textsuperscript{+}): Calcd for C\textsubscript{25}H\textsubscript{22}IN\textsubscript{2}O\textsubscript{3}, [M+H]\textsuperscript{+} \(m/z\) 525.0675. Found 525.0665.
4. Synthesis and Characterization of 2a-ah

(1) General Procedures

To a dried Schlenk tube were added Pd(TFA)$_2$ (3.32 mg, 0.01 mmol) and ligand (S)-E, (S)-F or (S)-G (0.015 mmol) under N$_2$, 3.0 mL of anhydrous N,N-dimethylacetamide (DMA) was then introduced via syringe. After stirring for 1 h, 1 (0.2 mmol, dissolved in 1 mL of DMA), BnNMe$_2$ (1.0 mmol, 5 equiv) and TFA (0.4 mmol, 2 equiv) were added via syringe. The mixture was vigorously stirred in a pre-warmed oil bath at 150 °C for 24 h. The solvent was then removed under vacuum, and the residue was purified by column chromatography on silica to give the desired product 2. The enantiomeric excess was determined by chiral HPLC analysis.

(2) Preparation of Racemic Products Rac-2a-ah

Racemic products Rac-2a-ah were prepared according to the above procedures in the absence of ligand.
(3) Characterization of 2a-ah

(S)-3α-Methyl-1-phenyl-3α,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one (2a): Pale yellow solid, mp = 127-128 °C; Eluent: petroleum ether/EtOAc 4:1; Yield: 76%;
HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 95:5; flow: 1.0 mL/min; λ = 220 nm. 25 °C.
97% ee (tr (minor) = 9.5 min, tr (major) = 28.9 min).
HRMS (ESI+): Calcd for C_{17}H_{17}N_{2}O, [M+H]⁺ m/z 265.1341. Found 265.1332.

1H NMR (400 MHz, CDCl$_3$) δ 7.88 (d, J = 8.4 Hz, 2H), 7.42-7.35 (m, 2H), 7.35-7.27 (m, 2H),
7.26-7.18 (m, 2H), 7.15 (t, J = 7.4 Hz, 1H), 4.72 (d, J = 13.7 Hz, 1H), 4.07 (d, J = 13.7 Hz, 1H),
3.10 (d, J = 16.7 Hz, 1H), 2.66 (d, J = 16.8 Hz, 1H), 1.65 (s, 3H);
13C NMR (100 MHz, CDCl$_3$) δ 170.35, 143.76, 138.53, 136.33, 128.97, 128.34, 128.20, 124.66, 123.37, 122.07, 119.48, 70.21, 60.11, 44.38, 25.99.
IR (cm⁻¹): 3032 (w), 2966 (m), 2926 (m), 2845 (w), 1588 (vs), 1547 (m), 1482 (s), 1419 (m), 1353 (s), 1326 (m), 1306 (m), 1094 (m), 753 (vs), 816 (m), 733 (s), 694 (s).

(S)-3α-Ethyl-1-phenyl-3α,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one (2b): Pale yellow solid, mp = 116-117 °C; Eluent: petroleum ether/EtOAc 4:1; Yield: 74%;
HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 95:5; flow: 1.0 mL/min; λ = 220 nm. 25 °C.
99% ee (tr (minor) = 9.0 min, tr (major) = 23.4 min).
HRMS (ESI+): Calcd for C_{18}H_{19}N_{2}O, [M+H]⁺ m/z 279.1492. Found 279.1492.

1H NMR (400 MHz, CDCl$_3$) δ 7.89 (d, J = 8.2 Hz, 2H), 7.38 (t, J = 7.9 Hz, 2H), 7.34-7.26 (m, 2H), 7.22-7.11 (m, 3H), 4.72 (d, J = 13.9 Hz, 1H), 4.07 (d, J = 13.9 Hz, 1H), 3.11 (d, 1H), 2.67 (d, J = 18.2 Hz, 1H), 2.02-1.89 (m, 2H), 0.91 (t, J = 6.8 Hz, 3H);
13C NMR (100 MHz, CDCl$_3$) δ 170.40, 142.39, 138.43, 136.98, 128.97, 128.23, 128.11, 124.59, 123.28, 122.22, 119.47, 73.33, 60.60, 43.86, 31.73, 8.33.
IR (cm⁻¹): 3062 (w), 2969 (m), 2926 (m), 2851 (w), 1691 (vs), 1593 (m), 1485 (s), 1460 (m), 1414 (m), 1359 (s), 1327 (m), 1308 (m), 1097 (m), 758 (vs), 832 (m), 731 (s), 694 (s).

-S28-
(S)-1-Phenyl-3α-propyl-3α,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one (2c): Light yellow oil; Eluent: petroleum ether/EtOAc 4:1; Yield: 79%;
HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 90:10; flow: 1.0 mL/min; λ = 220 nm. 25 ºC.
98% ee (tR (minor) = 6.3 min, tR (major) = 16.9 min).
HRMS (ESI+): Calcd for C_{19}H_{21}N_2O, [M+H]^+ m/z 293.1654. Found 293.1651.

1H NMR (400 MHz, CDCl₃) δ 7.88 (d, J = 8.5 Hz, 2H), 7.39 (t, J = 7.9 Hz, 2H), 7.35-7.27 (m, 2H), 7.23-7.12 (m, 3H), 4.72 (d, J = 14.0 Hz, 1H), 4.07 (d, J = 14.0 Hz, 1H), 3.11 (d, J = 16.9 Hz, 1H), 2.69 (d, J = 16.9 Hz, 1H), 1.99-1.82 (m, 2H), 1.60-1.50 (m, 1H), 1.26-1.15 (m, 1H), 0.90 (t, J = 7.4 Hz, 3H); 13C NMR (100 MHz, CDCl₃) δ 170.36, 142.87, 138.41, 136.84, 129.00, 128.12, 124.66, 123.12, 122.46, 119.73, 75.77, 61.47, 42.92, 36.58, 17.33, 16.56. IR (cm⁻¹): 3030 (w), 2957 (m), 2931 (w), 2871 (w), 1697 (vs), 1594 (s), 1542 (s), 1493 (m), 1459 (m), 1419 (w), 1353 (m), 1308 (m), 1028 (w), 751 (vs), 732 (m), 708 (s), 691 (w).

(R)-3α-Isopropyl-1-phenyl-3α,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one (2d): Pale yellow solid, mp = 103-104 ºC; Eluent: petroleum ether/EtOAc 4:1; Yield: 82%;
HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 95:5; flow: 1.0 mL/min; λ = 220 nm. 25 ºC.
98% ee (tR (minor) = 8.8 min, tR (major) = 20.0 min).
HRMS (ESI+): Calcd for C_{10}H_{21}N_2O, [M+H]^+ m/z 293.1654. Found 293.1648.

1H NMR (400 MHz, CDCl₃) δ 7.87 (d, J = 7.9 Hz, 2H), 7.40 (t, J = 7.9 Hz, 2H), 7.34-7.25 (m, 2H), 7.21-7.12 (m, 3H), 4.70 (d, J = 14.6 Hz, 1H), 4.06 (d, J = 14.6 Hz, 1H), 3.10 (d, J = 17.2 Hz, 1H), 2.90 (d, J = 17.3 Hz, 1H), 2.19 (hept, J = 6.7 Hz, 1H), 1.03 (d, J = 6.8 Hz, 3H), 0.89 (d, J = 6.7 Hz, 3H); 13C NMR (100 MHz, CDCl₃) δ 169.75, 143.38, 137.99, 137.04, 128.96, 128.07, 124.66, 123.12, 122.46, 119.73, 75.77, 61.47, 42.92, 36.58, 17.73, 16.56. IR (cm⁻¹): 3057 (w), 2964 (m), 2923 (w), 2871 (w), 1690 (vs), 1591 (m), 1487 (m), 1353 (s), 1307(w), 1070 (m), 768 (vs), 730 (m), 693 (s).
(R)-3α-Cyclopropyl-1-phenyl-3α,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one (2e): Pale yellow solid, mp = 163-164 °C; Eluent: petroleum ether/EtOAc 4:1; Yield: 81%;
HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 95:5; flow: 1.0 mL/min; λ = 220 nm. 25 °C.
98% ee (t<sub>R</sub> (minor) = 9.7 min, t<sub>R</sub> (major) = 27.7 min).
HRMS (ESI<sup>+</sup>): Caled for C<sub>19</sub>H<sub>19</sub>N<sub>2</sub>O, [M+H]<sup>+</sup> m/z 291.1497. Found 291.1391.

1H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.82 (d, J = 7.8 Hz, 2H), 7.38 (t, J = 8.0 Hz, 2H), 7.35-7.23 (m, 3H), 7.20-7.10 (m, 2H), 4.67 (d, J = 14.0 Hz, 1H), 4.04 (d, J = 14.0 Hz, 1H), 3.14 (d, J = 16.9 Hz, 1H), 2.80 (d, J = 16.9 Hz, 1H), 1.40-1.32 (m, 1H), 0.56-0.35 (m, 4H); 13C NMR (100 MHz, CDCl<sub>3</sub>) δ 170.17, 143.92, 137.97, 136.32, 129.04, 128.28, 128.22, 124.63, 123.10, 122.48, 119.38, 71.85, 60.75, 43.43, 19.31, 0.85, 0.35. IR (cm<sup>-1</sup>): 3013 (w), 2923 (w), 2853 (w), 1691 (vs), 1485 (m), 1458 (s), 1413 (w), 1351 (m), 1048 (w), 1025 (m), 1028 (m), 758 (vs), 732 (m), 731 (s), 693 (s).

(R)-3α-Cyclopentyl-1-phenyl-3α,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one (2f): Pale yellow solid, mp = 97-98 °C; Eluent: petroleum ether/EtOAc 4:1; Yield: 83%;
HPLC analysis of 2f: Daicel Chiralpak IB; hexane/iPrOH: 85:15; flow: 1.0 mL/min; λ = 220 nm. 25 °C. 98% ee (t<sub>R</sub> (minor) = 5.8 min, t<sub>R</sub> (major) = 11.4 min).
HRMS (ESI<sup>+</sup>): Caled for C<sub>21</sub>H<sub>23</sub>N<sub>2</sub>O, [M+H]<sup>+</sup> m/z 319.1810. Found 319.1804.

1H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.87 (d, J = 7.9 Hz, 2H), 7.39 (t, J = 7.9 Hz, 2H), 7.32-7.20 (m, 3H), 7.18-7.11 (m, 2H), 4.71 (d, J = 14.5 Hz, 1H), 4.06 (d, J = 14.5 Hz, 1H), 3.13 (d, J = 17.2 Hz, 1H), 2.89 (d, J = 17.2 Hz, 1H), 2.46 (quint, J = 8.8, 8.2 Hz, 1H), 1.86-1.77 (m, 1H), 1.71-1.49 (m, 4H), 1.47-1.33 (m, 3H); 13C NMR (100 MHz, CDCl<sub>3</sub>) δ 169.73, 143.98, 138.01, 136.78, 128.97, 128.11, 128.05, 124.62, 123.07, 122.45, 119.68, 74.27, 61.47, 49.52, 43.63, 27.54, 26.79, 26.05, 25.22. IR (cm<sup>-1</sup>): 3029 (w), 2949 (m), 2855 (w), 1694 (vs), 1592 (m), 1486 (s), 1457 (w), 1418 (m), 1306 (s), 1306 (m), 1075 (m), 1028 (m), 757 (vs), 731 (m), 692 (s).
(S)-3α-Phenethyl-1-phenyl-3α,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one (2g): Light yellow oil; Eluent: petroleum ether/EtOAc 4:1; Yield: 82%.

HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 95:5; flow: 1.0 mL/min; λ = 220 nm. 25 °C. 98% ee (tR (minor) = 12.0 min, tR (major) = 29.0 min).

HRMS (ESI+): Calcd for C24H23N2O, [M+H]+ m/z 355.1810. Found 355.1805.

1H NMR (600 MHz, CDCl3) δ 7.89 (d, J = 8.7 Hz, 2H), 7.39 (t, J = 8.0 Hz, 2H), 7.36-7.28 (m, 2H), 7.26-7.19 (m, 4H), 7.18-7.12 (m, 2H), 7.10 (d, J = 8.0 Hz, 2H), 4.77 (d, J = 13.8 Hz, 1H), 4.09 (d, J = 13.7 Hz, 1H), 3.15 (d, J = 17.0 Hz, 1H), 2.90-2.80 (m, 1H), 2.70 (d, J = 16.9 Hz, 1H), 2.49-2.39 (m, 1H), 2.32-2.24 (m, 1H), 2.24-2.13 (m, 1H); 13C NMR (100 MHz, CDCl3) δ 170.20, 142.07, 141.94, 138.41, 136.95, 129.07, 128.49, 128.45, 128.38, 128.33, 125.92, 124.67, 123.44, 122.17, 119.39, 72.89, 60.66, 44.22, 40.74, 30.55. IR (cm⁻¹): 3026 (w), 2927 (w), 2854 (w), 1696 (vs), 1594 (m), 1491 (s), 1457 (m), 1352 (s), 1309 (s), 1028 (w), 754 (vs), 729 (m), 695 (s), 620 (w).

(S)-1-Phenyl-3α-(3-phenylpropyl)-3α,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one (2h): Light yellow oil; Eluent: petroleum ether/EtOAc 4:1; Yield: 83%.

HPLC analysis of 2h: Daicel Chiralpak IB; hexane/iPrOH: 90:10; flow: 1.0 mL/min; λ = 220 nm. 25 °C. 97% ee (tR (minor) = 7.9 min, tR (major) = 15.4 min).

HRMS (ESI+): Calcd for C25H25N2O, [M+H]+ m/z 369.1967. Found 369.1962.

1H NMR (400 MHz, CDCl3) δ 7.86 (d, J = 8.1 Hz, 2H), 7.39 (t, J = 7.9 Hz, 2H), 7.32-7.12 (m, 7H), 7.09 (d, J = 6.9 Hz, 3H), 4.71 (d, J = 13.9 Hz, 1H), 4.06 (d, J = 13.9 Hz, 1H), 3.09 (d, J = 16.9 Hz, 1H), 2.71-2.52 (m, 3H), 2.03-1.84 (m, 3H), 1.56-1.41 (m, 1H); 13C NMR (100 MHz, CDCl3) δ 170.35, 142.38, 142.03, 138.43, 136.91, 129.05, 128.49, 128.41, 128.32, 128.19, 125.92, 124.67, 123.34, 122.22, 119.51, 73.04, 60.59, 44.24, 38.22, 35.90, 25.61. IR (cm⁻¹): 3026 (w), 2927 (w), 2854 (w), 1696 (vs), 1594 (m), 1491 (s), 1457 (m), 1352 (s), 1309 (s), 1028 (w), 754 (vs), 729 (m), 695 (s), 620 (w).
(S)-3a-Benzyl-1-phenyl-3a,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one (2i): Pale yellow solid, mp = 140-141 °C; Eluent: petroleum ether/EtOAc 4:1; Yield: 80%.
HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 95:5; flow: 1.0 mL/min; λ = 220 nm. 25 °C. 98% ee (tR (minor) = 14.3 min, tR (major) = 26.9 min).
HRMS (ESI+): Calcd for C_{23}H_{21}N_{2}O. [M+H]^{+} m/z 341.1654. Found 341.1648.

δ H NMR (400 MHz, CDCl_{3}) δ 7.79 (d, J = 8.7 Hz, 2H), 7.40-7.22 (m, 5H), 7.20-7.08 (m, 7H), 4.50 (d, J = 14.5 Hz, 1H), 4.00 (d, J = 14.4 Hz, 1H), 3.25-3.16 (m, 2H), 3.12 (d, J = 17.0 Hz, 1H), 2.92 (d, J = 17.0 Hz, 1H); δ C NMR (100 MHz, CDCl_{3}) δ 169.15, 142.98, 138.03, 137.07, 135.76, 130.70, 128.89, 128.42, 128.01, 127.87, 126.81, 124.63, 123.30, 122.71, 119.65, 73.64, 60.36, 45.40, 43.65. IR (cm⁻¹): 3071 (w), 3026 (w), 2927 (w), 2853 (w), 1682 (vs), 1591 (m), 1486 (s), 1456 (m), 1363 (s), 1312 (m), 1025 (m), 992 (w), 770 (m), 749 (s), 731 (m), 695 (vs), 660 (m).

(S)-1-Phenyl-3a-(2,4,6-trimethylbenzyl)-3a,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one (2j): Light yellow oil; Eluent: petroleum ether/EtOAc 4:1; Yield: 78%.
HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 95:5; flow: 1.0 mL/min; λ = 220 nm. 25 °C. 98% ee (tR (minor) = 11.7 min, tR (major) = 13.2 min).
HRMS (ESI+): Calcd for C_{26}H_{27}N_{2}O. [M+H]^{+} m/z 383.2123. Found 383.2118.

δ H NMR (600 MHz, CDCl_{3}) δ 7.50 (d, J = 8.4 Hz, 2H), 7.37-7.29 (m, 5H), 7.18-7.11 (m, 2H), 6.83 (s, 2H), 4.31 (d, J = 16.1 Hz, 1H), 4.08 (d, J = 16.1 Hz, 1H), 3.29 (d, J = 14.9 Hz, 1H), 3.11 (d, J = 4.7 Hz, 1H), 3.09 (d, J = 2.8 Hz, 1H), 2.98 (d, J = 16.7 Hz, 1H), 2.31 (s, 6H), 2.23 (s, 3H); δ C NMR (100 MHz, CDCl_{3}) δ 167.93, 146.30, 138.02, 137.67, 137.13, 136.36, 130.50, 129.38, 128.87, 128.65, 128.24, 125.42, 123.33, 123.00, 121.67, 75.80, 58.80, 42.17, 37.80, 21.15, 20.92.
IR (cm⁻¹): 2951 (w), 2918 (w), 2858 (w), 1698 (vs), 1593 (m), 1490 (s), 1457 (m), 1351 (s), 1307 (s), 1026 (w), 989 (w), 851 (s), 754 (vs), 692 (s), 626 (w).

(S)-3a-([1,1'-Biphenyl]-4-ylmethyl)-1-phenyl-3a,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one (2k): Light yellow oil; Eluent: petroleum ether/EtOAc 4:1; Yield: 88%;

HPLC analysis: Daicel Chiralpak ID; hexane/iPrOH: 97:3; flow: 1.0 mL/min; λ = 220 nm. 99% ee (t₁ (major) = 46.4 min, t₂ (minor) = 52.7 min).

HRMS (ESI⁺): Calcd for C₂₉H₂₅N₂O, [M+H]⁺ m/z 417.1967. Found 417.1958.

¹H NMR (400 MHz, CDCl₃) δ 7.80 (d, J = 8.5 Hz, 2H), 7.47 (d, J = 8.1 Hz, 2H), 7.40-7.19 (m, 12H), 7.17-7.06 (m, 2H), 4.52 (d, J = 14.4 Hz, 1H), 4.00 (d, J = 14.4 Hz, 1H), 3.29-3.17 (m, 2H), 3.12 (d, J = 17.0 Hz, 1H), 2.93 (d, J = 17.1 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 169.25, 142.88, 140.84, 139.47, 138.11, 136.31, 134.91, 131.10, 128.89, 128.72, 128.43, 128.01, 127.16, 127.01, 126.51, 124.62, 123.33, 122.69, 119.57, 73.72, 60.38, 44.88, 43.76. IR (cm⁻¹): 3028 (w), 2916 (w), 1696 (vs), 1594 (m), 1489 (s), 1458 (s), 1309 (s), 1074 (w), 847 (w), 821 (vs), 757 (s), 692 (w).

(S)-3a-(Naphthalen-1-ylmethyl)-1-phenyl-3a,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one (2l): Light yellow oil; Eluent: petroleum ether/EtOAc 4:1; Yield: 84%;

HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 95:5; flow: 1.0 mL/min; λ = 220 nm. 98% ee (t₁ (minor) = 24.2 min, t₂ (major) = 28.7 min).

HRMS (ESI⁺): Calcd for C₂₇H₂₃N₂O, [M+H]⁺ m/z 391.1810. Found 391.1809.

¹H NMR (600 MHz, CDCl₃) δ 8.15 (d, J = 8.2 Hz, 1H), 7.74 (d, J = 7.7 Hz, 1H), 7.64 (d, J = 8.1 Hz, 1H), 7.50 (d, J = 8.0 Hz, 2H), 7.41-7.31 (m, 4H), 7.28-7.19 (m, 5H), 7.09-7.03 (m, 2H), 4.31 (d, J = 14.8 Hz, 1H), 3.92 (d, J = 14.9 Hz, 1H), 3.81 (d, J = 14.4 Hz, 1H), 3.60 (d, J = 14.4 Hz, 1H), 3.15 (d, J = 17.0 Hz, 1H), 3.07 (d, J = 17.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 168.64,
143.79, 137.53, 137.15, 133.80, 128.75, 128.64, 128.51, 128.09, 127.71, 125.73, 125.43, 124.96, 124.90, 124.63, 123.28, 122.88, 120.05, 77.48, 77.16, 76.84, 74.30, 60.25, 43.66, 41.35. IR (cm⁻¹): 3036 (w), 2914 (w), 2830 (w), 1689 (vs), 1594 (m), 1490 (s), 1457 (m), 1395 (s), 1326 (s), 1062 (w), 802 (w), 776 (s), 745 (vs), 689 (s), 625 (w).

(S)-3α-(Naphthalen-2-ylmethyl)-1-phenyl-3α,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one (2m): Pale yellow solid, mp = 116-118 °C; Eluent: petroleum ether/EtOAc 4:1; Yield: 85%; HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 95:5; flow: 1.0 mL/min; λ = 220 nm. 25 °C. 98% ee (tR (minor) = 19.2 min, tR (major) = 32.0 min).

HRMS (ESI⁺): Calcd for C₂₇H₂₃N₂O, [M+H]⁺ m/z 391.1807. Found 391.1807.

¹H NMR (600 MHz, CDCl₃) δ 7.80 (d, J = 7.7 Hz, 2H), 7.73-7.70 (m, 1H), 7.63-7.58 (m, 3H), 7.39-7.32 (m, 6H), 7.30-7.23 (m, 2H), 7.14 (t, J = 7.4 Hz, 1H), 7.07 (d, J = 7.5 Hz, 1H), 4.48 (d, J = 14.4 Hz, 1H), 4.00 (d, J = 14.4 Hz, 1H), 3.42-3.32 (m, 2H), 3.15 (d, J = 16.9 Hz, 1H), 2.98 (d, J = 16.9 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 169.32, 142.72, 142.72, 138.12, 137.11, 133.48, 133.14, 132.33, 129.66, 129.05, 128.93, 128.47, 128.01, 127.66, 127.58, 127.24, 125.84, 125.54, 124.67, 123.35, 122.76, 119.57, 73.87, 60.36, 45.27, 43.94. IR (cm⁻¹): 3049 (w), 2914 (w), 2849 (w), 1689 (vs), 1593 (m), 1490 (s), 1458 (m), 1356 (s), 1306 (s), 1063 (w), 818 (w), 776 (s), 745 (vs), 689 (s), 633 (w).

(S)-3α-Benzyl-1-(p-tolyl)-3α,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one (2n): Pale yellow solid, mp = 128-129 °C; Eluent: petroleum ether/EtOAc 4:1; Yield: 78%; HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 95:5; flow: 1.0 mL/min; λ = 220 nm. 25 °C. 25 °C. 98% ee (tR (minor) = 13.9 min, tR (major) = 22.3 min).

HRMS (ESI⁺): Calcd for C₂₅H₂₃N₂O, [M+H]⁺ m/z 355.1810. Found 355.1802.
\( ^1 \)H NMR (400 MHz, CDCl₃) \( \delta \) 7.65 (d, \( J = 8.4 \) Hz, 2H), 7.35-7.24 (m, 3H), 7.22-7.07 (m, 8H), 4.47 (d, \( J = 14.6 \) Hz, 1H), 4.00 (d, \( J = 14.5 \) Hz, 1H), 3.25-3.16 (m, 2H), 3.11 (d, \( J = 16.9 \) Hz, 1H), 2.92 (d, \( J = 16.9 \) Hz, 1H), 2.35 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl₃) \( \delta \) 168.78, 143.13, 137.22, 135.90, 134.46, 130.77, 129.48, 128.43, 128.00, 127.90, 126.82, 123.32, 122.79, 119.95, 73.75, 60.27, 45.43, 43.67, 21.06.

IR (cm\(^{-1}\)): 3051 (w), 2913 (w), 2846 (w), 1686 (vs), 1593 (m), 1491 (s), 1455 (m), 1354 (s), 1306 (s), 1064 (w), 819 (w), 744 (vs), 686 (m).

\((S)-3a\)-Benzy1-1-(m-tolyl)-3a,8-dihydro-1H-pyrazolo[5,1-a]isoidol-2(3H)-one (2o): Light yellow oil; Eluent: petroleum ether/EtOAc 4:1; Yield: 77%;

HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 95:5; flow: 1.0 mL/min; \( \lambda = 220 \) nm. 25 °C.

98% ee (\( t_R \) (minor) = 12.5 min, \( t_R \) (major) = 22.7 min).

HRMS (ESI\(^+\)): Calcd for C\(_{24}\)H\(_{23}\)N\(_2\)O, [M+H]\(^+\) m/z 355.1810. Found 355.1806.

\( ^1 \)H NMR (400 MHz, CDCl₃) \( \delta \) 7.62 (s, 1H), 7.57 (d, \( J = 8.2 \) Hz, 1H), 7.35-7.30 (m, 1H), 7.29-7.23 (m, 6H), 6.97 (d, \( J = 7.6 \) Hz, 1H), 4.50 (d, \( J = 14.5 \) Hz, 1H), 4.00 (d, \( J = 14.5 \) Hz, 1H), 3.25-3.16 (m, 2H), 3.11 (d, \( J = 16.9 \) Hz, 1H), 2.92 (d, \( J = 17.0 \) Hz, 1H), 2.37 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl₃) \( \delta \) 169.10, 143.01, 138.76, 137.97, 137.17, 135.86, 130.78, 128.75, 128.42, 127.99, 127.87, 126.81, 125.57, 123.32, 122.77, 120.51, 116.99, 73.67, 60.32, 45.34, 43.73, 21.79. IR (cm\(^{-1}\)): 3062 (w), 3030 (w), 2915 (w), 2856 (w), 1684 (vs), 1604 (m), 1584 (s), 1489 (m), 1364 (s), 1204 (s), 779 (w), 753 (s), 729 (s), 695 (vs), 664 (s).

\((S)-3a\)-Benzy1-1-(o-tolyl)-3a,8-dihydro-1H-pyrazolo[5,1-a]isoidol-2(3H)-one (2p): Pale yellow solid, mp = 133-134 °C; Eluent: petroleum ether/EtOAc 4:1; Yield: 75%;

HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 98:2; flow: 1.0 mL/min; \( \lambda = 220 \) nm. 25 °C. >99% ee (\( t_R \) (major) = 36.0 min, \( t_R \) (minor) = 42.8 min).

HRMS (ESI\(^+\)): Calcd for C\(_{24}\)H\(_{23}\)N\(_2\)O, [M+H]\(^+\) m/z 355.1810. Found 355.1802.
\(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 7.35 (d, \(J = 7.0\) Hz, 1H), 7.33-7.20 (m, 8H), 7.18-7.12 (m, 3H), 7.10 (d, \(J = 7.1\) Hz, 1H), 3.92 (s, 2H), 3.20 (d, \(J = 13.8\) Hz, 1H), 3.14-3.00 (m, 3H), 2.06 (s, 3H);

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 167.22, 144.88, 138.26, 136.89, 136.16, 135.50, 131.13, 130.85, 128.65, 128.38, 128.09, 127.80, 127.34, 126.94, 126.71, 123.36, 123.20, 76.04, 58.01, 45.05, 42.13, 18.28.

IR (cm\(^{-1}\)): 3028 (w), 2969 (m), 2920 (w), 1685 (vs), 1601 (w), 1582 (w), 1488 (m), 1447 (s), 1369 (s), 779 (w), 1072 (w), 765 (s), 699 (vs), 660 (s), 638 (s).

\((S)\)-3\(\alpha\)-Benzy1-1-(3,4-dimethylphenyl)-3\(\alpha\),8-dihydro-1\(H\)-pyrazolo[5,1-\(a\)]isoindol-2(3\(H\))-one (2q): Pale yellow solid, mp = 110-111 °C; Eluent: petroleum ether/EtOAc 4:1; Yield: 78%;

HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 95:5; flow: 1.0 mL/min; \(\lambda = 220\) nm. 25 °C. 98% ee (\(t_R\) (minor) = 13.4 min, \(t_R\) (major) = 20.5 min).

HRMS (ESI\(^+\)): Calcd for C\(_{25}\)H\(_{25}\)N\(_2\)O, [M+H\(^+\)]\(m/z\) 369.1967. Found 369.1961.

\(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 7.56 (s, 1H), 7.47 (d, \(J = 8.2\) Hz, 1H), 7.32 (t, \(J = 7.4\) Hz, 1H), 7.29-7.24 (m, 2H), 7.19-7.12 (m, 6H), 7.09 (d, \(J = 7.9\) Hz, 1H), 4.45 (d, \(J = 14.5\) Hz, 1H), 4.00 (d, \(J = 14.6\) Hz, 1H), 3.26-3.15 (m, 2H), 3.10 (d, \(J = 16.9\) Hz, 1H), 2.92 (d, \(J = 16.9\) Hz, 1H), 2.28 (s, 3H), 2.25 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 168.70, 143.11, 137.29, 137.17, 135.96, 135.76, 133.31, 130.82, 129.97, 128.38, 127.93, 127.86, 126.79, 123.31, 122.82, 121.44, 117.67, 73.74, 60.18, 45.33, 43.69, 20.19, 19.39. IR (cm\(^{-1}\)): 3030 (w), 2967 (m), 2917 (w), 2861 (w), 1694 (vs), 1609 (w), 1576 (w), 1498 (m), 1358 (s), 895 (w), 876 (w), 761 (s), 727 (s), 693 (m), 675 (s), 615 (w).

\((S)\)-3\(\alpha\)-Benzy1-1-(3,5-dimethylphenyl)-3\(\alpha\),8-dihydro-1\(H\)-pyrazolo[5,1-\(a\)]isoindol-2(3\(H\))-one (2r): Pale yellow solid, Mp = 113-114 °C; Eluent: petroleum ether/EtOAc 4:1; Yield: 79%;

HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 95:5; flow: 1.0 mL/min; \(\lambda = 220\) nm. 25 °C. 98% ee (\(t_R\) (minor) = 11.9 min, \(t_R\) (major) = 18.5 min).

-S36 -
HRMS (ESI+): Calcd for C_{25}H_{25}N_{2}O, [M+H]+ m/z 369.1967. Found 369.1960.

^1^H NMR (400 MHz, CDCl₃) δ 7.40 (s, 2H), 7.34-7.29 (m, 1H), 7.28-7.23 (m, 2H), 7.18-7.12 (m, 5H), 7.10 (d, J = 7.9 Hz, 1H), 6.80 (s, 1H), 4.48 (d, J = 14.5 Hz, 1H), 3.99 (d, J = 14.5 Hz, 1H), 3.26-3.14 (m, 2H), 3.10 (d, J = 16.9 Hz, 1H), 2.91 (d, J = 16.9 Hz, 1H), 2.33 (s, 6H); ^1^C NMR (100 MHz, CDCl₃) δ 169.04, 142.96, 138.55, 137.86, 137.22, 135.91, 130.83, 128.37, 127.92, 127.82, 126.78, 126.60, 123.31, 122.79, 117.81, 73.66, 60.21, 45.22, 43.75, 21.67.

IR (cm⁻¹): 3059 (w), 3031 (w), 2932 (m), 2860 (w), 1683 (vs), 1591 (w), 1459 (w), 1363 (s), 1289 (m), 1066 (w), 848 (m), 753 (w), 730 (s), 697 (vs), 665 (s).

(S)-1-(4-Methoxyphenyl)-3α-methyl-3α,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one (2s):
Light yellow oil; Eluent: petroleum ether/EtOAc 4:1; Yield: 74%;
HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 95:5; flow: 1.0 mL/min; λ = 220 nm. 25 °C.
98% ee (t<sub>R</sub> (minor) = 16.9 min, t<sub>R</sub> (major) = 29.9 min).

HRMS (ESI+): Calcd for C_{18}H_{19}N_{2}O_{2}, [M+H]+ m/z 295.1447. Found 295.1441.

^1^H NMR (400 MHz, CDCl₃) δ 7.74 (d, J = 9.1 Hz, 2H), 7.35-7.28 (m, 2H), 7.24 (t, J = 5.8 Hz, 1H), 7.20 (d, J = 7.0 Hz, 1H), 6.93 (d, J = 9.0 Hz, 2H), 4.66 (d, J = 13.8 Hz, 1H), 4.08 (d, J = 13.8 Hz, 1H), 3.81 (s, 3H), 3.10 (d, J = 16.8 Hz, 1H), 2.66 (d, J = 16.6 Hz, 1H), 1.65 (s, 3H); ^1^C NMR (100 MHz, CDCl₃) δ 169.63, 156.92, 144.01, 136.48, 131.70, 128.35, 128.23, 123.40, 122.15, 121.72, 114.22, 70.38, 55.64, 44.29, 26.14. IR (cm⁻¹): 2957 (w), 2924 (m), 2836 (w), 1689 (vs), 1608 (w), 1585 (w), 1505 (s), 1357 (s), 1296 (m), 1243 (vs), 1065 (s), 795 (s), 762 (s), 729 (m), 660 (w).

(S)-3α-Benzyl-1-(4-methoxyphenyl)-3α,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one (2t):
Pale yellow solid, mp = 191-193 °C; Eluent: petroleum ether/EtOAc 4:1; Yield: 75%;
HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 95:5; flow: 1.0 mL/min; λ = 220 nm. 25 °C.
98% ee (t<sub>R</sub> (minor) = 27.5 min, t<sub>R</sub> (major) = 32.2 min).
HRMS (ESI⁺): Calcd for C_{24}H_{23}N_{2}O_2, [M+H]⁺ m/z 371.1760. Found 371.1750.

^1^H NMR (600 MHz, CDCl₃) δ 7.65 (d, J = 9.1 Hz, 2H), 7.33 (t, J = 7.5 Hz, 1H), 7.28-7.24 (m, 2H), 7.19-7.12 (m, 5H), 7.10 (d, J = 7.4 Hz, 1H), 6.91 (d, J = 9.1 Hz, 2H), 4.41 (d, J = 14.6 Hz, 1H), 4.00 (d, J = 14.6 Hz, 1H), 3.81 (s, 3H), 3.25-3.11 (m, 2H), 3.10 (d, J = 16.9 Hz, 1H), 2.93 (d, J = 16.9 Hz, 1H); ^1^C NMR (100 MHz, CDCl₃) δ 168.33, 156.85, 143.28, 137.25, 135.89, 131.19, 130.72, 128.42, 127.99, 127.90, 126.82, 123.80, 121.86, 114.13, 73.84, 60.11, 55.59, 45.47, 43.47. IR (cm⁻¹): 3022 (w), 2955 (m), 2923 (w), 2852 (w), 1675 (vs), 1602 (w), 1544 (w), 1502 (s), 1373 (s), 1243 (s), 837 (s), 755 (m), 729 (m), 697 (vs), 665 (w).

(S)-3a-Benzyl-1-(4-fluorophenyl)-3a,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one (2u): Pale yellow solid, mp = 119-120 °C; Eluent: petroleum ether/EtOAc 4:1; Yield: 81%.

HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 95:5; flow: 1.0 mL/min; λ = 220 nm. 25 °C. 98% ee (t <sub>R</sub> (minor) = 14.8 min, t <sub>R</sub> (major) = 29.1 min).

HRMS (ESI⁺): Calcd for C_{26}H_{22}FNO_2, [M+H]⁺ m/z 359.1560. Found 359.1553.

^1^H NMR (600 MHz, CDCl₃) δ 7.80-7.68 (m, 2H), 7.34 (t, J = 7.4 Hz, 1H), 7.28 (t, J = 6.7 Hz, 2H), 7.17-7.10 (m, 6H), 7.08-7.03 (m, 2H), 4.49 (d, J = 14.4 Hz, 1H), 3.98 (d, J = 14.4 Hz, 1H), 3.26-3.15 (m, 2H), 3.11 (d, J = 17.0 Hz, 1H), 2.93 (d, J = 17.0 Hz, 1H); ^1^C NMR (100 MHz, CDCl₃) δ 168.97, 159.56 (d, J <sub>CF</sub> = 244.1 Hz), 142.97, 136.88, 135.63, 134.14 (d, J <sub>CF</sub> = 2.5 Hz), 130.58, 128.49, 128.10, 127.90, 126.88, 123.31, 122.69, 121.30 (d, J <sub>CF</sub> = 7.8 Hz), 115.53 (d, J <sub>CF</sub> = 22.6 Hz), 73.72, 60.29, 45.45, 43.38; ^1^F NMR (283 MHz, CDCl₃) δ -117.47. IR (cm⁻¹): 3084 (w), 3027 (m), 3006 (w), 2924 (w), 2855 (w), 1681 (vs), 1602 (w), 1503 (s), 1456 (m), 1421 (s), 1236 (m), 907 (m), 755 (w), 729 (s), 697 (s), 665 (w).

(S)-3a-Benzyl-1-(4-chlorophenyl)-3a,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one (2v): Pale yellow solid, mp = 147-148 °C; Eluent: petroleum ether/EtOAc 4:1; Yield: 81%.

-S38 -
HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 95:5; flow: 1.0 mL/min; λ = 220 nm. 25 °C. 98% ee (t<sub>R</sub> (minor) = 14.7 min, t<sub>R</sub> (major) = 31.4 min).

HRMS (ESI<sup>+</sup>): Calcd for C<sub>23</sub>H<sub>20</sub>ClN<sub>2</sub>O, [M+H]<sup>+</sup> m/z 375.1264. Found 375.1261.

1H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.73 (d, J = 8.9 Hz, 2H), 7.38-7.27 (m, 5H), 7.18-7.09 (m, 6H), 4.55 (d, J = 14.2 Hz, 1H), 3.98 (d, J = 14.2 Hz, 1H), 3.28-3.15 (m, 2H), 3.11 (d, J = 17.0 Hz, 1H), 2.92 (d, J = 17.1 Hz, 1H); 13C NMR (150 MHz, CDCl<sub>3</sub>) δ 169.42, 142.80, 136.72, 136.68, 135.53, 130.56, 129.50, 128.89, 128.54, 127.93, 126.93, 123.34, 122.65, 120.52, 73.67, 60.42, 45.43, 43.45. IR (cm<sup>-1</sup>): 3085 (w), 3055 (m), 3030 (w), 2930 (w), 2906 (w), 2846 (w), 1695 (vs), 1590 (w), 1486 (s), 1414 (m), 1362 (s), 829 (m), 758 (m), 695 (vs), 672 (w).

(S)-3α-Benzyl-1-(4-bromophenyl)-3α,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one (2w): Pale yellow solid, mp = 144-145 °C; Eluent: petroleum ether/EtOAc 4:1; Yield: 80%;

HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 95:5; flow: 1.0 mL/min; λ = 220 nm. 25 °C. 98% ee (t<sub>R</sub> (minor) = 13.7 min, t<sub>R</sub> (major) = 39.6 min).

HRMS (ESI<sup>+</sup>): Calcd for C<sub>23</sub>H<sub>20</sub>BrN<sub>2</sub>O, [M+H]<sup>+</sup> m/z 419.0759. Found 419.0757.

1H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.68 (d, J = 8.9 Hz, 2H), 7.47 (d, J = 9.0 Hz, 2H), 7.39-7.32 (m, 1H), 7.32-7.24 (m, 3H), 7.17-7.09 (m, 10H), 4.55 (d, J = 14.2 Hz, 2H), 3.98 (d, J = 14.2 Hz, 1H), 3.25-3.16 (m, 2H), 3.10 (d, J = 17.0 Hz, 1H), 2.92 (d, J = 17.0 Hz, 1H); 13C NMR (100 MHz, CDCl<sub>3</sub>) δ 169.52, 142.78, 137.20, 136.73, 135.53, 131.87, 130.59, 128.58, 128.20, 127.97, 126.97, 123.38, 122.67, 120.85, 117.26, 73.68, 60.45, 45.44, 43.50. IR (cm<sup>-1</sup>): 3085 (w), 3055 (m), 3030 (w), 2930 (w), 2906 (w), 2846 (w), 1693 (vs), 1588 (w), 1483 (s), 1461 (m), 1343 (s), 1068 (m), 828 (m), 757 (s), 729 (w), 697 (vs), 669 (s).

(S)-3α-Benzyl-1-(4-(trifluoromethyl)phenyl)-3α,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one (2x): Pale yellow solid, Mp = 171-173 °C; Eluent: petroleum ether/EtOAc 4:1; Yield: 84%;
HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 95:5; flow: 1.0 mL/min; λ = 220 nm. 25 °C. 98% ee (t_R (minor) = 14.0 min, t_R (major) = 41.2 min).

HRMS (ESI\(^+\)): Calcd for C_{24}H_{20}F_3N_2O, [M+H]\(^+\) m/z 409.1528. Found 409.1520.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.91 (d, \(J = 8.7\) Hz, 2H), 7.61 (d, \(J = 8.7\) Hz, 2H), 7.39-7.28 (m, 3H), 7.19-7.06 (m, 6H), 4.63 (d, \(J = 14.1\) Hz, 1H), 3.99 (d, \(J = 14.1\) Hz, 1H), 3.26-3.17 (m, 2H), 3.13 (d, \(J = 17.1\) Hz, 1H), 2.94 (d, \(J = 17.1\) Hz, 1H); \(^1\)\(^3\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 170.27, 142.63, 140.98, 136.53, 135.38, 130.55, 128.65, 128.29, 127.98, 127.02, 126.11 (q, \(^3\)J\(_{C,F}\) = 3.7 Hz), 126.05, 125.83 (q, \(^2\)J\(_{C,F}\) = 32.6 Hz), 124.30 (q, \(^1\)J\(_{C,F}\) = 270.0 Hz), 123.40, 122.63, 118.69, 73.70, 60.59, 45.44, 43.48. \(^1\)\(^9\)F NMR (283 MHz, CDCl\(_3\)) \(\delta\) -61.89.

IR (cm\(^{-1}\)): 3085 (w), 3027 (w), 2918 (w), 2853 (w), 1686 (vs), 1608 (m), 1512 (w), 1361 (m), 1327 (s), 1170 (m), 1117 (s), 1065 (m), 844 (s), 730 (w), 698 (vs), 666 (w).

(S)-3a-Benzyl-1-(4-nitrophenyl)-3a,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one \((2y)\):

Pale yellow solid, mp = 158-159 °C; Eluent: petroleum ether/EtOAc 4:1; Yield: 82%;

HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 70:30; flow: 1.0 mL/min; λ = 220 nm. 25 °C. 98% ee (t_R (minor) = 11.6 min, t_R (major) = 24.9 min).

HRMS (ESI\(^+\)): Calcd for C_{23}H_{20}N_3O_3, [M+H]\(^+\) m/z 386.1505. Found 386.1504.

\(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 8.22 (d, \(J = 9.2\) Hz, 2H), 7.94 (d, \(J = 9.2\) Hz, 2H), 7.42-7.37 (m, 1H), 7.36-7.32 (m, 2H), 7.20 (d, \(J = 7.8\) Hz, 1H), 7.17-7.13 (m, 2H), 7.11-7.04 (m, 3H), 4.73 (d, \(J = 13.8\) Hz, 1H), 4.00 (d, \(J = 13.8\) Hz, 1H), 3.23 (s, 2H), 3.14 (d, \(J = 17.2\) Hz, 1H), 2.97 (d, \(J = 17.2\) Hz, 1H); \(^1\)\(^3\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 171.02, 143.35, 143.33, 142.35, 136.01, 135.01, 130.35, 128.77, 128.44, 128.01, 127.12, 124.82, 123.42, 122.50, 118.11, 73.62, 60.68, 45.45, 43.19. IR (cm\(^{-1}\)): 3028 (w), 2920 (w), 1711 (s), 1589 (m), 1491 (s), 1458 (m), 1314 (vs), 1109 (m), 1117 (s), 899 (s), 753 (m), 700 (s), 637 (w).
(S)-4-(3α-Benzyl-2-oxo-2,3,3α,8-tetrahydro-1H-pyrazolo[5,1-a]isoindol-1-yl)benzonitrile (2z): Pale yellow solid, mp = 168-169 °C; Eluent: petroleum ether/EtOAc 4:1; Yield: 83%;
HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 80:20; flow: 1.0 mL/min; λ = 220 nm. 25 °C. 98% ee (tR (minor) = 14.3 min, tR (major) = 25.6 min).
HRMS (ESI+): Calcd for C24H20N3O, [M+H]+ m/z 366.1604. Found 366.1604.

1H NMR (600 MHz, CDCl3) δ 7.90 (d, J = 8.9 Hz, 2H), 7.62 (d, J = 8.9 Hz, 2H), 7.41-7.35 (m, 1H), 7.35-7.30 (m, 2H), 7.18 (d, J = 8.1 Hz, 1H), 7.16-7.12 (m, 2H), 7.11-7.05 (m, 3H), 4.68 (d, J = 13.9 Hz, 1H), 3.98 (d, J = 13.8 Hz, 1H), 3.21 (s, 2H), 3.12 (d, J = 17.2 Hz, 1H), 2.95 (d, J = 17.2 Hz, 1H); 13C NMR (150 MHz, CDCl3) δ 170.72, 142.41, 141.68, 136.12, 135.09, 133.00, 130.36, 128.68, 128.35, 127.94, 127.03, 123.35, 122.50, 119.07, 118.57, 106.93, 75.39, 60.61, 45.40, 43.25. IR (cm⁻¹): 3124 (w), 3088 (w), 3029 (w), 2928 (w), 2838 (w), 2218 (s), 1703 (vs), 1600 (s), 1499 (s), 1417 (s), 1367 (m), 775 (m), 750 (m), 701 (s), 673 (w).

(S)-1-Benzyl-3α-methyl-3α,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one (2aa): Light yellow oil; Eluent: petroleum ether/EtOAc 4:1; Yield: 77%;
HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 95:5; flow: 1.0 mL/min; λ = 220 nm. 25 °C. 99% ee (tR (minor) = 12.2 min, tR (major) = 18.5 min).
HRMS (ESI+): Calcd for C18H19N2O, [M+H]+ m/z 279.1497. Found 279.1488.

1H NMR (400 MHz, CDCl3) δ 7.40-7.28 (m, 5H), 7.27-7.21 (m, 2H), 7.17-7.12 (m, 1H), 7.09 (d, J = 6.7 Hz, 1H), 4.74-4.62 (m, 2H), 4.32 (d, J = 13.6 Hz, 1H), 3.89 (d, J = 13.6 Hz, 1H), 2.91 (d, J = 16.5 Hz, 1H), 2.46 (d, J = 16.5 Hz, 1H), 1.43 (s, 3H); 13C NMR (100 MHz, CDCl3) δ 171.49, 143.60, 136.73, 128.89, 128.65, 128.18, 128.07, 127.84, 123.20, 122.01, 71.62, 61.03, 48.52, 42.62, 25.91. IR (cm⁻¹): 3031 (w), 2963 (w), 2922 (w), 2838 (w), 1683 (vs), 1455 (m), 1402 (s), 1265 (m), 1116 (m), 1075 (m), 759 (m), 731 (m), 700 (vs), 653 (w).
(S)-1,3a-Dibenzyl-3a,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one (2ab): Pale yellow solid, mp = 137-138 °C; Eluent: petroleum ether/EtOAc 4:1; Yield: 79%;
HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 95:5; flow: 1.0 mL/min; λ = 220 nm. 25 °C. 99% ee (tR (minor) = 18.6 min, tR (major) = 21.9 min).
HRMS (ESI+): Calcd for C24H23N2O, [M+H]+ m/z 355.1806. Found 355.1806.

3H NMR (600 MHz, CDCl3) δ 7.39-7.29 (m, 5H), 7.27-7.23 (m, 1H), 7.21-7.15 (m, 2H), 7.14-7.07 (m, 3H), 7.00 (d, J = 7.5 Hz, 1H), 6.94-6.87 (m, 2H), 4.57-4.41 (m, 2H), 4.12 (d, J = 14.3 Hz, 1H), 3.86 (d, J = 14.3 Hz, 1H), 3.00 (s, 2H), 2.93 (d, J = 16.8 Hz, 1H), 2.73 (d, J = 16.8 Hz, 1H); 13C NMR (100 MHz, CDCl3) δ 170.35, 142.80, 137.36, 136.81, 135.94, 130.73, 129.03, 128.67, 128.16, 127.82, 127.76, 127.72, 126.56, 123.10, 122.62, 75.01, 60.67, 48.25, 45.05, 42.05. IR (cm⁻¹): 3031 (w), 2916 (w), 2847 (w), 1673 (vs), 1604 (m), 1409 (s), 1353 (m), 1293 (m), 1069 (m), 769 (s), 756 (m), 700 (vs), 665 (w).

(S)-1-Cyclohexyl-3a-methyl-3a,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one (2ac): Light yellow oil; Eluent: petroleum ether/EtOAc 4:1; Yield: 74%;
HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 80:20; flow: 1.0 mL/min; λ = 220 nm. 25 °C. 98% ee (tR (minor) = 4.6 min, tR (major) = 5.7 min).
HRMS (ESI+): Calcd for C17H23N2O, [M+H]+ m/z 271.1810. Found 271.1799.

3H NMR (400 MHz, CDCl3) δ 7.31-7.25 (m, 2H), 7.22-7.12 (m, 2H), 4.60 (d, J = 13.3 Hz, 1H), 4.16-4.02 (m, 2H), 2.88 (d, J = 16.3 Hz, 1H), 2.32 (d, J = 16.4 Hz, 1H), 1.91-1.78 (m, 3H), 1.75-1.54 (m, 4H), 1.51 (s, 3H) 1.47-1.31 (m, 2H), 1.23-1.07 (m, 1H); 13C NMR (100 MHz, CDCl3) δ 172.32, 143.28, 137.06, 128.13, 127.99, 123.07, 121.95, 72.09, 63.68, 53.37, 42.23, 31.77, 30.04, 25.87, 25.46. IR (cm⁻¹): 3043 (w), 2926 (w), 2854 (w), 1681 (vs), 1589 (m), 1482 (m), 1449 (s), 1250 (s), 1073 (m), 890 (m), 765 (s), 737 (s), 655 (w).
(S)-3α-Benzyl-1-cyclohexyl-3α,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one (2ad): Pale yellow solid, mp = 134-135 °C; Eluent: petroleum ether/EtOAc 4:1; Yield: 76%;

HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 98:2; flow: 1.0 mL/min; λ = 220 nm. 25 °C.
98% ee (t<sub>R</sub> (minor) = 22.3 min, t<sub>R</sub> (major) = 30.2 min).

HRMS (ESI<sup>+</sup>): Calcd for C<sub>23</sub>H<sub>27</sub>N<sub>2</sub>O, [M+H]<sup>+</sup> m/z 347.2123. Found 347.2121.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.23-7.10 (m, 7H), 7.10-7.04 (m, 2H), 4.53 (d, J = 13.6 Hz, 1H), 4.16-3.99 (m, 3H), 3.20 (d, J = 14.3 Hz, 1H), 3.06 (d, J = 14.3 Hz, 1H), 2.93 (d, J = 16.7 Hz, 1H), 2.62 (d, J = 16.8 Hz, 1H), 1.95-1.74 (m, 5H), 1.73-1.65 (m, 1H), 1.59 (qd, J = 12.3, 3.2 Hz, 1H), 1.48-1.32 (m, 2H), 1.18 (qt, J = 13.0, 3.3 Hz, 1H);
<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 171.37, 141.62, 137.61, 136.78, 130.80, 127.92, 127.77, 127.60, 126.42, 122.93, 122.89, 75.46, 63.72, 54.17, 44.19, 43.38, 31.92, 30.87, 25.92, 25.74, 25.56.

IR (cm<sup>-1</sup>): 3025 (w), 2931 (w), 2856 (w), 1674 (vs), 1602 (m), 1431 (m), 1405 (s), 1255 (m), 1206 (m), 731 (m), 697 (s), 673 (s), 636 (w).

(S)-3α-Benzyl-6-fluoro-1-phenyl-3α,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one (2ae):

Light yellow oil; Eluent: petroleum ether/EtOAc 4:1; Yield: 84%;

HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 95:5; flow: 1.0 mL/min; λ = 220 nm. 25 °C.
98% ee (t<sub>R</sub> (minor) = 16.3 min, t<sub>R</sub> (major) = 26.5 min).

HRMS (ESI<sup>+</sup>): Calcd for C<sub>23</sub>H<sub>20</sub>FNO, [M+H]<sup>+</sup> m/z 359.1560. Found 359.1557.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.77 (d, J = 8.1 Hz, 2H), 7.37 (t, J = 8.0 Hz, 2H), 7.23-7.12 (m, 7H), 7.01 (td, J = 8.7, 2.0 Hz, 1H), 6.78 (d, J = 8.3 Hz, 1H), 4.44 (d, J = 14.9 Hz, 1H), 3.97 (d, J = 14.8 Hz, 1H), 3.18 (s, 2H), 3.09 (d, J = 17.0 Hz, 1H), 2.93 (d, J = 17.0 Hz, 1H);
<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 168.88, 163.03 (d, <sup>1</sup>J<sub>C-F</sub> = 246.4 Hz), 139.40 (d, <sup>3</sup>J<sub>C-F</sub> = 8.5 Hz), 138.59 (d, <sup>4</sup>J<sub>C-F</sub> = 1.8 Hz), 137.87, 135.58, 130.69, 128.97, 127.96, 126.93, 124.82, 124.14 (d, <sup>3</sup>J<sub>C-F</sub> = 9.1 Hz), 119.74, 115.26 (d, <sup>2</sup>J<sub>C-F</sub> = 23.0 Hz), 110.5 (d, <sup>2</sup>J<sub>C-F</sub> = 23.1 Hz), 73.26, 60.04, 45.45, 43.75; <sup>19</sup>F NMR (283 MHz, CDCl<sub>3</sub>) δ -113.51. IR (cm<sup>-1</sup>): 3062 (w), 3030 (w), 2917 (w), 2848 (w), 1696 (vs), 1595 (m), 1489 (s), 1405 (s), 1355 (m), 1311 (m), 1260 (m), 861 (m), 819 (m), 751 (vs), 695 (s).

-S43 -
(S)-3α-Benzyl-6-chloro-1-phenyl-3α,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one (2af):
Light yellow oil; Eluent: petroleum ether/EtOAc 4:1; Yield: 86%;
HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 95:5; flow: 1.0 mL/min; λ = 220 nm. 25 °C.
98% ee (tR (minor) = 18.3 min, tR (major) = 33.1 min).
HRMS (ESI+): Calcd for C2₃H₂₀ClN₂O, [M+H]+ m/z 375.1264. Found 375.1257.
1H NMR (400 MHz, CDCl₃) δ 7.76 (d, J = 7.8 Hz, 2H), 7.41-7.35 (m, 2H), 7.30 (dd, J = 8.0, 1.7 Hz, 1H), 7.20-7.12 (m, 7H), 7.08 (s, 1H), 4.43 (d, J = 14.9 Hz, 1H), 3.97 (d, J = 14.9 Hz, 1H), 3.18 (s, 2H), 3.08 (d, J = 17.0 Hz, 1H), 2.93 (d, J = 17.0 Hz, 1H); 13C NMR (100 MHz, CDCl₃) δ 168.74, 141.49, 139.15, 137.77, 135.42, 134.23, 130.67, 128.98, 128.30, 127.98, 126.96, 124.86, 124.00, 123.61, 119.73, 73.42, 59.86, 45.20, 43.59. IR (cm⁻¹): 3062 (w), 3030 (w), 2921 (w), 2850 (w), 1696 (s).

(S)-3α-Benzyl-5-fluoro-1-phenyl-3α,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one (2ag):
Light yellow oil; Eluent: petroleum ether/EtOAc 4:1; Yield: 83%;
HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 95:5; flow: 1.0 mL/min; λ = 220 nm. 25 °C.
98% ee (tR (minor) = 16.7 min, tR (major) = 21.7 min).
HRMS (ESI+): Calcd for C2₃H₂₀FN₂O, [M+H]+ m/z 359.1560. Found 359.1550.
1H NMR (400 MHz, CDCl₃) δ 7.78 (d, J = 7.9 Hz, 2H), 7.42-7.34 (m, 2H), 7.21-7.12 (m, 6H), 7.09-7.02 (m, 1H), 7.01-6.93 (m, 2H), 4.47 (d, J = 14.2 Hz, 1H), 3.95 (d, J = 14.2 Hz, 1H), 3.19 (s, 2H), 3.11 (d, J = 17.0 Hz, 1H), 2.92 (d, J = 17.0 Hz, 1H); 13C NMR (100 MHz, CDCl₃) δ 168.79, 167.63 (d, 3JCF = 4.6 Hz), 162.88 (d, 1JCF = 245.7 Hz), 145.06 (d, 3JCF = 7.8 Hz), 137.87, 135.36, 132.44, 130.69, 128.96, 128.00, 126.99, 124.77, 124.66, 119.62, 115.75 (d, 2JCF = 22.8 Hz), 110.06 (d, 3JCF = 23.5 Hz), 73.64, 59.86, 45.21, 43.46; 19F NMR (283 MHz, CDCl₃) δ -113.74. IR
(cm⁻¹): 3064 (w), 3030 (w), 2923 (w), 2847 (w), 1693 (vs), 1594 (m), 1492 (s), 1458 (s), 1352 (m),
1311 (m), 1075 (m), 758 (m), 727 (m), 691 (s).

Methyl (S)-3α-benzyl-2-oxo-1-phenyl-2,3,3α,8-tetrahydro-1H-pyrazolo[5,1-a]isoindole-5-carboxylate (2ah): Light yellow oil; Eluent: petroleum ether/EtOAc 4:1; Yield: 78%;
HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 85:15; flow: 1.0 mL/min; λ = 220 nm. 25 °C.
98% ee (tR (minor) = 12.5 min, tR (major) = 26.1 min).
HRMS (ESI⁺): Calcd for C₂₅H₂₃N₂O₃, [M+H]⁺ m/z 399.1709. Found 399.1699.

1H NMR (400 MHz, CDCl₃) δ 8.03-7.93 (m, 2H), 7.82-7.73 (m, 2H), 7.40-7.35 (m, 2H), 7.20-7.10
(m, 7H), 4.51 (d, J = 15.4 Hz, 1H), 4.03 (d, J = 15.4 Hz, 1H), 3.96 (s, 3H), 3.25 (s, 2H), 3.13 (d, J
= 17.0 Hz, 1H), 2.96 (d, J = 17.0 Hz, 1H); 13C NMR (100 MHz, CDCl₃) δ 168.79, 166.74, 143.64,
142.55, 137.88, 135.42, 130.73, 130.40, 130.13, 129.00, 128.00, 126.98, 124.84, 124.14, 123.43,
119.70, 73.59, 60.38, 52.46, 45.39, 43.64. IR (cm⁻¹): 3062 (w), 3030 (w), 2958 (w), 2919 (w),
2849 (w), 1695 (vs), 1595 (m), 1489 (s), 1456 (s), 1354 (m), 1310 (s), 794 (m), 753 (vs), 695 (s),
630 (w).
5. Scale Synthesis of 2i

To a dried Schlenk tube were added Pd(TFA)_2 (35.9 mg, 0.108 mmol) and ligand (S)-F (95.1 mg, 0.161 mmol) under N_2, 25.0 mL of anhydrous N,N-dimethylacetamide (DMA) was then introduced via syringe. After stirring for 1 h, substrate 1i (1.0 g, dissolved in 8 mL of DMA), BnNMe_2 (10.75 mmol, 5 equiv) and TFA (4.3 mmol, 2 equiv) were added via syringe. The mixture was vigorously stirred in a pre-warmed oil bath at 150 °C for 48 h. The solvent was then removed under vacuum, and the residue was purified by chromatography on silica to give the desired product 2i (0.6 g, 82% yield, 98% ee).

6. Procedure for Hydroarylation Using Aryl Bromide 3

To a dried Schlenk tube were added Pd(TFA)_2 (3.32 mg, 0.01 mmol) and ligand (S)-F (8.85 mg, 0.015 mmol) under N_2, 3.0 mL of anhydrous N,N-dimethylacetamide (DMA) was then introduced via syringe. After stirring for 1 h, 3 (0.2 mmol, dissolved in 1 mL of DMA), BnNMe_2 (1.0 mmol, 5 equiv) and TFA (0.4 mmol, 2 equiv) were added via syringe. The mixture was vigorously stirred in a pre-warmed oil bath at 150 °C for 24 h. The solvent was then removed under vacuum, and the residue was purified by chromatography on silica to give the desired product 2a (38% yield, 97% ee).

1-(2-Bromobenzyl)-5-methyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (3): Pale yellow solid, 
Mp = 158-159 °C; Eluent: EtOAc; HRMS (ESI^+): Calcd for C_{17}H_{16}BrN_2O, [M+H]^+ ml/z 343.0446. Found 343.0441. ^1 H NMR (400 MHz, CDCl_3) δ 7.55-7.44 (m, 2H), 7.41 (t, J = 7.8 Hz, 2H), 7.28-7.22 (m, 3H), 7.18 (td, J = 7.7, 1.5 Hz, 1H), 6.62 (s, 1H), 6.54 (dd, J = 7.5, 1.1 Hz, 1H), 5.27
(s, 2H), 2.47 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 158.26, 150.17, 133.33, 131.97, 131.76, 130.27, 130.06, 129.55, 128.32, 128.22, 127.16, 121.71, 93.21, 50.19, 13.15.

7. Application of the Synthesized Compound (S)-2i

To a solution of (S)-3a-benzyl-1-phenyl-3a,8-dihydro-1H-pyrazolo[5,1-a]isoindol-2(3H)-one ((S)-2i, 68 mg, 0.2 mmol, 98% ee) in THF (4 mL) was added LiAlH$_4$ (38 mg, 1.0 mmol) at room temperature and the mixture was stirred at 70 °C for 4 h. After which, the mixture was quenched with water at room temperature and extracted with ethyl acetate. The organic layers were washed with brine and dried over Na$_2$SO$_4$. After filtered and concentrated under vacuum, the residue was purified with flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 1:25 (v/v), to afford (S)-4 (62 mg, 95%, 98% ee). White solid, mp = 97-98 °C; HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 99:1; flow: 0.5 mL/min; λ = 220 nm. 25 °C. 98% ee (t$_R$ (minor) = 31.1 min, t$_R$ (major) = 32.4 min). HRMS (ESI$^+$): Calcd for C$_{23}$H$_{23}$N$_2$, [M+H]$^+$ m/z 327.1861. Found 327.1864.

8. Procedure for Hydroarylation Using o-Iodobenzyoyl Derivatives

(1) Synthesis of Substrates 5a-d

Compounds 5 were synthesized from the corresponding pyrazol-3-one and 2-iodobenzyoyl chloride according to the literature procedure (Maruoka et al., 2013).
(2) General Procedures

To a dried Schlenk tube were added Pd(TFA)$_2$ (3.32 mg, 0.01 mmol) and ligand (S)-F (8.85 mg, 0.015 mmol) under N$_2$, 3.0 mL of anhydrous N,N-dimethylacetamide (DMA) was then introduced via syringe. After stirring for 1 h, 5 (0.2 mmol, dissolved in 1mL of DMA), BnMe$_2$ (1.0 mmol, 5 equiv) and TFA (0.4 mmol, 2 equiv) were added via syringe. The mixture was vigorously stirred in a pre-warmed oil bath at 130 °C for 24 h. The solvent was then removed under vacuum, and the residue was purified by chromatography on silica to give the desired product 6. The enantiomeric excess was determined by chiral HPLC analysis.

Racemic products Rac-6a-d were prepared according to the above procedures in the absence of ligand

(3) Characterization Data of Substrates 5a-d and 6a-d

1-(2-Iodobenzoyl)-5-methyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (5a): Pale yellow solid, mp = 218-219 °C; Eluent: petroleum ether/EtOAc 2:1; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.68 (d, $J$ = 7.8 Hz, 1H), 7.16 (t, $J$ = 7.4 Hz, 2H), 7.12-7.06 (m, 1H), 7.02 (t, $J$ = 7.1 Hz, 1H), 6.97-6.91 (m, 3H), 6.86 (dd, $J$ = 7.5, 1.5 Hz, 1H), 5.63 (s, 1H), 2.60 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 167.74, 166.78, 155.74, 139.87, 139.01, 138.02, 131.78, 129.86, 128.95, 127.53, 127.24, 124.27, 102.70, 92.04, 15.98.

5-Ethyl-1-(2-iodobenzoyl)-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (5b): Pale yellow solid, mp = 204-205 °C; Eluent: petroleum ether/EtOAc 2:1; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.65 (d, $J$ = 7.8 Hz, 1H), 7.14 (t, $J$ = 7.3 Hz, 2H), 7.12-7.08 (m, 1H), 7.02 (t, $J$ = 7.1 Hz, 1H), 6.98-6.91 (m, 3H), 6.86 (dd, $J$ = 7.5, 1.5 Hz, 1H), 5.63 (s, 1H), 2.59 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 167.74, 166.78, 155.74, 139.87, 139.01, 138.02, 131.78, 129.86, 128.95, 127.53, 127.24, 124.27, 102.70, 92.04, 15.98.
Hz, 1H), 7.20-7.04 (m, 3H), 6.99 (t, J = 7.4 Hz, 1H), 6.95-6.85 (m, 3H), 6.82 (d, J = 7.2 Hz, 1H), 5.67 (s, 1H), 3.02 (q, J = 7.2 Hz, 2H), 1.40 (t, J = 7.3 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 167.97, 166.85, 161.96, 140.01, 138.86, 138.06, 131.59, 129.76, 128.87, 127.40, 127.12, 124.11, 100.75, 91.92, 22.78, 11.81.

1-(2-Iodobenzoyl)-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (5c): Pale yellow solid, mp = 197-198 °C; Eluent: petroleum ether/EtOAc 2:1; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.65 (d, J = 7.8 Hz, 1H), 7.14 (t, J = 7.4 Hz, 2H), 7.08 (t, J = 7.3 Hz, 1H), 6.99 (t, J = 7.5 Hz, 1H), 6.94-6.86 (m, 3H), 6.82 (d, J = 7.6 Hz, 1H), 5.66 (s, 1H), 2.98 (t, J = 7.6 Hz, 2H), 1.93-1.81 (m, 2H), 1.11 (t, J = 7.4 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 168.05, 166.86, 160.59, 140.08, 138.91, 138.16, 131.60, 129.80, 128.92, 127.41, 127.15, 124.13, 101.47, 91.95, 31.10, 21.04, 13.89.

1-(2-Iodobenzoyl)-5-isopropyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (5d): Pale yellow solid, mp = 208-209 °C; Eluent: petroleum ether/EtOAc 2:1; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.64 (d, J = 7.8 Hz, 1H), 7.14 (t, J = 7.4 Hz, 2H), 7.07 (t, J = 7.2 Hz, 1H), 6.98 (t, J = 7.5 Hz, 1H), 6.93-6.83 (m, 3H), 6.79 (d, J = 7.5 Hz, 1H), 5.67 (s, 1H), 3.59 (hept, J = 6.6 Hz, 1H), 1.45 (d, J = 6.8 Hz, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 168.24, 167.41, 166.94, 140.39, 138.88, 138.29, 131.50, 129.79, 128.93, 127.37, 127.09, 123.98, 99.50, 91.85, 28.23, 22.15.

(S)-3α-Methyl-1-phenyl-3,3α-dihydro-1H-pyrazolo[5,1-a]isoindole-2,8-dione (6a): Pale yellow solid, mp = 157-158 °C; Eluent: petroleum ether/EtOAc 3:1.
HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 80:20; flow: 1.0 mL/min; λ = 220 nm. 25 °C.
91% ee (t<sub>R</sub> (minor) = 10.9 min, t<sub>R</sub> (major) = 13.3 min);

<sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.93 (d, J = 7.6 Hz, 1H), 7.78 (d, J = 9.7 Hz, 2H), 7.72 (t, J = 8.1 Hz, 1H), 7.58 (t, J = 7.9 Hz, 1H), 7.54 (d, J = 7.6 Hz, 1H), 7.44 -7.38 (m, 2H), 7.20 (t, J = 7.5 Hz, 1H), 2.86-2.77 (m, 2H), 1.76 (s, 3H);

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 171.92, 171.20, 149.30, 139.14, 134.26, 129.69, 128.98, 128.83, 125.58, 125.23, 122.33, 118.55, 66.92, 45.69, 23.09.

(S)-3α-Ethyl-1-phenyl-3,3α-dihydro-1H-pyrazolo[5,1-a]isoindole-2,8-dione (6b): Pale yellow solid, mp = 149-150 °C; Eluent: petroleum ether/EtOAc 3:1;

HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 80:20; flow: 1.0 mL/min; λ = 220 nm. 25 °C.
87% ee (t<sub>R</sub> (minor) = 10.1 min, t<sub>R</sub> (major) = 12.4 min)

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.92 (d, J = 7.7 Hz, 1H), 7.79 (d, J = 8.5 Hz, 2H), 7.71 (t, J = 7.6 Hz, 1H), 7.57 (t, J = 7.5 Hz, 1H), 7.48 (d, J = 7.7 Hz, 1H), 7.41 (t, J = 7.6 Hz, 2H), 7.19 (t, J = 7.2 Hz, 1H), 2.83 (s, 2H), 2.19 – 2.02 (m, 2H), 0.84 (t, J = 7.2 Hz, 3H);

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 172.61, 171.39, 147.97, 139.08, 134.22, 129.62, 129.53, 128.96, 125.55, 125.03, 122.36, 118.35, 70.20, 44.84, 29.04, 8.04.

(S)-1-Phenyl-3α-propyl-3,3α-dihydro-1H-pyrazolo[5,1-a]isoindole-2,8-dione (6c): Pale yellow solid, mp = 138-139 °C; Eluent: petroleum ether/EtOAc 3:1;

HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 80:20; flow: 1.0 mL/min; λ = 220 nm. 25 °C.
88% ee (t<sub>R</sub> (minor) = 8.9 min, t<sub>R</sub> (major) = 11.0 min)

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.90 (d, J = 7.7 Hz, 1H), 7.78 (d, J = 8.6 Hz, 2H), 7.70 (t, J = 7.6 Hz, 1H), 7.55 (t, J = 7.5 Hz, 1H), 7.49 (d, J = 7.8 Hz, 1H), 7.41 (t, J = 7.8 Hz, 2H), 7.19 (t, J = 7.0 Hz, 1H), 2.82 (s, 2H), 2.11-1.95 (m, 2H), 1.52-1.37 (m, 1H), 1.16-1.00 (m, 1H), 0.86 (t, J = 7.3 Hz,
3-H; $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 172.51, 171.32, 148.36, 139.04, 134.18, 129.56, 129.31, 128.95, 125.50, 124.98, 122.35, 69.80, 44.99, 38.37, 17.05, 14.14.

3α-Isopropyl-1-phenyl-3,3α-dihydro-1H-pyrazolo[5,1-a]isoindole-2,8-dione (6d): Pale yellow solid, mp = 142-143 °C; Eluent: petroleum ether/EtOAc 3:1;

HPLC analysis: Daicel Chiralpak IB; hexane/iPrOH: 80:20; flow: 1.0 mL/min; $\lambda$ = 220 nm. 25 °C. 89% ee ($t_R$ (minor) = 10.0 min, $t_R$ (major) = 12.3 min)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.91 (d, $J$ = 7.6 Hz, 1H), 7.81 (d, $J$ = 8.4 Hz, 2H), 7.69 (t, $J$ = 7.6 Hz, 1H), 7.55 (t, $J$ = 7.5 Hz, 1H), 7.48 (d, $J$ = 7.6 Hz, 1H), 7.41 (t, $J$ = 7.9 Hz, 2H), 7.18 (t, $J$ = 7.3 Hz, 1H), 3.03 (d, $J$ = 16.7 Hz, 1H), 2.85 (d, $J$ = 16.6 Hz, 1H), 2.36 (hept, $J$ = 6.9 Hz, 1H), 1.03 (d, $J$ = 6.9 Hz, 3H), 0.91 (d, $J$ = 6.7 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 173.22, 171.48, 149.17, 138.91, 134.24, 129.48, 129.37, 128.98, 125.63, 124.90, 122.50, 118.13, 72.36, 43.05, 34.52, 16.92.

9. X-Ray Crystallographic Data for (S)-2a, (S)-E, (S)-F and (S)-G

(1) Crystal report of compound (S)-2a

Figure S1. Crystal structure of (S)-2a showing 25% probability displacement ellipsoids, related to Table 1.

Table S1. Crystal Data and Structure Refinement for (S)-2a, related to Table 1.

| Identification code | CCDC 1822025 |
|---------------------|--------------|

-S51-
| Property                          | Value                                      |
|----------------------------------|--------------------------------------------|
| Empirical formula               | C17H16N2O                                  |
| Formula weight                   | 264.32                                     |
| Temperature/K                    | 293(2)                                     |
| Crystal system                   | orthorhombic                               |
| Space group                      | P2₁2₁2₁                                   |
| a/Å                              | 8.6230(3)                                  |
| b/Å                              | 9.0471(4)                                  |
| c/Å                              | 18.2985(5)                                 |
| α/°                              | 90                                         |
| β/°                              | 90                                         |
| γ/°                              | 90                                         |
| Volume/Å³                        | 1427.52(9)                                 |
| Z                                | 4                                          |
| ρcalc g/cm³                      | 1.230                                      |
| μ/mm⁻¹                           | 0.613                                      |
| F(000)                           | 560.0                                      |
| Crystal size/mm³                 | 0.55 × 0.40 × 0.30                         |
| Radiation                        | CuKα (λ = 1.54184)                         |
| 2Θ range for data collection/°   | 9.666 to 148.988                           |
| Index ranges                     | -5 <= h <= 10, -10 <= k <= 11, -22 <= l <= 22 |
| Reflections collected            | 3465                                       |
| Independent reflections          | 2443[Rint = 0.0147, Rsigma = 0.0242]        |
| Data/restraints/parameters       | 2443/0/183                                 |
| Goodness-of-fit on F²            | 1.050                                      |
| Final R indexes [I>=2σ (I)]     | R₁ = 0.0328, wR₂ = 0.0874                  |
| Final R indexes [all data]      | R₁ = 0.0354, wR₂ = 0.0904                  |
| Largest diff. peak/hole / e Å⁻³  | 0.109/-0.107                              |
| Flack parameter                  | -0.1(3)                                    |
(2) Crystal report of compound (S)-E

![Crystal structure of (S)-E](image)

Figure S2. Crystal structure of (S)-E showing 60% probability displacement ellipsoids for non-H atoms, related to Figure 3.

Table S2. Crystal Data and Structure Refinement for (S)-E, related to Figure 3.

| Property                        | Value                  |
|---------------------------------|------------------------|
| Identification code             | CCDC 1842685           |
| Empirical formula               | C_{40}H_{34}P_{2}      |
| Formula weight                  | 576.61                 |
| Temperature/K                   | 99.9(5)                |
| Crystal system                  | orthorhombic           |
| Space group                     | P2₁/T2₁              |
| a/Å                             | 10.07990(10)           |
| b/Å                             | 15.64660(10)           |
| c/Å                             | 19.5369(2)             |
| α/°                             | 90                    |
| β/°                             | 90                    |
| γ/°                             | 90                    |
| Volume/Å³                       | 3081.28(5)             |
| Z                               | 4                     |
| ρ_{calc}/g/cm³                  | 1.243                  |
| μ/mm⁻¹                          | 1.477                  |
| F(000)                          | 1216                   |
| Crystal size/mm³                | 0.8 × 0.2 × 0.1        |
Radiation: \( \text{CuK}\alpha (\lambda = 1.54184) \)

\( 2\theta \) range for data collection: 7.238 to 193.384

Index ranges: -12 \( \leq h \leq 9 \), -19 \( \leq k \leq 19 \), -24 \( \leq l \leq 24 \)

Reflections collected: 25919

Independent reflections: 6419 \([R_{int} = 0.0437, R_{sigma} = 0.0331]\)

Data/restraints/parameters: 6419 /0/ 379

Goodness-of-fit on \( F^2 \): 1.039

Final R indexes [\( I \geq 2\sigma (I) \)]: \( R_1 = 0.0295, wR_2 = 0.0769 \)

Final R indexes [all data]: \( R_1 = 0.0308, wR_2 = 0.0781 \)

Largest diff. peak/hole / e Å\(^3\): 0.345/ -0.244

Flack parameter: -0.011(8)

(3) Crystal report of compound (S)-F

![Crystal structure of (S)-F showing 25% probability displacement ellipsoids for non-H atoms, related to Figure 3.](image)

**Table S3. Crystal Data and Structure Refinement for (S)-F, related to Figure 3.**

| Identification code | CCDC 1822026 |
|---------------------|--------------|
| Empirical formula   | \( \text{C}_{41}\text{H}_{36}\text{P}_2 \) |
| Formula weight      | 590.64       |
| Temperature/K       | 293(2)       |
| Crystal system      | monoclinic   |
Space group C2

a/Å 20.4128(4)
b/Å 10.4888(2)
c/Å 15.8277(3)
α/° 90
β/° 99.378(2)
γ/° 90

Volume/Å³ 3343.51(11)

Z 4

ρ calc 1.173

μ/mm⁻¹ 1.372

F(000) 1248

Crystals size/mm³ 0.2 × 0.2 × 0.1

Radiation CuKα (λ = 1.54184)

2Θ range for data collection/° 8.782 to 148.846

Index ranges -23 ≤ h ≤ 25, -12 ≤ k ≤ 11, -15 ≤ l ≤ 19

Reflections collected 7520

Independent reflections 4917 [R int = 0.0170, R sigma = 0.0261]

Data/restraints/parameters 4917/1/388

Goodness-of-fit on F² 1.022

Final R indexes [I>2σ (I)] R₁ = 0.0354, wR₂ = 0.1032

Final R indexes [all data] R₁ = 0.0366, wR₂ = 0.1055

Largest diff. peak/hole / e Å⁻³ 0.38/-0.15

Flack parameter 0.022(11)

(4) Crystal report of compound (S)-G
Figure S4. Crystal structure of (S)-G showing 60% probability displacement ellipsoids for non-H atoms, related to Figure 3.

Table S4. Crystal Data and Structure Refinement for (S)-G, related to Figure 3.

| Property                  | Value                                      |
|---------------------------|--------------------------------------------|
| Identification code       | CCDC 1842686                               |
| Empirical formula         | C_{42}H_{38}P_{2}                          |
| Formula weight            | 604.66                                     |
| Temperature/K             | 99.9(5)                                    |
| Crystal system            | monoclinic                                 |
| Space group               | C2                                         |
| a/Å                       | 20.3682(2)                                 |
| b/Å                       | 10.54400(10)                               |
| c/Å                       | 15.6750(2)                                 |
| α/°                       | 90                                         |
| β/°                       | 99.9320(10)                                |
| γ/°                       | 90                                         |
| Volume/Å³                 | 3315.95(6)                                 |
| Z                         | 4                                          |
| ρ calc/g/cm³              | 1.211                                      |
| μ/mm⁻¹                    | 1.395                                      |
| F(000)                    | 1280                                       |
| Crystal size/mm³          | 0.45 ×0.4×0.32                             |
| Radiation                 | CuKα (λ = 1.54184)                         |
| Property                                      | Value                                      |
|----------------------------------------------|--------------------------------------------|
| 2θ range for data collection/°               | 8.816 to 134.986                           |
| Index ranges                                 | -23 <= h <= 24, -12 <= k <= 12, -18 <= l <= 18 |
| Reflections collected                        | 11595                                      |
| Independent reflections                      | 5431 [R_int = 0.0244, R_sigma = 0.0295]     |
| Data/restraints/parameters                   | 5431 /1/ 397                               |
| Goodness-of-fit on F^2                       | 1.054                                      |
| Final R indexes [I>=2σ (I)]                  | R_1 = 0.0263, wR_2 = 0.0687                |
| Final R indexes [all data]                   | R_1 = 0.0264, wR_2 = 0.0688                |
| Largest diff. peak/hole / e Å\(^{-3}\)       | 0.202/ -0.251                              |
| Flack parameter                              | 0.012(7)                                   |
10. References

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11. HPLC Analysis of Products M-4, 2a-ah, 4 and 6

**Figure S5.** HPLC of *Rac*-M-4E, related to Figure 2.

**Figure S6.** HPLC of (R)-M-4E, related to Figure 2.
Figure S7. HPLC of (S)-M-4E, related to Figure 2.

Figure S8. HPLC of Rac-M-4F, related to Figure 2.
Figure S9. HPLC of (R)-M-4F, related to Figure 2.

Figure S10. HPLC of (S)-M-4F, related to Figure 2.
Figure S11. HPLC of Rac-M-4G, related to Figure 2.

Figure S12. HPLC of (R)-M-4G, related to Figure 2.
**Figure S13.** HPLC of (S)-M-4G, related to Figure 2.

| Peak | RetTime | Type | Width | Area   | Height | Area %  |
|------|---------|------|-------|--------|--------|---------|
| #    | [min]   | [min]| mAU  | *s | [mAU ] |        |
| 1    | 8.330   | MM   | 0.1924| 43.82491 | 3.79612 | 0.9911  |
| 2    | 11.268  | BB   | 0.2503| 4378.00195 | 270.00085 | 99.0089 |

**Figure S14.** HPLC of Rac-2a, related to Table 1.

| Peak | RetTime | Type | Width | Area   | Height | Area %  |
|------|---------|------|-------|--------|--------|---------|
| #    | [min]   | [min]| mAU  | *s | [mAU ] |        |
| 1    | 9.543   | BV   | 0.1933| 3589.92920 | 280.00446 | 49.9524 |
| 2    | 26.537  | BB   | 0.4839| 3596.77075 | 115.11349 | 50.0476 |

-S63-
Figure S15. HPLC of (S)-2a, related to Table 1.

Figure S16. HPLC of (S)-2a, related to Table 1.
Figure S17. HPLC of \( (S) \)-2a, related to Table 1.

| Peak | Ret Time (min) | Type | Width (min) | Area   | Height (mAU) | Area % | mAU | *s | [mAU] |
|------|----------------|------|-------------|--------|--------------|--------|-----|----|-------|
| 1    | 9.538          | BB   | 0.1961      | 123.97203 | 9.58267     | 2.1489 | 1   | 123.97203 | 9.58267 |
| 2    | 28.047         | BB   | 0.5174      | 5645.06152 | 170.44727  | 97.8511 | 1   | 5645.06152 | 170.44727 |

Figure S18. HPLC of Rac-2b, related to Table 2.

| Peak | Ret Time (min) | Type | Width (min) | Area   | Height (mAU) | Area % | mAU | *s | [mAU] |
|------|----------------|------|-------------|--------|--------------|--------|-----|----|-------|
| 1    | 9.006          | VV   | 0.1761      | 5851.36523 | 509.76456   | 49.6755 | 1   | 5851.36523 | 509.76456 |
| 2    | 23.640         | BB   | 0.4368      | 5927.81445 | 212.07364   | 50.3245 | 1   | 5927.81445 | 212.07364 |
Figure S19. HPLC of (S)-2b, related to Table 2.

Figure S20. HPLC of (S)-2b, related to Table 2.
**Figure S21.** HPLC of (S)-2b, related to Table 2.

| Peak | RetTime | Type | Width | Area  | Height | Area  |
|------|---------|------|-------|-------|--------|-------|
| #    | [min]   |      | [min] | mAU   | s      | mAU   | %     |
| 1    | 9.020   | VB   | 0.2267| 21.98778 | 1.44772 | 0.5486|
| 2    | 23.434  | BB   | 0.4289| 3986.19263 | 144.78496 | 99.4514|

**Figure S22.** HPLC of Rac-2c, related to Table 2.

| Peak | RetTime | Type | Width | Area  | Height | Area  |
|------|---------|------|-------|-------|--------|-------|
| #    | [min]   |      | [min] | mAU   | s      | mAU   | %     |
| 1    | 6.287   | BV   | 0.1307| 1.09849e4 | 1299.38330 | 48.4757|
| 2    | 16.912  | BB   | 0.3779| 1.16757e4 | 491.01810  | 51.5243|
Figure S23. HPLC of (S)-2c, related to Table 2.

Figure S24. HPLC of Rac-2d, related to Table 2.
Figure S25. HPLC of (S)-2d, related to Table 2.

| Peak | Ret Time | Type | Width | Area   | Height | Area % |
|------|----------|------|-------|--------|--------|--------|
| 1    | 8.840    | BV   | 0.1784| 100.66415| 8.62471| 1.0669 |
| 2    | 20.039   | BB   | 0.3934| 9334.23828| 366.26318| 98.9331|

Figure S26. HPLC of Rac-2e, related to Table 2.

| Peak | Ret Time | Type | Width | Area   | Height | Area % |
|------|----------|------|-------|--------|--------|--------|
| 1    | 9.673    | BV   | 0.2119| 9961.88477| 709.32764| 48.0556 |
| 2    | 27.834   | BB   | 0.6147| 1.07680e4| 278.16705| 51.9444 |
Figure S27. HPLC of (S)-2e, related to Table 2.

Figure S28. HPLC of Rac-2b, related to Table 2.
Figure S29. HPLC of (S)-2f, related to Table 2.

| Peak | RetTime | Type | Width | Area     | Height | Area     | %     |
|------|---------|------|-------|----------|--------|----------|-------|
| #    | [min]   |      | [min] | mAU      | s      | mAU      |       |
| 1    | 5.840   | BV   | 0.1112| 264.65854| 36.34045| 0.8958   |       |
| 2    | 11.398  | BB   | 0.2463| 2.92813e4| 1874.67334| 99.1042 |       |

Figure S30. HPLC of Rac-2g, related to Table 2.

| Peak | RetTime | Type | Width | Area     | Height | Area     | %     |
|------|---------|------|-------|----------|--------|----------|-------|
| #    | [min]   |      | [min] | mAU      | s      | mAU      |       |
| 1    | 11.925  | BB   | 0.2647| 6541.70215| 374.91364| 49.3920  |       |
| 2    | 29.506  | BB   | 0.6237| 6702.75586| 168.16367| 50.6080  |       |
Figure S31. HPLC of (S)-2g, related to Table 2.

Figure S32. HPLC of Rac-2h, related to Table 2.
Figure S33. HPLC of (S)-2h, related to Table 2.

Figure S34. HPLC of Rac-2i, related to Table 2.
Figure S35. HPLC of (S)-2i, related to Table 2.

Figure S36. HPLC of Rac-2j, related to Table 2.
Figure S37. HPLC of (S)-2j, related to Table 2.

Figure S38. HPLC of Rac-2k, related to Table 2.
Figure S39. HPLC of (S)-2k, related to Table 2.

Figure S40. HPLC of Rac-2l, related to Table 2.
Figure S41. HPLC of (S)-2l, related to Table 2.

Figure S42. HPLC of Rac-2m, related to Table 2.
Figure S43. HPLC of (S)-2m, related to Table 2.

Figure S44. HPLC of Rac-2n, related to Table 2.
Figure S45. HPLC of (S)-2n, related to Table 2.

Figure S46. HPLC of Rac-2o, related to Table 2.
Figure S47. HPLC of (S)-2o, related to Table 2.

Figure S48. HPLC of Rac-2p, related to Table 2.
Figure S49. HPLC of (S)-2p, related to Table 2.

| Peak | RetTime | Type | Width | Area   | Height | Area % |
|------|---------|------|-------|--------|--------|--------|
| 1    | 36.036  | BB   | 1.3335| 1.44537e4 | 155.68726 | 99.8319 |
| 2    | 42.843  | BV   | 0.6311| 24.34075 | 4.57325e-1 | 0.1681 |

Figure S50. HPLC of Rac-2q, related to Table 2.

| Peak | RetTime | Type | Width | Area   | Height | Area % |
|------|---------|------|-------|--------|--------|--------|
| 1    | 13.153  | BB   | 0.3230| 1.13799e4 | 527.50494 | 49.6336 |
| 2    | 20.518  | BB   | 0.4618| 1.15479e4 | 378.99115 | 50.3664 |
Figure S51. HPLC of (S)-2q, related to Table 2.

| #  | RetTime | Type | Width | Area   | Height | Area %   |
|----|---------|------|-------|--------|--------|----------|
| 1  | 13.404  | BB   | 0.3276| 265.64832 | 12.16198 | 1.1817   |
| 2  | 20.506  | BB   | 0.4796| 2.22140e4 | 702.40350 | 98.8183  |

Figure S52. HPLC of Rac-2r, related to Table 2.

| #  | RetTime | Type | Width | Area   | Height | Area %   |
|----|---------|------|-------|--------|--------|----------|
| 1  | 11.637  | BB   | 0.2928| 3.10593e4 | 1594.40588 | 49.3227  |
| 2  | 18.454  | BB   | 0.4230| 3.19124e4 | 1149.20239 | 50.6773  |
Figure S53. HPLC of (S)-2r, related to Table 2.

| Peak | RetTime | Type | Width [min] | Area [mAU] | Height [μmAU] | Area % |
|------|---------|------|-------------|------------|---------------|------|
| 1    | 11.873  | MM   | 0.2958      | 463.04886  | 26.09230      | 1.2381 |
| 2    | 18.494  | BB   | 0.4325      | 3.69373e+4 | 1303.53076    | 98.7619 |

Figure S54. HPLC of Rac-2s, related to Table 2.

| Peak | RetTime | Type | Width [min] | Area [mAU] | Height [μmAU] | Area % |
|------|---------|------|-------------|------------|---------------|------|
| 1    | 16.617  | VB   | 0.4104      | 3691.99683 | 133.33612     | 49.9703 |
| 2    | 29.907  | BB   | 0.6465      | 3696.38452 | 86.59996      | 50.0297 |
Figure S55. HPLC of (S)-2s, related to Table 2.

| Peak RetTime Type | Width | Area     | Height | Area     |
|-------------------|-------|----------|--------|----------|
| # | [min] | [min] | mAU    | *s | [mAU]     | %  |
| 1 | 16.898 | MM   | 0.4593 | 72.46369 | 2.62971 | 98.7519 |
| 2 | 29.865 | BB   | 0.6595 | 5733.41797 | 132.40321 | 98.7519 |

Figure S56. HPLC of Rac-2t, related to Table 2.

| Peak RetTime Type | Width | Area     | Height | Area     |
|-------------------|-------|----------|--------|----------|
| # | [min] | [min] | mAU    | *s | [mAU]     | %  |
| 1 | 26.260 | BB   | 0.7740 | 8104.12500 | 154.03474 | 49.9894 |
| 2 | 31.877 | BB   | 0.8117 | 8107.55762 | 147.49445 | 50.0106 |
Figure S57. HPLC of (S)-2t, related to Table 2.

| Peak RetTime | Type | Width | Area  | Height | Area % |
|--------------|------|-------|-------|--------|--------|
| # | [min] | [min] | mAU | *s  | [mAU ] | % |
| 1 | 27.531 | BB | 0.6606 | 127.94970 | 2.43108 | 1.1436 |
| 2 | 32.241 | BB | 0.8437 | 1.10603e4 | 192.90025 | 98.8564 |

Figure S58. HPLC of Rac-2u, related to Table 2.

| Peak RetTime | Type | Width | Area  | Height | Area % |
|--------------|------|-------|-------|--------|--------|
| # | [min] | [min] | mAU | *s  | [mAU ] | % |
| 1 | 14.589 | BB | 0.3118 | 1572.08752 | 76.73154 | 50.2386 |
| 2 | 29.251 | BB | 0.5738 | 1557.15442 | 41.85207 | 49.7614 |
Figure S59. HPLC of (S)-2u, related to Table 2.

Figure S60. HPLC of Rac-2v, related to Table 2.
Figure S61. HPLC of (S)-2v, related to Table 2.

| Peak | RetTime | Type | Width [min] | Area | Height [mAU *s] | Area [mAU] | %     |
|------|---------|------|-------------|------|-----------------|----------------|-------|
| 1    | 14.749  | BB   | 0.3081      | 149.78223 | 7.38171         | 1.1152       | 98.8848 |
| 2    | 31.365  | BB   | 0.6672      | 1.32815e4 | 305.58240       | 98.8848      | 98.8848 |

Figure S62. HPLC of Rac-2w, related to Table 2.

| Peak | RetTime | Type | Width [min] | Area | Height [mAU *s] | Area [mAU] | %     |
|------|---------|------|-------------|------|-----------------|----------------|-------|
| 1    | 15.444  | BB   | 0.3190      | 4121.93701 | 196.51964      | 49.7478       | 50.2522 |
| 2    | 33.662  | BB   | 0.6729      | 4163.72314 | 95.27980       | 50.2522       | 50.2522 |

-S87-
Figure S6. HPLC of (S)-2w, related to Table 2.

Figure S6. HPLC of Rac-2x, related to Table 2.
Figure S65. HPLC of (S)-2x, related to Table 2.

Figure S66. HPLC of Rac-2y, related to Table 2.
Figure S67. HPLC of (S)-2y, related to Table 2.

Figure S68. HPLC of (S)-2y, related to Table 2.
Figure S69. HPLC of (S)-2y, related to Table 2.

| Peak | RetTime | Type | Width | Area    | Height | Area    | %   |
|------|---------|------|-------|---------|--------|---------|-----|
| 1    | 11.630  | BB   | 0.2570| 92.18953| 5.49088| 0.9880  |
| 2    | 24.860  | BB   | 0.5487| 9238.61914| 258.08063| 99.0120|

Figure S70. HPLC of Rac-2z, related to Table 2.

| Peak | RetTime | Type | Width | Area    | Height | Area    | %   |
|------|---------|------|-------|---------|--------|---------|-----|
| 1    | 14.429  | BB   | 0.3207| 443.24789| 21.10505| 50.0349|
| 2    | 26.599  | BB   | 0.5786| 442.62976| 11.69038| 49.9651|
Figure S71. HPLC of (S)-2z, related to Table 2.

| Peak | RetTime | Type | Width | Area    | Height | Area  | %    |
|------|---------|------|-------|---------|--------|-------|------|
| #    | [min]   |      | [min] | mAU     | *s     | [mAU] |      |
| 1    | 14.296  | MM   | 0.1764| 496.04568| 46.85562| 0.8510|      |
| 2    | 25.627  | BB   | 0.6423| 5.77949e4| 1357.44946| 99.1490|      |

Figure S72. HPLC of Rac-2aa, related to Table 2.

| Peak | RetTime | Type | Width | Area    | Height | Area  | %    |
|------|---------|------|-------|---------|--------|-------|------|
| #    | [min]   |      | [min] | mAU     | *s     | [mAU] |      |
| 1    | 12.071  | BV   | 0.2808| 1.14189e4| 602.43781| 49.7547|      |
| 2    | 18.398  | BV   | 0.3866| 1.15315e4| 451.83405| 50.2453|      |
Figure S73. HPLC of (S)-2aa, related to Table 2.

| Peak # | RetTime (min) | Type | Width (min) | Area (mAU) | Height (s) | Area (mAU) | % |
|--------|---------------|------|-------------|------------|------------|------------|---|
| 1      | 12.217        | BB   | 0.2822      | 50.22261   | 2.66774    | 0.7430     |   |
| 2      | 18.466        | BB   | 0.3784      | 6709.56104 | 268.92368  | 99.2570    |   |

Figure S74. HPLC of Rac-2ab, related to Table 2.

| Peak # | RetTime (min) | Type | Width (min) | Area (mAU) | Height (s) | Area (mAU) | %  |
|--------|---------------|------|-------------|------------|------------|------------|---|
| 1      | 18.115        | BB   | 0.4351      | 1.46261e4  | 501.21518  | 49.9847    |   |
| 2      | 21.783        | BB   | 0.5075      | 1.46351e4  | 433.38348  | 50.0153    |   |
**Figure S75.** HPLC of (S)-2ab, related to Table 2.

| Peak | RetTime | Type | Width | Area    | Height | Area    | %  |
|------|---------|------|-------|---------|--------|---------|----|
| 1    | 18.577  | BB   | 0.4162| 83.20202| 3.04637| 0.6770  |    |
| 2    | 21.868  | BB   | 0.5042| 1.22065e4 | 364.56906 | 99.3230 |    |

**Figure S76.** HPLC of Rac-2ac, related to Table 2.

| Peak | RetTime | Type | Width | Area    | Height | Area    | %  |
|------|---------|------|-------|---------|--------|---------|----|
| 1    | 4.632   | BV   | 0.1050| 1.78426e4 | 2641.08325 | 49.1888 |    |
| 2    | 5.666   | BV   | 0.1181| 1.84312e4 | 2416.49292 | 50.8112 |    |
Figure S7. HPLC of (S)-2ac, related to Table 2.

Figure S78. HPLC of Rac-2ad, related to Table 2.
Figure S79. HPLC of (S)-2ad, related to Table 2.

Figure S80. HPLC of Rac-2ae, related to Table 2.
Figure S81. HPLC of (S)-2ae, related to Table 2.

| Peak | RetTime | Type | Width | Area    | Height | Area    | %     |
|------|---------|------|-------|---------|--------|---------|-------|
| 1    | 16.321  | BB   | 0.3653| 227.38745| 9.44409| 1.1354  |       |
| 2    | 26.542  | BB   | 0.6357| 1.98004e4| 465.82135| 98.8646 |       |

Figure S82. HPLC of Rac-2af, related to Table 2.

| Peak | RetTime | Type | Width | Area    | Height | Area    | %     |
|------|---------|------|-------|---------|--------|---------|-------|
| 1    | 17.844  | BB   | 0.3968| 1.00765e4| 385.40063| 49.5704 |       |
| 2    | 32.916  | BB   | 0.7245| 1.02511e4| 215.25081| 50.4296 |       |
Figure S83. HPLC of (S)-2af, related to Table 2.

Figure S84. HPLC of Rac-2ag, related to Table 2.
Figure S85. HPLC of (S)-2ag, related to Table 2.

Figure S86. HPLC of Rac-2ah, related to Table 2.
Figure S87. HPLC of (S)-2ah, related to Table 2.

Figure S88. HPLC of Rac-4, related to Figure 4.
Figure S89. HPLC of (S)-4, related to Figure 4.

Figure S90. HPLC of Rac-6a, related to Figure 6.
Figure S91. HPLC of (S)-6a, related to Figure 6.

Figure S92. HPLC of Rac-6b, related to Figure 6.
Figure S93. HPLC of (S)-6b, related to Figure 6.

Figure S94. HPLC of Rac-6c, related to Figure 6.
**Figure S95.** HPLC of (S)-6c, related to Figure 6.

**Figure S96.** HPLC of Rac-6d, related to Figure 6.
Figure S9. HPLC of (S)-6d, related to Figure 6.
12. NMR Spectra of M-1, M-2, M-3, M-4, (S)-E, (S)-F, (S)-G, 1a-ah, 2a-ah, 3, 4, 5 and 6

Figure S98. $^1$H NMR of Rac-M-1E, related to Figure 2.

Figure S99. $^{13}$C NMR of Rac-M-1E, related to Figure 2.
Figure S100. $^{19}F$ NMR of Rac-M-1E, related to Figure 2.

Figure S101. $^1H$ NMR of Rac-M-2E, related to Figure 2.
Figure S102. $^{13}$C NMR of Rac-M-2E, related to Figure 2.

Figure S103. $^{19}$F NMR of Rac-M-2E, related to Figure 2.
Figure S104. $^{31}\text{P}$ NMR of Rac-M-2E, related to Figure 2.

Figure S105. $^1\text{H}$ NMR of Rac-M-3E, related to Figure 2.
Figure S106. $^{13}$C NMR of Rac-M-3E, related to Figure 2.

Figure S107. $^{19}$F NMR of Rac-M-3E, related to Figure 2.
Figure S10. $^{31}$P NMR of Rac-M-3E, related to Figure 2.

Figure S109. $^1$H NMR of Rac-M-4E, related to Figure 2.
Figure S110. $^{13}$C NMR of Rac-M-4E, related to Figure 2.

Figure S111. $^{31}$P NMR of Rac-M-4E, related to Figure 2.
Figure S112. $^1$H NMR of (S)-E, related to Figure 2.

Figure S113. $^{13}$C NMR of (S)-E, related to Figure 2.
Figure S114. $^{31}$P NMR of (S)-E, related to Figure 2.

Figure S115. $^1$H NMR of Rac-M-1F, related to Figure 2.
Figure S116. $^{13}$C NMR of Rac-M-1F, related to Figure 2.

Figure S117. $^{19}$F NMR of Rac-M-1F, related to Figure 2.
Figure S118. $^1$H NMR of Rac-M-2F, related to Figure 2.

Figure S119. $^{13}$C NMR of Rac-M-2F, related to Figure 2.
Figure S120. $^{19}$F NMR of Rac-M-2F, related to Figure 2.

Figure S121. $^{31}$P NMR of Rac-M-2F, related to Figure 2.
Figure S122. $^1$H NMR of Rac-M-3F, related to Figure 2.

Figure S123. $^{13}$C NMR of Rac-M-3F, related to Figure 2.
Figure S124. $^{19}$F NMR of Rac-M-3F, related to Figure 2.

Figure S125. $^{31}$P NMR of Rac-M-3F, related to Figure 2.
Figure S12. $^1$H NMR of Rac-M-4F, related to Figure 2.

Figure S12. $^{13}$C NMR of Rac-M-4F, related to Figure 2.
Figure S12. $^{31}$P NMR of Rac-M-4F, related to Figure 2.

Figure S129. $^1$H NMR of (S)-F, related to Figure 2.
Figure S130. $^{13}$C NMR of (S)-F, related to Figure 2.

Figure S131. $^{31}$P NMR of (S)-F, related to Figure 2.
Figure S132. $^1$H NMR of Rac-M-1G, related to Figure 2.

Figure S133. $^{13}$C NMR of Rac-M-1G, related to Figure 2.
Figure S134. $^{19}$F NMR of Rac-M-1G, related to Figure 2.

Figure S135. $^1$H NMR of Rac-M-2G, related to Figure 2.
Figure S13. $^{13}$C NMR of Rac-M-2G, related to Figure 2.

Figure S137. $^{19}$F NMR of Rac-M-2G, related to Figure 2.
Figure S138. $^{31}$P NMR of Rac-M-2G, related to Figure 2.

Figure S139. $^1$H NMR of Rac-M-3G, related to Figure 2.
Figure S140. $^{13}$C NMR of Rac-M-3G, related to Figure 2.

Figure S141. $^{19}$F NMR of Rac-M-3G, related to Figure 2.
Figure S142. $^{31}$H NMR of Rac-M-3G, related to Figure 2.

Figure S143. $^1$H NMR of Rac-M-4G, related to Figure 2.
Figure S144. $^{13}$C NMR of Rac-M-4G, related to Figure 2.

Figure S145. $^{31}$P NMR of Rac-M-4G, related to Figure 2.
Figure S146. $^1$H NMR of (S)-G, related to Figure 2.

Figure S147. $^{13}$C NMR of (S)-G, related to Figure 2.
Figure S148. $^{31}$P NMR of (S)-G, related to Figure 2.

Figure S149. $^1$H NMR of 1a, related to Table 2.
Figure S150. $^{13}$C NMR of 1a, related to Table 2.

Figure S151. $^{13}$C NMR of 1b, related to Table 2.
Figure S152. $^{13}$C NMR of 1b, related to Table 2.

Figure S153. $^1$H NMR of 1c, related to Table 2.
Figure S154. $^{13}$C NMR of 1c, related to Table 2.

Figure S155. $^1$H NMR of 1d, related to Table 2.
Figure S15. $^{13}$C NMR of 1d, related to Table 2.

Figure S15. $^1$H NMR of 1e, related to Table 2.
Figure S158. $^{13}$C NMR of 1e, related to Table 2.

Figure S159. $^1$H NMR of 1f, related to Table 2.
Figure S160. $^{13}$C NMR of 1f, related to Table 2.

Figure S161. $^1$H NMR of 1g, related to Table 2.
Figure S162. $^{13}$C NMR of 1g, related to Table 2.

Figure S163. $^1$H NMR of 1h, related to Table 2.
Figure S164. $^{13}$C NMR of 1h, related to Table 2.

Figure S165. $^1$H NMR of 1i, related to Table 2.
Figure S16. $^{13}$C NMR of 1i, related to Table 2.

Figure S167. $^1$H NMR of 1j, related to Table 2.
Figure S168. $^{13}$C NMR of 1j, related to Table 2.

Figure S169. $^1$H NMR of 1k, related to Table 2.
Figure S170. $^{13}$C NMR of 1k, related to Table 2.

Figure S171. $^1$H NMR of 1l, related to Table 2.
Figure S172. $^{13}$C NMR of 1l, related to Table 2.

Figure S173. $^1$H NMR of 1m, related to Table 2.
Figure S174. $^{13}$C NMR of 1m, related to Table 2.

Figure S175. $^1$H NMR of 1n, related to Table 2.
Figure S176. $^{13}\text{C}$ NMR of 1n, related to Table 2.

Figure S177. $^1\text{H}$ NMR of 1o, related to Table 2.
Figure S178. $^{13}$C NMR of 1o, related to Table 2.

Figure S179. $^1$H NMR of 1p, related to Table 2.
Figure S180. $^{13}$C NMR of 1p, related to Table 2.

Figure S181. $^1$H NMR of 1q, related to Table 2.
Figure S182. $^{13}$C NMR of 1q, related to Table 2.

Figure S183. $^1$H NMR of 1r, related to Table 2.
Figure S184. $^{13}$C NMR of 1r, related to Table 2.

Figure S185. $^1$H NMR of 1s, related to Table 2.
Figure S186. $^{13}$C NMR of 1s, related to Table 2.

Figure S187. $^1$H NMR of 1t, related to Table 2.
Figure S188. $^{13}$C NMR of 1t, related to Table 2.

Figure S189. $^1$H NMR of 1u, related to Table 2.
Figure S190. $^{13}$C NMR of 1u, related to Table 2.

Figure S191. $^{19}$F NMR of 1u, related to Table 2.
Figure S192. $^1$H NMR of $1v$, related to Table 2.

Figure S193. $^{13}$C NMR of $1v$, related to Table 2.
Figure S194. $^1$H NMR of 1w, related to Table 2.

Figure S195. $^{13}$C NMR of 1w, related to Table 2.
Figure S16. $^1$H NMR of 1x, related to Table 2.

Figure S17. $^{13}$C NMR of 1x, related to Table 2.
Figure S198. $^{19}$F NMR of 1x, related to Table 2.

Figure S199. $^1$H NMR of 1y, related to Table 2.
Figure S200. $^{13}$C NMR of 1y, related to Table 2.

Figure S201. $^1$H NMR of 1z, related to Table 2.
Figure S202. $^{13}$C NMR of 1z, related to Table 2.

Figure S203. $^1$H NMR of 1aa, related to Table 2.
Figure S204. $^{13}$C NMR of 1aa, related to Table 2.

Figure S205. $^1$H NMR of 1ab, related to Table 2.
Figure S206. $^{13}$C NMR of 1ab, related to Table 2.

Figure S207. $^1$H NMR of 1ac, related to Table 2.
Figure S208. $^{13}$C NMR of 1ac, related to Table 2.

Figure S209. $^1$H NMR of 1ad, related to Table 2.
Figure S210. $^{13}$C NMR of 1ad, related to Table 2.

Figure S211. $^1$H NMR of 1ae, related to Table 2.
Figure S212. $^{13}$C NMR of 1ae, related to Table 2.

Figure S213. $^{19}$F NMR of 1ae, related to Table 2.
Figure S214. $^1$H NMR of 1af, related to Table 2.

Figure S215. $^{13}$C NMR of 1af, related to Table 2.
Figure S216. $^1$H NMR of 1ag, related to Table 2.

Figure S217. $^{13}$C NMR of 1ag, related to Table 2.
Figure S218. $^{19}$F NMR of 1ag, related to Table 2.

Figure S219. $^1$H NMR of 1ah, related to Table 2.
Figure S220. $^{13}$C NMR of 1ah, related to Table 2.
Figure S221. $^1$H NMR of 2a, related to Table 2.

Figure S222. $^{13}$C NMR of 2a, related to Table 2.
Figure S223. $^1$H NMR of 2b, related to Table 2.

Figure S224. $^{13}$C NMR of 2b, related to Table 2.
Figure S225. $^1$H NMR of 2c, related to Table 2.

Figure S226. $^{13}$C NMR of 2c, related to Table 2.
Figure S227. $^1$H NMR of 2d, related to Table 2.

Figure S228. $^{13}$C NMR of 2d, related to Table 2.
Figure S229. $^1$H NMR of 2e, related to Table 2.

Figure S230. $^{13}$C NMR of 2e, related to Table 2.
Figure S231. $^1$H NMR of 2f, related to Table 2.

Figure S232. $^{13}$C NMR of 2f, related to Table 2.
Figure S233. $^1$H NMR of 2g, related to Table 2.

Figure S234. $^{13}$C NMR of 2g, related to Table 2.
Figure S235. $^1$H NMR of 2h, related to Table 2.

Figure S236. $^{13}$C NMR of 2h, related to Table 2.
Figure S237. $^1$H NMR of 2i, related to Table 2.

Figure S238. $^{13}$C NMR of 2i, related to Table 2.
Figure S239. $^1$H NMR of 2j, related to Table 2.

Figure S240. $^{13}$C NMR of 2j, related to Table 2.
Figure S241. $^1$H NMR of 2k, related to Table 2.

Figure S242. $^{13}$C NMR of 2k, related to Table 2.
Figure S243. $^1$H NMR of 2l, related to Table 2.

Figure S244. $^{13}$C NMR of 2l, related to Table 2.
Figure S245. $^1$H NMR of 2m, related to Table 2.

Figure S246. $^{13}$C NMR of 2m, related to Table 2.
Figure S247. $^1$H NMR of 2n, related to Table 2.

Figure S248. $^{13}$C NMR of 2n, related to Table 2.
Figure S249. $^1$H NMR of 2o, related to Table 2.

Figure S250. $^{13}$C NMR of 2o, related to Table 2.
Figure S251. $^1$H NMR of 2p, related to Table 2.

Figure S252. $^{13}$C NMR of 2p, related to Table 2.
Figure S253. $^1$H NMR of 2q, related to Table 2.

Figure S254. $^{13}$C NMR of 2q, related to Table 2.
Figure S255. $^1$H NMR of 2r, related to Table 2.

Figure S256. $^{13}$C NMR of 2r, related to Table 2.
Figure S257. $^1$H NMR of 2s, related to Table 2.

Figure S258. $^{13}$C NMR of 2s, related to Table 2.
Figure S259. $^1$H NMR of 2t, related to Table 2.

Figure S260. $^{13}$C NMR of 2t, related to Table 2.
Figure S261. $^1$H NMR of 2u, related to Table 2.

Figure S262. $^{13}$C NMR of 2u, related to Table 2.
Figure S263. $^{19}$F NMR of 2u, related to Table 2.

Figure S264. $^1$H NMR of 2v, related to Table 2.
Figure S265. $^{13}$C NMR of 2v, related to Table 2.

Figure S266. $^1$H NMR of 2w, related to Table 2.
Figure S267. $^{13}$C NMR of 2w, related to Table 2.

Figure S268. $^1$H NMR of 2x, related to Table 2.
Figure S269. $^{13}$C NMR of 2x, related to Table 2.

Figure S270. $^{19}$F NMR of 2x, related to Table 2.
Figure S271. $^1$H NMR of 2y, related to Table 2.

Figure S272. $^{13}$C NMR of 2y, related to Table 2.
Figure S273. $^1$H NMR of 2z, related to Table 2.

Figure S274. $^{13}$C NMR of 2z, related to Table 2.
Figure S275. $^1$H NMR of 2aa, related to Table 2.

Figure S276. $^{13}$C NMR of 2aa, related to Table 2.
Figure S277. $^1$H NMR of 2ab, related to Table 2.

Figure S278. $^{13}$C NMR of 2ab, related to Table 2.
Figure S279. $^1$H NMR of 2ac, related to Table 2.

Figure S280. $^{13}$C NMR of 2ac, related to Table 2.
Figure S281. $^1$H NMR of 2ad, related to Table 2.

Figure S282. $^{13}$C NMR of 2ad, related to Table 2.
Figure S283. $^1$H NMR of 2ae, related to Table 2.

Figure S284. $^{13}$C NMR of 2ae, related to Table 2.
Figure S285. $^{19}$F NMR of 2ae, related to Table 2.

Figure S286. $^1$H NMR of 2af, related to Table 2.
Figure S287. $^{13}$C NMR of 2af, related to Table 2.

Figure S288. $^1$H NMR of 2ag, related to Table 2.
Figure S289. $^{13}$C NMR of 2ag, related to Table 2.

Figure S290. $^{19}$F NMR of 2ag, related to Table 2.
Figure S291. $^1$H NMR of 2ah, related to Table 2.

Figure S292. $^{13}$C NMR of 2ah, related to Table 2.
Figure S293. $^1$H NMR of 3, related to Figure 4.

Figure S294. $^{13}$C NMR of 3, related to Figure 4.
Figure S295. $^1$H NMR of 4, related to Figure 4.

Figure S296. $^{13}$C NMR of 4, related to Figure 4.
Figure S297. $^1$H NMR of 5a, related to Figure 6.

Figure S298. $^{13}$C NMR of 5a, related to Figure 6.
Figure S299. $^1$H NMR of 5b, related to Figure 6.

Figure S300. $^{13}$C NMR of 5b, related to Figure 6.
Figure S301. $^1$H NMR of 5c, related to Figure 6.

Figure S302. $^{13}$C NMR of 5c, related to Figure 6.
Figure S303. $^1$H NMR of 5d, related to Figure 6.

Figure S304. $^{13}$C NMR of 5d, related to Figure 6.
Figure S305. $^1$H NMR of 6a, related to Figure 6.

Figure S306. $^{13}$C NMR of 6a, related to Figure 6.
Figure S307. $^1$H NMR of 6b, related to Figure 6.

Figure S308. $^{13}$C NMR of 6b, related to Figure 6.
Figure S309. $^1$H NMR of 6c, related to Figure 6.

Figure S310. $^{13}$C NMR of 6c, related to Figure 6.
Figure S311. $^1$H NMR of 6d, related to Figure 6.

Figure S312. $^{13}$C NMR of 6d, related to Figure 6.