Atroposelective Synthesis of Biaryl Diamines and Amino Alcohols via Chiral Phosphoric Acid Catalyzed para-Aminations of Anilines and Phenols

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HIGHLIGHTS
Versatile methods for asymmetric synthesis of biaryl diamines and amino alcohols
Atroposelective para-aminations of biaryl anilines and phenols
Kinetic resolution of racemic biaryl anilines
Facile transformations of chiral products

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Atroposelective Synthesis of Biaryl Diamines and Amino Alcohols via Chiral Phosphoric Acid Catalyzed para-Aminations of Anilines and Phenols

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SUMMARY
A versatile method for atroposelective synthesis of chiral biaryl diamines and amino alcohols has been developed via para-amination of anilines and phenols with azodicarboxylates enabled by chiral phosphoric acid catalysis. Meanwhile, highly efficient kinetic resolution of the racemic biaryl anilines has also been realized through these reactions, giving selectivity factor up to 246. The gram-scale reaction and facile derivatizations of the chiral products well demonstrate the potential of these reactions in the development of novel chiral ligands and catalysts.

INTRODUCTION
Biaryl compounds possessing axial chirality are ubiquitous among biologically active natural products and pharmaceuticals and have been extensively exploited as chiral ligands/catalysts in asymmetric catalysis. To this end, their highly efficient and asymmetric catalytic synthesis has drawn increasing research interests, and various elegant methods have been developed in the last two decades. However, in contrast to the numerous well-developed methods for asymmetric synthesis of BINOL-type biaryl diols and amino alcohols, methods for their asymmetric catalytic synthesis remain elusive. One representative chiral biaryl diamine, 1,1'-Binaphthyl-2,2'-diamine (BINAM), has been widely exploited in the development of chiral ligands and organocatalysts. However, only limited asymmetric catalytic methods have been developed for its enantioselective synthesis, including asymmetric [3,3]-sigmatropic rearrangement (De et al., 2013; Li et al., 2013) and kinetic resolution (Cheng et al., 2014). 2-Amino-2'-hydroxy-1,1'-binaphthyl (NOBIN) (Smrcina et al., 1992, 1993), which is considered as the hybrid analogue of BINOL and BINAM, represents one type of privileged biaryl amino alcohol scaffold for constructing chiral ligands (Galzerano et al., 2009; Tan et al., 2011; Telfer and Kuroda, 2003; Uraguchi et al., 2009; Wang et al., 2005). However, methods for their asymmetric catalytic synthesis was also limited to kinetic resolutions (Lu et al., 2014; Shirakawa et al., 2013) and enantioselective direct arylation of 2-naphthylamines (Chen et al., 2017). Although the aforementioned elegant methods have provided access to enantioenriched biaryl diamines and amino alcohols, respectively, versatile methods for their asymmetric synthesis remain elusive. Recently, Tan and co-workers reported the asymmetric synthesis of BINAM- and NOBIN-type biaryl diamines and amino alcohols with azodicarboxylates by chiral phosphoric acid catalysis, constructing N-containing chiral quaternary centers. Nevertheless, most of these methods are still limited to ortho-aminations.
of naphthols and naphthylamines; asymmetric reactions involving para-aminations of common anilines and phenols (Leblanc and Boudreault, 1995; Tang et al., 2017; Yadav et al., 2002; Zaltsgendler et al., 1993) are still elusive. Herein, we report a versatile protocol for atroposelective synthesis of biaryl diamines and amino alcohols via para-aminations of anilines and phenols (Diener et al., 2015; Gustafson et al., 2010; Miyaji et al., 2015, 2017; Mori et al., 2013a, b) with azodicarboxylates via chiral phosphoric acid catalysis (Akiyama, 2007; Akiyama et al., 2004; Akiyama and Mori, 2015; Li and Song, 2018; Parmar et al., 2014; Terada, 2010; Uraguchi and Terada, 2004) (Scheme 1C).

**RESULTS AND DISCUSSION**

**Optimization of Reaction Conditions**

Our study commenced with using biaryl aniline 1a as substrate and dibenzyl azodicarboxylate 2 as amination reagent under the catalysis of CPA catalysts (Table 1). Interestingly, in the presence of CPA catalyst A1 (10 mol%), the amination reaction between 1a and azodicarboxylate 2 (1.1 equiv.) in toluene (with 5 Å molecular sieves) proceeded smoothly at ambient temperature to afford the triazane 4a (Egger et al., 1983; Tang et al., 2017) as the major product (60% yield), whereas the desired para-amination product 3a was obtained only in 13% yield with 47% enantiomeric excess (ee) (entry 1). Next, a variety of BINOL-derived chiral phosphoric acid catalysts were examined (entries 2–7), and encouragingly the TCYP catalyst (cat A7) provided the desired product 3a in 80% yield with 98% ee, with the undesired N-amination product 4a and diamination product 5a isolated in <10% yield (entry 7). Next, a range of solvents were also investigated (entries 8–10), and CHCl₃ turned out to be the optimal one, in which the desired product 3a was produced in 91% yield with 98% ee (entry 9). The role of the molecular sieves was also demonstrated; in the absence of 5 Å molecular sieves, the axially chiral biaryl 3a was obtained only in 66% yield (entry 11).
The reduction of catalyst loading was also studied; however, decreasing the catalyst loading to 5 mol % at room temperature led to a diminished yield (entry 12). Interestingly, conducting this reaction with 5 mol % catalyst at 40°C gave product 3a in 87% yield with the same ee (entry 13). The axially chiral biaryl product 3a has high configurational stability, whose ee was retained after storing on bench for more than 2 months at ambient temperature and heating at 100°C in toluene for 36 h.

### Substrate Scope

With the optimal conditions in hand, we next sought to explore the compatibility of substrate scope of this reaction (Scheme 2). A range of substituted 2-naphthylamine moieties could be well tolerated in the biaryl aniline substrates, affording the axially chiral amination products with high enantioselectivities (3b–3d). A series of substitutions at the ortho- and meta-positions of the aniline moieties in substrates was also compatible with the optimal conditions (3f–3h). It is worth mentioning that the direct amination of substrates 1g and 1h afforded products as inseparable diastereomer mixtures due to the presence of extra...
C-N axial chirality; therefore, these products were directly converted into –NH₂-containing product 3g and 3h by catalytic hydrogenations. The absolute configurations of the axially chiral products 3 were assigned as (S) by analogy to product 3g, whose structure was unambiguously confirmed by X-ray crystallography (see Supplemental Information). The 2-naphthylamine scaffold in the substrates could also be switched to 3-substituted anilines (3i-3k), which also produced the biaryl amination products with high enantioselectivities under the standard conditions. Switching the N-protecting group from -Boc to –Cbz was also well...
 tolerated with the optimal conditions, which produced product 3l with excellent enantioselectivity. However, using the N-protecting group-free biaryl aniline as substrates provided the triazane product as the major product.

With the excellent performance of constructing chiral biaryl diamines via asymmetric para-amination reactions, we envisioned that these reactions could also be adopted in the kinetic resolution of racemic biaryl anilines. Thus, a variety of 2-substituted biaryl anilines possessing axial chirality were synthesized and their kinetic resolution via para-amination reactions with azodicarboxylate 2 (0.6 equiv.) was investigated (Scheme 3). Under the catalysis of (R)-TRIP catalyst (cat A6, 10 mol %) in DCM at room temperature, the kinetic resolutions of these substrates proceeded with high efficiencies to afford both recovered aniline substrates and para-amination products with high enantioselectivities (with s factor up to 246, 3m-3p).

The absolute configurations of the axially chiral products and recovered starting materials were assigned by analogy to recovered 1m, whose structure was unambiguously confirmed by X-ray crystallography (see Supplemental Information).

To achieve enantioselective synthesis of biaryl amino alcohols, the 2-naphthylamine moieties in the substrates were switched to 2-naphthol moieties. However, the amination reactions of the corresponding biaryl anilines 6 provided only N-amination triazane products 7 but not para-amination products 7p. Interestingly, the desired biaryl amino alcohols were obtained while phenols 6 were employed as electron-rich arenes instead of anilines. Under the catalysis of (R)-C8-TRIP catalyst (cat A8) in CHCl3 at ambient temperature, the para-amination of biaryl phenol 6a with azodicarboxylate 2 afforded the biaryl amino alcohol 7a in 56% yield with 86% ee (for further details, see Table S1 in the Supplemental Information). Switching the protecting group from O-Me to O-MOM was compatible with the optimal conditions, providing the axially chiral amination product with comparable stereoselectivity (7b). The substrate scope for the 2-naphthol moieties in the substrates were explored under the standard conditions, which showed that a range of substituted 2-naphthol scaffolds (with various substitutions at the 4-, 6-, and 7-positions) could be accommodated, affording biaryl amino alcohols in good yields and high enantioselectivities (7c-7g).

**Mechanistic Discussion**

To gain more insight into the reaction mechanism, several control experiments were performed (Scheme 5). The amination reaction of N-Me biaryl aniline substrate 1q proceeded smoothly under
the standard conditions to give the desired para-amination product \(3q\) in 56% yield with 92% ee. However, applying the same conditions on \(N,N\)-dimethyl aniline substrate \(1r\) provided only the para-amination product \(3r\) in 25% yield with 5% ee (with the \(N\)-amination product as the major by-product), which indicated that the potential hydrogen bonding between CPA catalyst and the aniline \(N\)-H group played a key role in controlling both chemoselectivity and stereoselectivity in this reaction (Scheme 5A).Interestingly, subjection of the \(N\)-amination triazane product \(4a\) into the optimal conditions without adding azodicarboxylate \(2\) also gave the para-amination product \(3a\) in 58% yield with 98% ee after 16 h, with the aniline substrate \(1a\) isolated in 28% yield, which suggested the reversible nature of the triazane formation step (Scheme 5B). Based on the above-mentioned experimental study and previous work (Bai et al., 2019; Drouet et al., 2011; Dumoulin et al., 2015), a plausible reaction mechanism is proposed, in which bifunctional activation (Parmar et al., 2014; Simón and Goodman, 2008; Yamanaka et al., 2007) of both the aniline substrate and azodicarboxylate via dual hydrogen-bonding interaction with the CPA catalyst is postulated (Scheme 5C). Under the catalysis of CPA catalyst, there are two alternative reaction pathways between aniline substrates and azodicarboxylates: (1) direct nucleophilic addition of the –NH\(_2\) group to the azodicarboxylate facilitated the generation of the triazane products (path a), which is also reversible under these conditions; and (2) the para-selective amination of aniline substrates would give the dearomatized addition product \(\text{INT A}\), possessing a chiral center (path b). On subsequent aromatization, \(\text{INT A}\) underwent the central-to-axial chirality transfer (Qi et al., 2017; Raut et al., 2017) to provide the axial biaryl diamine products.

Transformations of Products

To evaluate the practicability of these reactions, a gram-scale amination reaction of \(1a\) was performed, which provided the axially chiral biaryl \(3a\) in 70% yield with 99% ee, with reduced catalyst loading (2 mol %, Scheme 6A). The derivatizations of the chiral products were also studied to prove the value of these reactions. By means of the Sandmeyer reaction, the directing –NH\(_2\) group was transformed into...
an iodide group via diazotization of 3a with NaNO₂ followed by treatment with NaI to afford 8a, which could be further employed in Suzuki coupling with phenylboronic acid to give product 9a in 81% yield (Scheme 6B). Notably, the ee of chiral biaryl product was retained through these steps of transformations, including the Suzuki coupling step (105 °C, overnight), again demonstrating the high configurational stability of these atropisomeric products. The catalytic hydrogenation of 7a using Pd/C as catalyst facilely reduced the substituted hydrazine moiety to give the biaryl product 10a in 90% yield (Scheme 6C). A two-step procedure of catalytic hydrogenation followed by deprotection of the N-Boc group converted chiral product 3n into biaryl diamine 11n in 82% yield, without erosion of the enantioselectivity (Scheme 6D). Finally, a primary-amine/thiourea bifunctional catalyst 13a was straightforwardly synthesized from the chiral product 3a within 4 steps, with complete retention of the enantiomeric purity (Scheme 6E). The application of this bifunctional catalyst was preliminarily demonstrated in an asymmetric Michael reaction of 3-methyl oxindole 14 with cinnamaldehyde 15 (Galzerano et al., 2009), which readily provided the product 16 (after reduction) in 53% yield with 6:1 d.r. and 73% ee without optimization (Scheme 6F).

Conclusion
We have disclosed a versatile method for asymmetric synthesis of biaryl diamines and amino alcohols, which was realized through chiral phosphoric acid catalyzed enantioselective para-aminations of biaryl amines and phenols with azodicarboxylates. These reactions are also well employed in the highly efficient kinetic resolution of racemic biaryl amines, which give s factor up to 246. Preliminary mechanistic studies were performed to elucidate the reaction mechanism, in which a dual hydrogen-bonding activation mode was proposed in the key chirality induction step. The facile transformations of chiral products into atropisomeric biaryl diamine
Scheme 6. Gram-Scale Synthesis of 3a and Derivatizations of the Chiral Products

Gram-scale preparation of 3a:

\[ \text{1a, 1002 mg} \]

\[ \text{2} \]

\[ \text{(R)-cat A7 (2 mol\%)} \]

\[ \text{CHCl}_3, 5 \text{ Å MS} \]

\[ 40 ^\circ \text{C} \]

\[ \text{3a, 70\% yield, 99\% ee} \]

Derivatization of the chiral products:

\[ \text{3a, 99\% ee} \]

\[ \text{NaNO}_2, \text{Nal, TsOH} \]

\[ \text{MeCN/H}_2\text{O} \]

\[ \text{8a, 50\%, 99\% ee} \]

\[ \text{PhB(OH)}_2 \]

\[ \text{Pd}(_\text{dba})_3 \]

\[ \text{S-Phos} \]

\[ \text{toluene, 105 ^\circ \text{C}} \]

\[ \text{9a, 81\%, 99\% ee} \]

\[ \text{3n, 96\% ee} \]

\[ \text{H}_2, \text{Pd/C} \]

\[ \text{10a, 90\%, 86\% ee} \]

\[ \text{11n, 82\%, 96\% ee} \]

\[ \text{3a, 99\% ee} \]

\[ \text{1) H}_2, \text{Pd/C} \]

\[ \text{2) HCl} \]

\[ \text{12a, 55\%, 99\% ee} \]

\[ \text{13a, 51\%, 99\% ee} \]

Preliminary application of amine-thioeura catalyst 13a:

\[ \text{14} \]

\[ \text{15} \]

\[ \text{1) 13a (10 mol\%), PhCOOH (50 mol\%), toluene} \]

\[ \text{2) NaBH}_4 \]

\[ \text{16, 53\%, 6:1 dr, 73\% ee} \]
and amino alcohol derivatives with novel and diversified scaffolds well demonstrate the value of these reactions, especially in the field of developments of novel chiral catalysts and ligands.

Limitations of the Study

The synthesis of the substrates usually needs multiple steps. Different directing groups are required in the synthesis of biaryl diamines and biaryl amino alcohols.

There are also some limitations of the substrate scope (Scheme 7): (1) electron-donating groups were required at the 2-position of the naphthyl moiety; substrates with alkyl groups at this position barely provided the para-amination products (S1a and S1b); (2) kinetic resolution of racemic biaryl phenol substrate did not provide good kinetic resolution performance (S1c); (3) substitutions at the 2-position of the phenol moiety and 3-position of the naphthol moiety were not compatible in the asymmetric para-amination reactions of biaryl phenols (S1d and S1e).

METHODS

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

DATA AND CODE AVAILABILITY

The X-ray crystallographic coordinates for structures reported in this study have been deposited at the Cambridge Crystallographic Data Centre (CCDC) under accession number CCDC: 1923360 (3g), 1938295 (7c), and 1923362 ((S)-1m). These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

SUPPLEMENTAL INFORMATION

Supplemental Information can be found online at https://doi.org/10.1016/j.isci.2019.11.024.

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AUTHOR CONTRIBUTIONS

D.W., W.L., and M.T. performed the experiments. N.Y. performed the crystallographic studies. X.Y. conceived the concept, directed the project, and wrote the paper.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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Supplemental Information

Atroposelective Synthesis of Biaryl Diamines and Amino Alcohols via Chiral Phosphoric Acid Catalyzed \textit{para}-Aminations of Anilines and Phenols

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Table S1. Reaction conditions optimization for para-amination of biaryl phenol 6a, related to Scheme 4.

![Scheme 4](image)

| Entry | R          | Catalyst | Solvent | Additives | Yield (%) | Ee (%) |
|-------|------------|----------|---------|-----------|-----------|--------|
| 1     | COOEt      | A6       | CHCl₃   | -         | 52        | 40     |
| 2     | Boc        | A6       | CHCl₃   | -         | 45        | 61     |
| 3     | Cbz        | A6       | CHCl₃   | -         | 38        | 69     |
| 4     | Cbz        | A6       | CHCl₃   | 4 Å MS    | 64        | 73     |
| 5     | Cbz        | A6       | CHCl₃   | 5 Å MS    | 63        | 83     |
| 6     | Cbz        | A6       | Toluene | 5 Å MS    | 46        | 66     |
| 7     | Cbz        | A6       | DCM     | 5 Å MS    | 46        | 78     |
| 8     | Cbz        | A6       | CCI₄    | 5 Å MS    | 37        | 74     |
| 9     | Cbz        | A6       | Et₂O    | 5 Å MS    | NR        | -      |
| 10    | Cbz        | A2       | CHCl₃   | 5 Å MS    | 42        | 55     |
| 11    | Cbz        | A3       | CHCl₃   | 5 Å MS    | 49        | 35     |
| 12    | Cbz        | A4       | CHCl₃   | 5 Å MS    | 60        | 13     |
| 13    | Cbz        | A5       | CHCl₃   | 5 Å MS    | 58        | 37     |
| 14    | Cbz        | A7       | CHCl₃   | 5 Å MS    | 51        | 84     |
| 15    | Cbz        | A8       | CHCl₃   | 5 Å MS    | 56        | 86     |

*Unless otherwise noted, reactions were performed with 6a (0.1 mmol), 2 (0.15 mmol), CPA catalyst (0.01 mmol) in solvents (0.5 mL) for 36 h at ambient temperature. Yields were isolated yields. Enantiomeric excesses (ees) were determined by HPLC analysis on a chiral stationary phase.
Supplemental Figures for HPLC spectra:

**Figure S1.** HPLC spectrum of racemic-3a, related to Table 1.

**Figure S2.** HPLC spectrum of 3a, related to Table 1.
Figure S3. Full HPLC spectrum of 3a, related to Table 1.

![Full HPLC spectrum of 3a](image1)

| #  | Time  | Type | Area  | Height | Width | Area % | Symmetry |
|----|-------|------|-------|--------|-------|--------|----------|
| 1  | 13.609| BE   | 5605.3| 216.5  | 0.3551| 99.034 | 0.875    |
| 2  | 15.157| BE   | 54.7  | 2.3    | 0.2815| 0.966  | 0.675    |

Figure S4. HPLC spectrum of racemic-3b, related to Scheme 2.

![HPLC spectrum of racemic-3b](image2)

| #  | Time  | Type | Area  | Height | Width | Area % | Symmetry |
|----|-------|------|-------|--------|-------|--------|----------|
| 1  | 13.731| BE   | 2760.1| 58.2   | 0.3507| 50.155 | 0.884    |
| 2  | 16.255| BE   | 2683.3| 73.3   | 0.4287| 49.845 | 0.887    |
Figure S5. HPLC spectrum of 3b, related to Scheme 2.

Figure S6. Full HPLC spectrum of 3b, related to Scheme 2.
Figure S7. HPLC spectrum of racemic-3c, related to Scheme 2.

Figure S8. HPLC spectrum of 3c, related to Scheme 2.
Figure S9. Full HPLC spectrum of 3b, related to Scheme 2.

![HPLC spectrum of 3b](image1)

| # | Time | Type | Area | Height | Width | Area% | Symmetry |
|---|------|------|------|--------|-------|-------|----------|
| 1 | 16.651 | BV R | 196.3 | 7 | 0.3274 | 0.532 | 0.718 |
| 2 | 24.211 | VV R | 36716.2 | 685.4 | 0.63 | 99.468 | 0.597 |

Figure S10. HPLC spectrum of racemic-3d, related to Scheme 2.

![HPLC spectrum of racemic-3d](image2)

| # | Time | Type | Area | Height | Width | Area% | Symmetry |
|---|------|------|------|--------|-------|-------|----------|
| 1 | 16.956 | MM | 136.5 | 4.5 | 0.3007 | 49.448 | 0.954 |
| 2 | 20.379 | MM | 139.6 | 3.6 | 0.6447 | 50.552 | 0.975 |
Figure S11. HPLC spectrum of 3d, related to Scheme 2.

|   | Time  | Type | Area  | Height | Width  | Area% | Symmetry |
|---|-------|------|-------|--------|--------|-------|----------|
| 1 | 17.276| MM   | 150.4 | 4.8    | 0.5195 | 0.776 | 0.864    |
| 2 | 20.763| VV R | 19225.1| 463.4  | 0.4856 | 99.224| 0.749    |

Figure S12. Full HPLC spectrum of 3b, related to Scheme 2.

|   | Time  | Type | Area  | Height | Width  | Area% | Symmetry |
|---|-------|------|-------|--------|--------|-------|----------|
| 1 | 17.319| MM   | 30.1  | 1.9    | 0.4276 | 0.425 | 0.699    |
| 2 | 20.765| VV R | 11713.8| 280.5  | 0.4903 | 99.575| 0.757    |
Figure S13. HPLC spectrum of racemic-3e, related to Scheme 2.

| #  | Time  | Type | Area   | Height | Width | Area%  | Symmetry |
|----|-------|------|--------|--------|-------|--------|----------|
| 1  | 12.37 | BB   | 5852.5 | 297.7  | 0.28*2| 50.062 | 0.885    |
| 2  | 14.098| BB   | 5855.5 | 290.7  | 0.3456| 49.338 | 0.832    |

Figure S14. HPLC spectrum of 3e, related to Scheme 2.

| #  | Time  | Type | Area   | Height | Width | Area%  | Symmetry |
|----|-------|------|--------|--------|-------|--------|----------|
| 1  | 12.838| MF   | 34680.9| 1497.9 | 0.3859| 96.362 | 0.735    |
| 2  | 14.206| PM   | 1309.2 | 46.7   | 0.4676| 3.638  | 0.923    |
Figure S15. Full HPLC spectrum of 3b, related to Scheme 2.

Figure S16. HPLC spectrum of racemic-3f, related to Scheme 2.
Figure S17. HPLC spectrum of 3f, related to Scheme 2.

Figure S18. Full HPLC spectrum of 3b, related to Scheme 2.
Figure S19. HPLC spectrum of racemic-3g, related to Scheme 2.

![HPLC spectrum of racemic-3g](image1)

| #  | Time  | Type | Area     | Height | Width | Area% | Symmetry |
|----|-------|------|----------|--------|-------|-------|----------|
| 1  | 10.254| BR   | 5408.2   | 250    | 0.3249| 90.133| 0.514    |
| 2  | 16.35 | BR   | 5673.4   | 147.8  | 0.4524| 49.847| 0.585    |

Figure S20. HPLC spectrum of 3g, related to Scheme 2.

![HPLC spectrum of 3g](image2)

| #  | Time  | Type | Area     | Height | Width | Area% | Symmetry |
|----|-------|------|----------|--------|-------|-------|----------|
| 1  | 10.232| YY R | 12350.6  | 565.8  | 0.3034| 99.777| 0.543    |
| 2  | 16.841| MM   | 28.1     | 9.9E-1 | 0.4729| 0.223 | 2.437    |
Figure S21. Full HPLC spectrum of 3b, related to Scheme 2.

Figure S22. HPLC spectrum of racemic-3h, related to Scheme 2.
Figure S23. HPLC spectrum of 3h, related to Scheme 2.

![HPLC spectrum of 3h](image1)

| #  | Time | Type | Area  | Height | Width | Area% | Symmetry |
|----|------|------|-------|--------|-------|-------|----------|
| 1  | 8.209| BB   | 22.9  | 1.6    | 0.166 | 0.230 | 0.751    |
| 2  | 9.896| BB   | 9944.4| 573.2  | 0.2519| 99.773| 0.618    |

Figure S24. Full HPLC spectrum of 3b, related to Scheme 2.

![Full HPLC spectrum of 3b](image2)

| #  | Time | Type | Area  | Height | Width | Area% | Symmetry |
|----|------|------|-------|--------|-------|-------|----------|
| 1  | 8.209| BB   | 22.9  | 1.6    | 0.166 | 0.230 | 0.751    |
| 2  | 9.896| BB   | 9944.4| 573.2  | 0.2519| 99.773| 0.618    |
Figure S25. HPLC spectrum of racemic-3i, related to Scheme 2.

Figure S26. HPLC spectrum of 3i, related to Scheme 2.
Figure S27. Full HPLC spectrum of 3b, related to Scheme 2.

|    | Time (min) | Type | Area  | Height | Width  | Area% | Symmetry |
|----|------------|------|-------|--------|--------|-------|----------|
| 1  | 11.973     | BB   | 1306.6| 503.5  | 0.255  | 98.957| 0.845    |
| 2  | 13.365     | BB   | 137.7 | 6.5    | 0.2509 | 1.043 | 0.807    |

Figure S28. HPLC spectrum of racemic-3j, related to Scheme 2.

|    | Time (min) | Type | Area  | Height | Width  | Area% | Symmetry |
|----|------------|------|-------|--------|--------|-------|----------|
| 1  | 14.075     | VR   | 3210.1| 133.1  | 0.2848 | 49.400| 0.987    |
| 2  | 14.824     | VR   | 3288  | 121.2  | 0.3261 | 50.600| 0.897    |
Figure S29. HPLC spectrum of 3j, related to Scheme 2.

Figure S30. Full HPLC spectrum of 3b, related to Scheme 2.
Figure S31. HPLC spectrum of racemic-3k, related to Scheme 2.

Figure S32. HPLC spectrum of 3k, related to Scheme 2.
Figure S33. Full HPLC spectrum of 3k, related to Scheme 2.

Figure S34. HPLC spectrum of racemic-3l, related to Scheme 2.
Figure S35. HPLC spectrum of 3I, related to Scheme 2.

Figure S36. Full HPLC spectrum of 3b, related to Scheme 2.
Figure S37. HPLC spectrum of racemic-1m, related to Scheme 3.

Figure S38. HPLC spectrum of (S)-1m, related to Scheme 3.
Figure S39. Full HPLC spectrum of (S)-1m, related to Scheme 3.

Figure S40. HPLC spectrum of racemic-3m, related to Scheme 3.
Figure S41. HPLC spectrum of 3m, related to Scheme 3.

Figure S42. Full HPLC spectrum of 3m, related to Scheme 3.
Figure S43. HPLC spectrum of racemic-1n, related to Scheme 3.

Figure S44. HPLC spectrum of (S)-1n, related to Scheme 3.
Figure S45. Full HPLC spectrum of (S)-1n, related to Scheme 3.

Figure S46. HPLC spectrum of racemic-3n, related to Scheme 3.
Figure S47. HPLC spectrum of 3n, related to Scheme 3.

Figure S48. Full HPLC spectrum of 3n, related to Scheme 3.
Figure S49. HPLC spectrum of racemic-1o, related to Scheme 3.

Figure S50. HPLC spectrum of (S)-1o, related to Scheme 3.
Figure S51. Full HPLC spectrum of (S)-1o, related to Scheme 3.

Figure S52. HPLC spectrum of racemic-3o, related to Scheme 3.
Figure S53. HPLC spectrum of 3o, related to Scheme 3.

Figure S54. Full HPLC spectrum of 3o, related to Scheme 3.
Figure S55. HPLC spectrum of racemic-1p, related to Scheme 3.

Figure S56. HPLC spectrum of (S)-1p, related to Scheme 3.
Figure S57. Full HPLC spectrum of (S)-1p, related to Scheme 3.

Figure S58. HPLC spectrum of racemic-3p, related to Scheme 3.
Figure S59. HPLC spectrum of 3p, related to Scheme 3.

Figure S60. Full HPLC spectrum of racemic-3p, related to Scheme 3.
Figure S61. HPLC spectrum of racemic-7a, related to Scheme 4

Figure S62. HPLC spectrum of 7a, related to Scheme 4
Figure S63. Full HPLC spectrum of racemic-7a, related to Scheme 4

Figure S64. HPLC spectrum of racemic-7b, related to Scheme 4
Figure S65. HPLC spectrum of 7b, related to Scheme 4

Figure S66. Full HPLC spectrum of 7b, related to Scheme 4
Figure S67. HPLC spectrum of racemic-7c, related to Scheme 4

![HPLC spectrum of racemic-7c](image)

| #  | Time | Type | Area  | Height | Width | Area % | Symmetry |
|----|------|------|-------|--------|-------|--------|----------|
| 1  | 9.183| MF   | 907.5 | 36.2   | 0.3961| 50.539 | 0.503    |
| 2  | 10.86 | FM   | 888.1 | 29.7   | 0.4999| 49.461 | 0.529    |

Figure S68. HPLC spectrum of 7c, related to Scheme 4

![HPLC spectrum of 7c](image)

| #  | Time | Type | Area  | Height | Width | Area % | Symmetry |
|----|------|------|-------|--------|-------|--------|----------|
| 1  | 9.172| BV R | 3947.7| 165.9  | 0.3251| 93.426 | 0.55     |
| 2  | 11.014| 88   | 277.8 | 9.5    | 0.3496| 6.574  | 0.656    |
Figure S69. Full HPLC spectrum of 7c, related to Scheme 4

Figure S70. HPLC spectrum of racemic-7d, related to Scheme 4
Figure S71. HPLC spectrum of 7d, related to Scheme 4

Figure S72. Full HPLC spectrum of 7a, related to Scheme 4
Figure S73. HPLC spectrum of racemic-7e, related to Scheme 4

![HPLC spectrum of racemic-7e](image1)

| #  | Time | Type | Area  | Height | Width | Area% | Symmetry |
|----|------|------|-------|--------|-------|-------|----------|
| 1  | 6.744| MM   | 1315.4| 402.4  | 0.587 | 48.990| 0.816    |
| 2  | 13.2 | PM   | 13596.4| 402.4  | 0.587 | 51.010| 0.913    |

Figure S74. HPLC spectrum of 7e, related to Scheme 4

![HPLC spectrum of 7e](image2)

| #  | Time | Type | Area  | Height | Width | Area% | Symmetry |
|----|------|------|-------|--------|-------|-------|----------|
| 1  | 6.927| MF   | 7214.9| 595.3  | 0.202 | 94.522| 0.840    |
| 2  | 13.7 | BR   | 418.2 | 12.4   | 0.362 | 5.478 | 0.871    |
**Figure S75.** Full HPLC spectrum of 7e, related to Scheme 4

![HPLC spectrum of 7e](image1)

| # | Time | Type | Area  | Height | Width | Area%  | Symmetry |
|---|------|------|-------|--------|-------|--------|----------|
| 1 | 6.527| NP   | 7214.9| 595.3  | 0.202 | 94.522 | 0.849    |
| 2 | 13.7 | BR   | 418.2 | 12.4   | 0.296 | 5.475  | 0.871    |

**Figure S76.** HPLC spectrum of racemic-7f, related to Scheme 4

![HPLC spectrum of racemic-7f](image2)

| #  | Time | Type | Area      | Height | Width | Area% | Symmetry |
|----|------|------|-----------|--------|-------|-------|----------|
| 1  | 3.415| R8   | 7413.8    | 227.3  | 0.464 | 59.096| 0.672    |
| 2  | 13.606| R8  | 7385.4    | 136.5  | 0.661 | 49.904| 0.755    |
Figure S77. HPLC spectrum of 7f, related to Scheme 4

Figure S78. Full HPLC spectrum of 7f, related to Scheme 4
Figure S79. HPLC spectrum of racemic-7g, related to Scheme 4

![HPLC spectrum of racemic-7g](image)

| #  | Time (min) | Type | Area  | Height | Width | Area% | Symmetry |
|----|------------|------|-------|--------|-------|-------|----------|
| 1  | 11.44      | MM   | 5356.8| 158.5  | 0.3582| 50.281| 0.657    |
| 2  | 20.133     | MM   | 5245.4| 84.5   | 1.0348| 95.705| 0.785    |

Figure S80. HPLC spectrum of 7g, related to Scheme 4

![HPLC spectrum of 7g](image)

| #  | Time (min) | Type | Area  | Height | Width | Area% | Symmetry |
|----|------------|------|-------|--------|-------|-------|----------|
| 1  | 11.292     | BB   | 7075.2| 211.4  | 0.403 | 93.419| 0.698    |
| 2  | 20.086     | BV R | 488.4 | 8.3    | 0.6593| 6.381 | 0.917    |
Figure S81. Full HPLC spectrum of 7g, related to Scheme 4.

Figure S82. HPLC spectrum of racemic-8a, related to Scheme 6.
Figure S83. HPLC spectrum of 8a, related to Scheme 6.

Figure S84. Full HPLC spectrum of 8a, related to Scheme 6.
Figure S85. HPLC spectrum of racemic-9a, related to Scheme 6.

Figure S86. HPLC spectrum of 9a, related to Scheme 6.
**Figure S87.** Full HPLC spectrum of 9a, related to Scheme 6.

**Figure S88.** HPLC spectrum of racemic-10a, related to Scheme 6.
Figure S89. HPLC spectrum of 10a, related to Scheme 6.

Figure S90. Full HPLC spectrum of 10a, related to Scheme 6.
Figure S91. HPLC spectrum of racemic-11n, related to Scheme 6.

Figure S92. HPLC spectrum of 11n, related to Scheme 6.
Figure S93. Full HPLC spectrum of 8a, related to Scheme 6.

![Full HPLC spectrum of 8a, related to Scheme 6.](image1)

| #  | Time | Type | Area  | Height | Width | Area%  | Symmetry |
|----|------|------|-------|--------|-------|--------|----------|
| 1  | 11.327 | MF   | 57.8  | 1.7    | 0.5638| 1.782  | 0        |
| 2  | 12.079 | FM   | 3187  | 112.1  | 0.4736| 98.218 | 0.444    |

Figure S94. HPLC spectrum of racemic-12a, related to Scheme 6.

![HPLC spectrum of racemic-12a, related to Scheme 6.](image2)

| #  | Time | Type | Area  | Height | Width | Area%  | Symmetry |
|----|------|------|-------|--------|-------|--------|----------|
| 1  | 16.767 | VV   | 3351.7 | 91.7   | 0.4571| 41.443 | 0.533    |
| 2  | 17.31  | V6   | 4735.9 | 105.3  | 0.5279| 58.557 | 0.505    |
Figure S95. HPLC spectrum of 12a, related to Scheme 6.

Figure S96. Full HPLC spectrum of 12a, related to Scheme 6.
Figure S97. HPLC spectrum of racemic-13a, related to Scheme 6.

Figure S98. HPLC spectrum of 13a, related to Scheme 6.
Figure S99. Full HPLC spectrum of 13a, related to Scheme 6.

![HPLC spectrum of 13a](image)

| #  | Time | Type | Area | Height | Width | Area%  | Symmetry |
|----|------|------|------|--------|-------|--------|----------|
| 1  | 15.649 | TVR | 14547.5 | 345.5 | 0.4957 | 100.000 | 0.511 |

Figure S100. HPLC spectrum of racemic-16, related to Scheme 6.

![HPLC spectrum of racemic-16](image)

| #  | Time | Type | Area | Height | Width | Area%  | Symmetry |
|----|------|------|------|--------|-------|--------|----------|
| 1  | 9.522 | MM  | 1438.9 | 76.3 | 0.3143 | 50.275 | 0.583 |
| 2  | 10.79 | MM  | 1423.2 | 67.1 | 0.3533 | 49.725 | 0.527 |
Figure S101. HPLC spectrum of 16, related to Scheme 6.

Figure S102. Full HPLC spectrum of 16, related to Scheme 6.
Supplemental Figures for NMR spectrums:

Figure S103. $^1$H NMR spectrum of substrate 1a, related to Table 1.

Figure S104. $^{13}$C NMR spectrum of substrate 1a, related to Table 1.
Figure S105. $^1$H NMR spectrum of substrate 1b, related to Scheme 2.

Figure S106. $^{13}$C NMR spectrum of substrate 1b, related to Scheme 2.
Figure S107. $^1$H NMR spectrum of substrate 1c, related to Scheme 2.

Figure S108. $^{13}$C NMR spectrum of substrate 1c, related to Scheme 2.
Figure S109. $^1$H NMR spectrum of substrate 1d, related to Scheme 2.

Figure S110. $^{13}$C NMR spectrum of substrate 1d, related to Scheme 2.
Figure S111. $^1$H NMR spectrum of substrate 1e, related to Scheme 2.

Figure S112. $^{13}$C NMR spectrum of substrate 1e, related to Scheme 2.
Figure S113. $^1$H NMR spectrum of substrate 1f, related to Scheme 2.

Figure S114. $^{13}$C NMR spectrum of substrate 1f, related to Scheme 2.
Figure S115. $^1$H NMR spectrum of substrate 1g, related to Scheme 2.

Figure S116. $^{13}$C NMR spectrum of substrate 1g, related to Scheme 2.
Figure S117. $^1$H NMR spectrum of substrate 1h, related to Scheme 2.

Figure S118. $^{13}$C NMR spectrum of substrate 1h, related to Scheme 2.
**Figure S119.** $^1$H NMR spectrum of substrate 1i, related to Scheme 2.

**Figure S120.** $^{13}$C NMR spectrum of substrate 1i, related to Scheme 2.
**Figure S121.** $^1$H NMR spectrum of substrate 1j, related to Scheme 2.

**Figure S122.** $^{13}$C NMR spectrum of substrate 1j, related to Scheme 2.
Figure S123. $^1$H NMR spectrum of substrate $1k$, related to Scheme 2.

Figure S124. $^{13}$C NMR spectrum of substrate $1k$, related to Scheme 2.
Figure S125. $^1$H NMR spectrum of substrate 1l, related to Scheme 2.

Figure S126. $^{13}$C NMR spectrum of substrate 1l, related to Scheme 2.
**Figure S127.** ¹H NMR spectrum of substrate 1m, related to Scheme 3.

**Figure S128.** ¹³C NMR spectrum of substrate 1m, related to Scheme 3.
Figure S129. $^1$H NMR spectrum of substrate 1n, related to Scheme 3.

Figure S130. $^{13}$C NMR spectrum of substrate 1n, related to Scheme 3.
Figure S131. $^1$H NMR spectrum of substrate 1o, related to Scheme 3.

Figure S132. $^{13}$C NMR spectrum of substrate 1o, related to Scheme 3.
Figure S133. $^1$H NMR spectrum of substrate 1p, related to Scheme 3.

Figure S134. $^{13}$C NMR spectrum of substrate 1p, related to Scheme 3.
Figure S135. $^1$H NMR spectrum of product 3a at room temperature, related to Table 1.

Figure S136. $^{13}$C NMR spectrum of product 3a at room temperature, related to Table 1.
Figure S137. $^1$H NMR spectrum of product 3a at 45 °C, related to Table 1.

Figure S138. $^{13}$C NMR spectrum of product 3a at 45 °C, related to Table 1.
Figure S139. $^1$H NMR spectrum of product 3a at -50 °C, related to Table 1.

Figure S140. $^{13}$C NMR spectrum of product 3a at -50 °C, related to Table 1.
Figure S141. $^1$H NMR spectrum of product 3b, related to Scheme 2.

Figure S142. $^{13}$C NMR spectrum of product 3b, related to Scheme 2.
Figure S143. $^1$H NMR spectrum of product 3c, related to Scheme 2.

Figure S144. $^{13}$C NMR spectrum of product 3c, related to Scheme 2.
Figure S145. $^1$H NMR spectrum of product 3d, related to Scheme 2.

Figure S146. $^{13}$C NMR spectrum of product 3d, related to Scheme 2.
Figure S147. $^1$H NMR spectrum of product 3e, related to Scheme 2.

Figure S148. $^{13}$C NMR spectrum of product 3e, related to Scheme 2.
Figure S149. $^1$H NMR spectrum of product 3f, related to Scheme 2.

Figure S150. $^{13}$C NMR spectrum of product 3f, related to Scheme 2.
Figure S151. $^1$H NMR spectrum of product 3g, related to Scheme 2.

Figure S152. $^{13}$C NMR spectrum of product 3g, related to Scheme 2.
Figure S153. $^1$H NMR spectrum of product 3h, related to Scheme 2.

Figure S154. $^{13}$C NMR spectrum of product 3h, related to Scheme 2.
Figure S155. $^1$H NMR spectrum of product 3i, related to Scheme 2.

Figure S156. $^{13}$C NMR spectrum of product 3i, related to Scheme 2.
Figure S157. $^1$H NMR spectrum of product 3j, related to Scheme 2.

Figure S158. $^{13}$C NMR spectrum of product 3j, related to Scheme 2.
**Figure S159.** $^1$H NMR spectrum of product 3k, related to Scheme 2.

**Figure S160.** $^{13}$C NMR spectrum of product 3k, related to Scheme 2.
Figure S161. $^1$H NMR spectrum of product 3I, related to Scheme 2.

Figure S162. $^{13}$C NMR spectrum of product 3I, related to Scheme 2.
Figure S163. $^1$H NMR spectrum of product 3m, related to Scheme 3.

Figure S164. $^{13}$C NMR spectrum of product 3m, related to Scheme 3.
Figure S165. $^1$H NMR spectrum of product 3n, related to Scheme 3.

Figure S166. $^{13}$C NMR spectrum of product 3n, related to Scheme 3.
Figure S167. $^1$H NMR spectrum of product 3o, related to Scheme 3.

Figure S168. $^{13}$C NMR spectrum of product 3o, related to Scheme 3.
Figure S169. $^1$H NMR spectrum of product 3p, related to Scheme 3.

Figure S170. $^{13}$C NMR spectrum of product 3p, related to Scheme 3.
Figure S171. $^1$H NMR spectrum of product 4a, related to Table 1.

Figure S172. $^{13}$C NMR spectrum of product 4a, related to Table 1.
Figure S173. $^1$H NMR spectrum of substrate 6a, related to Scheme 4.

Figure S174. $^{13}$C NMR spectrum of substrate 6a, related to Scheme 4.
Figure S175. $^1$H NMR spectrum of substrate 6b, related to Scheme 4.

Figure S176. $^{13}$C NMR spectrum of substrate 6b, related to Scheme 4.
**Figure S177.** $^1$H NMR spectrum of substrate 6c, related to Scheme 4.

**Figure S178.** $^{13}$C NMR spectrum of substrate 6c, related to Scheme 4.
Figure S179. $^1$H NMR spectrum of substrate 6d, related to Scheme 4.

Figure S180. $^{13}$C NMR spectrum of substrate 6d, related to Scheme 4.
Figure S181. $^1$H NMR spectrum of substrate 6e, related to Scheme 4.

Figure S182. $^{13}$C NMR spectrum of substrate 6e, related to Scheme 4.
Figure S183. $^1$H NMR spectrum of substrate 6f, related to Scheme 4.

Figure S184. $^{13}$C NMR spectrum of substrate 6f, related to Scheme 4.
Figure S185. $^1$H NMR spectrum of substrate 6g, related to Scheme 4.

Figure S186. $^{13}$C NMR spectrum of substrate 6g, related to Scheme 4.
**Figure S187.** $^1$H NMR spectrum of product 7a, related to Scheme 4.

**Figure S188.** $^{13}$C NMR spectrum of product 7a, related to Scheme 4.
Figure S189. $^1$H NMR spectrum of product 7b, related to Scheme 4.

Figure S190. $^{13}$C NMR spectrum of product 7b, related to Scheme 4.
Figure S191. $^1$H NMR spectrum of product 7c, related to Scheme 4.

Figure S192. $^{13}$C NMR spectrum of product 7c, related to Scheme 4.
Figure S193. $^1$H NMR spectrum of product 7d, related to Scheme 4.

Figure S194. $^{13}$C NMR spectrum of product 7d, related to Scheme 4.
Figure S195. $^1$H NMR spectrum of product 7e, related to Scheme 4.

Figure S196. $^{13}$C NMR spectrum of product 7e, related to Scheme 4.
**Figure S197.** $^1$H NMR spectrum of product 7f, related to Scheme 4.

**Figure S198.** $^{13}$C NMR spectrum of product 7f, related to Scheme 4.
**Figure S199.** $^1$H NMR spectrum of product 7g, related to Scheme 4.

**Figure S200.** $^{13}$C NMR spectrum of product 7g, related to Scheme 4.
**Figure S201.** $^1$H NMR spectrum of product 8a, related to Scheme 6.

**Figure S202.** $^{13}$C NMR spectrum of product 8a, related to Scheme 6.
**Figure S203.** $^1$H NMR spectrum of product 9a, related to **Scheme 6**.

**Figure S204.** $^{13}$C NMR spectrum of product 9a, related to **Scheme 6**.
Figure S205. $^1$H NMR spectrum of product 10a, related to Scheme 6.

Figure S206. $^{13}$C NMR spectrum of product 10a, related to Scheme 6.
**Figure S207.** $^1$H NMR spectrum of product 11n, related to **Scheme 6**.

**Figure S208.** $^{13}$C NMR spectrum of product 11n, related to **Scheme 6**.
Figure S209. $^1$H NMR spectrum of product 12a, related to Scheme 6.

Figure S210. $^{13}$C NMR spectrum of product 12a, related to Scheme 6.
Figure S211. $^1$H NMR spectrum of product 13a, related to Scheme 6.

Figure S212. $^{13}$C NMR spectrum of product 13a, related to Scheme 6.
Figure S213. $^1$H NMR spectrum of product 16, related to Scheme 6.
Supplemental figures and tables for X-Ray structures

Figure S214. X-ray structure of 3g, related to Scheme 2
| Identification code                  |                  |
|-------------------------------------|------------------|
| Empirical formula                   | C22H27N3O2       |
| Formula weight                      | 365.46           |
| Temperature / K                     | 150.0            |
| Crystal system                      | Orthorhombic     |
| Space group                         | P212121          |
| a / Å, b / Å, c / Å                 | 8.4379(2), 10.5541(3), 22.3081(6) |
| α°, β°, γ°                          | 90, 90, 90       |
| Volume / Å³                         | 1986.64(9)       |
| Z                                   | 4                |
| ρcalc / mg mm⁻³                     | 1.222            |
| μ / mm⁻¹                            | 0.629            |
| F(000)                              | 784.0            |
| Crystal size / mm³                  | 0.2 × 0.15 × 0.1 |
| Theta range for data collection     | 11.21 to 148.884°|
| Index ranges                        | -8 ≤ h ≤ 10, -13 ≤ k ≤ 13, -26 ≤ l ≤ 27 |
| Reflections collected               | 16588            |
| Independent reflections             | 4017[R(int) = 0.0214,R(sigma)=0.0187] |
| Data/restraints/parameters          | 4017/0/250       |
| Goodness-of-fit on F²               | 1.071            |
| Final R indexes [I>2σ (I)]          | R1 = 0.0398, wR2 = 0.1107 |
| Final R indexes [all data]          | R1 = 0.0405, wR2 = 0.1115 |
| Largest diff. peak/hole / e Å⁻³     | 0.31/-0.29       |
Figure S215. X-ray structure of (S)-1m, related to Scheme 3.
| Identification code                          |  |
|---------------------------------------------|---|
| **Empirical formula**                       | C$_{21}$H$_{21}$ClN$_2$O$_2$ |
| **Formula weight**                          | 368.85 |
| **Temperature / K**                         | 150.01 |
| **Crystal system**                          | Triclinic |
| **Space group**                             | P1 |
| **a / Å, b / Å, c / Å**                     | 8.1592(3), 10.4448(4), 12.8750(5) |
| **α°, β°, γ°**                               | 69.108(2), 89.972(2), 67.392(2) |
| **Volume / Å$^3$**                          | 934.37(6) |
| **Z**                                       | 2 |
| **ρcalc / mg mm$^{-3}$**                    | 1.311 |
| **μ / mm$^{-1}$**                            | 1.947 |
| **F(000)**                                  | 388.0 |
| **Crystal size / mm$^3$**                    | 0.2 × 0.15 × 0.1 |
| **Theta range for data collection**          | 9.856 to 144.234° |
| **Index ranges**                            | -9 ≤ h ≤ 8, -12 ≤ k ≤ 12, -15 ≤ l ≤ 15 |
| **Reflections collected**                   | 30818 |
| **Independent reflections**                 | 6979 [R(int) = 0.0652, R(sigma) = 0.0639] |
| **Data/restraints/parameters**               | 6979/3/477 |
| **Goodness-of-fit on F$^2$**                 | 1.050 |
| **Final R indexes [I>2σ (I)]**              | R1 = 0.0400, wR2 = 0.1036 |
| **Final R indexes [all data]**              | R1 = 0.0422, wR2 = 0.1061 |
| **Largest diff. peak/hole / e Å$^{-3}$**     | 0.33/-0.36 |
Figure S216. X-ray structure of 7c, related to Scheme 4.
Table S4: Crystal data for 7c, related to Scheme 4.

| Identification code |  |
|---------------------|--|
| **Empirical formula** | C_{69}H_{62}Cl_{2}N_{4}O_{14} |
| **Formula weight** | 1242.12 |
| **Temperature / K** | 150.0 |
| **Crystal system** | Monoclinic |
| **Space group** | Cc |
| **a / Å, b / Å, c / Å** | 30.4852(9), 10.4675(3), 19.5605(6) |
| **α°, β°, γ°** | 90, 96.8720(10), 90 |
| **Volume / Å³** | 6197.0(3) |
| **Z** | 4 |
| **ρ calc / mg mm⁻³** | 1.331 |
| **μ / mm⁻¹** | 1.528 |
| **F(000)** | 2600.0 |
| **Crystal size / mm³** | 0.2 × 0.15 × 0.1 |
| **Theta range for data collection** | 8.938° to 158.802° |
| **Index ranges** | -38 ≤ h ≤ 38, -13 ≤ k ≤ 13, -24 ≤ l ≤ 20 |
| **Reflections collected** | 63322 |
| **Independent reflections** | 11465[R(int) = 0.0749, R(sigma)=0.0644] |
| **Data/restraints/parameters** | 11465/2/808 |
| **Goodness-of-fit on F²** | 1.086 |
| **Final R indexes [I>2σ (I)]** | R1 = 0.0799, wR2 = 0.2268 |
| **Final R indexes [all data]** | R1 = 0.0854, wR2 = 0.2334 |
| **Largest diff. peak/hole / e Å⁻³** | 0.61/-0.54 |
Transparent Methods

General Information:

Unless otherwise noted, all commercial reagents were used without further purification. Dichloromethane, toluene, ether, THF were purified by passage through an activated alumina column under argon. Thin-layer chromatography (TLC) analysis of reaction mixtures were performed using Huanghai silica gel HSGF254 TLC plates, and visualized under UV or by staining with ceric ammonium molybdate or potassium permanganate. Flash column chromatography was carried out on Huanghai Silica Gel HHGJ-300, 300-400 mesh. Nuclear magnetic resonance (NMR) spectra were recorded using Bruker Avance III HD spectrometer (FT, 400 MHz for $^1$H, 101 MHz for $^{13}$C). $^1$H and $^{13}$C chemical shifts are reported in ppm downfield of tetramethylsilane and referenced to residual solvent peak (CHCl$_3$; $\delta$H = 7.26 and $\delta$C = 77.16, CD$_3$OD, $\delta$H = 3.31 and $\delta$C = 49.00, (CD$_3$)$_2$CO, $\delta$H = 2.05 and $\delta$C = 29.84). Multiplicities are reported using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad resonance. FT-IR spectra were recorded on PerkinElmer Frontier FT-IR Spectrometer, and absorption frequencies are reported in reciprocal centimeters (cm$^{-1}$). Mass spectral data were obtained from the Agilent Technologies 6230 TOF LC/MS spectrometer in electrospray ionization (ESI$^+$) mode. Optical rotations were measured with an Autopol V Plus/VI digital polarimeter. X-Ray structure analyses were performed using a Bruker D8 Venture X-ray single crystal diffractometer. Enantiomeric excesses were determined on an Agilent 1260 Chiral HPLC using IA, IB, IC columns under the detective wavelength of 254 nm. The racemic products were synthesized by using (±)-A5 or (±)-A6 as catalyst.

Synthesis of substrates:

Scheme S1, Synthesis of 1-bromo-2-naphthylamine S2, related to Scheme 2.

General procedure for synthesis S2: Substituted naphthalene S1 (3.5 mmol) was dissolved in dry MeOH (10 mL) in a pressure vessel, which was followed by adding (Boc)$_2$O (0.96 mL, 4.2 mmol). After stirring at 100 °C overnight, the reaction mixture was concentrated under vacuum to give a residue, which was then dissolved in MeCN (8 mL) and was added NBS (668 mg, 3.7 mmol) portion-wise at 0 °C. After stirring for 2 h at this temperature, the reaction mixture was quenched with H$_2$O (10 mL) and the aqueous layer was extracted with EtOAc for 3 times. The combined organic layers were dried over Na$_2$SO$_4$ and concentrated under vacuum to give a residue, which was purified with flash column chromatography to give the product S2. tert-butyl (1-bromo-6-methylnaphthalen-2-yl)carbamate (S2a)
This reaction was performed on 3.7 mmol scale of S1. Purification by flash column chromatography (petroleum ether/EtOAc = 20: 1) gave the product S2a (1.1 g, 89%).

$^1$H NMR (500 MHz, Chloroform-d) δ 8.30 (d, $J$ = 9.1 Hz, 1H), 8.03 (d, $J$ = 8.7 Hz, 1H), 7.70 (d, $J$ = 9.0 Hz, 1H), 7.55 (s, 1H), 7.38 (dd, $J$ = 8.7, 1.8 Hz, 1H), 7.26 (d, $J$ = 2.9 Hz, 1H), 2.50 (s, 3H), 1.57 (s, 9H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 153.0, 135.0, 134.3, 131.4, 130.7, 130.2, 127.9, 127.4, 126.6, 120.0, 110.5, 81.5, 28.7, 21.6. IR (cm$^{-1}$): $\nu$ = 3401, 2974, 1719, 1489, 1458, 1224, 1147, 1069, 809. m/z HRMS (ESI) found [M+H]$^+$ 336.0581, $C_{16}H_{19}BrNO_2^+$ requires 336.0594.

tert-butyl (1-bromo-6-phenylphenalen-2-yl)carbamate (S2b)

This reaction was performed on 2.05 mmol scale of S1. Purification by flash column chromatography (petroleum ether/EtOAc = 20: 1) gave the product S2b (1.1 g, 89%).

$^1$H NMR (500 MHz, Chloroform-d) δ 8.40 (d, $J$ = 9.0 Hz, 1H), 8.20 (d, $J$ = 8.8 Hz, 1H), 7.99 (d, $J$ = 1.9 Hz, 1H), 7.91 – 7.79 (m, 2H), 7.76 – 7.66 (m, 2H), 7.49 (t, $J$ = 7.8 Hz, 2H), 7.43 – 7.36 (m, 1H), 7.35 (s, 1H), 1.59 (s, 9H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 152.9, 140.7, 138.0, 135.2, 131.6, 131.5, 129.3, 128.9, 127.8, 127.6, 127.58, 127.3, 126.2, 120.3, 110.1, 81.6, 28.7. IR (cm$^{-1}$): $\nu$ = 3403, 2980, 1723, 1518, 1223, 1153, 767, 695. m/z HRMS (ESI) found [M+H]$^+$ 398.0740, $C_{21}H_{21}BrNO_2^+$ requires 398.0750.

Scheme S2, Synthesis of biaryl anilines and phenols, related to Scheme 2 and Scheme 4.

Method A for synthesis of substrate 1:

General procedure of method A for synthesis of substrate 1: A mixture of S2 (400 mg, 1.25 mmol), arylboronic acid S3 (1.87 mmol), tetrakis(triphenylphosphine) palladium(72 mg, 0.06mmol) and Ba(OH)$_2$ (639 mg, 3.74 mmol) were dissolved in 1,4-dioxane (24 mL) and H$_2$O (8mL). The mixture was purged with N$_2$ for 3 times and then heated to reflux overnight.
reaction mixture was then cooled to room temperature and filtered through celite to give the filtrate, which was extracted with EtOAc for 3 times. The combined organic layer was dried over Na$_2$SO$_4$ and concentrated under vacuum to give a residue, which was purified by flash column chromatography to give the product 1.

**Scheme S3.** Synthesis of biaryl anilines, related to Scheme 2.

**Method B for synthesis of substrate 1:**

**General procedure of method B for synthesis 1:**

**Step 1:** A mixture of S4 (2.9 mmol), 2,2',2',2'-tetramethyl-5,5'-bi(1,3,5-dioxaborinane) (688 mg, 3.05 mmol), and potassium acetate (568 mg, 5.8 mmol) were dissolved in dioxane (8 ml). The mixture was purged with N$_2$ for 3 times, which was followed by adding PdCl$_2$(dppf)-DCM (57 mg, 0.07 mmol). After refluxing for 3 h, the reaction mixture was cooled to room temperature and filtered through celite. The combined filtrates were concentrated under vacuum to afford a residue, which was purified by flash column chromatography to give the product S5 for the next step.

**Step 2:** A mixture of tert-butyl (1-bromonaphthalen-2-yl)carbamate (S2, 321 mg, 1 mmol), S5 (1.3 mmol), tetrakis(triphenylphosphine) palladium (46.2 mg, 0.04 mmol) and K$_2$CO$_3$ (331 mg, 2.4 mmol) were dissolved in 1,4-dioxane (10 mL) and H$_2$O (5mL). The mixture was purged with N$_2$ for 3 times, and then heated to reflux overnight. The reaction mixture was then cooled to room temperature and filtered through celite to give the filtrate, which was extracted with EtOAc for 3 times. The combined organic layers were dried over Na$_2$SO$_4$ and concentrated under vacuum to give a residue, which was purified by flash column chromatography to give the product 1.

tert-butyl (1-(3-aminophenyl)naphthalen-2-yl)carbamate (1a)
This reaction was performed on 0.47 mmol scale of S2 according to method A. Purification by flash column chromatography (petroleum ether/EtOAc = 9: 1) gave the product 1a (155 mg, 99%).

$^1$H NMR (400 MHz, Chloroform-d) $\delta$ 8.39 (d, $J = 9.1$ Hz, 1H), 7.84 (d, $J = 9.1$ Hz, 1H), 7.84 – 7.77 (m, 1H), 7.42 – 7.28 (m, 4H), 6.82 (ddd, $J = 8.0, 2.4, 1.0$ Hz, 1H), 6.71 (dt, $J = 7.5, 1.3$ Hz, 1H), 6.63 (t, $J = 2.0$ Hz, 1H), 6.48 (s, 1H), 3.80 (s, 2H), 1.48 (s, 9H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 153.3, 147.5, 137.2, 133.7, 133.1, 130.7, 130.3, 128.5, 128.1, 126.4, 126.2, 126.0, 124.5, 121.1, 119.5, 117.5, 115.2, 80.9, 28.7. IR (cm$^{-1}$): $f = 3467, 3409, 3364, 2979, 1703, 1490, 1236, 1152, 828, 751$. m/z HRMS (ESI) found [M+H]$^+$ 335.1750, C$_{21}$H$_{23}$N$_2$O$_2$ $^+$ requires 335.1754.

tert-butyl (1-(3-aminophenyl)-6-methylnaphthalen-2-yl)carbamate (1b)

This reaction was performed on 0.6 mmol scale of S2 according to method A. Purification by flash column chromatography (petroleum ether/EtOAc = 9: 1) gave the product 1b (204 mg, 98%).

$^1$H NMR (400 MHz, Chloroform-d) $\delta$ 8.31 (d, $J = 9.0$ Hz, 1H), 7.73 (d, $J = 9.1$ Hz, 1H), 7.56 (s, 1H), 7.33 (t, $J = 7.8$ Hz, 1H), 7.30 – 7.22 (t, 1H), 7.13 (d, $J = 8.6$ Hz, 1H), 6.79 (d, $J = 8.0$ Hz, 1H), 6.68 (d, $J = 7.5$ Hz, 1H), 6.61 (s, 1H), 6.43 (s, 1H), 3.79 (s, 2H), 2.45 (s, 3H), 1.46 (s, 9H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 153.4, 147.4, 137.4, 134.0, 132.8, 131.3, 130.6, 130.5, 128.7, 127.8, 127.1, 126.3, 125.9, 121.2, 119.7, 117.5, 115.2, 80.8, 28.7, 21.7. IR (cm$^{-1}$): $f = 3472, 3409, 3380, 2973, 1717, 1701, 1495, 1151, 816$. m/z HRMS (ESI) found [M+H]$^+$ 349.1906, C$_{22}$H$_{25}$N$_2$O$_2$ $^+$ requires 349.1911.

tert-butyl (1-(3-aminophenyl)-6-phenynaphthalen-2-yl)carbamate (1c)
This reaction was performed on 0.63 mmol scale of S2 according to method A. Purification by flash column chromatography (petroleum ether/EtOAc = 9: 1) gave the product 1c (247 mg, 96%).

$^1$H NMR (400 MHz, Chloroform-$d$) δ 8.44 (d, $J = 9.1$ Hz, 1H), 8.02 (d, $J = 2.0$ Hz, 1H), 7.90 (d, $J = 9.1$ Hz, 1H), 7.70 (d, $J = 7.6$ Hz, 2H), 7.59 (dd, $J = 8.9$, 2.0 Hz, 1H), 7.47 (dd, $J = 8.5$, 6.0 Hz, 3H), 7.42 – 7.31 (m, 2H), 6.83 (dd, $J = 8.0$, 2.4 Hz, 1H), 6.74 (d, $J = 7.5$ Hz, 1H), 6.66 (t, $J = 2.0$ Hz, 1H), 6.53 (s, 1H), 3.84 (s, 2H), 1.50 (s, 9H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 153.3, 147.5, 141.3, 137.1, 137.1, 133.8, 132.3, 130.7, 130.4, 129.2, 128.8, 127.6, 127.5, 126.6, 126.0, 125.9, 121.0, 119.9, 117.4, 115.3, 80.9, 28.7. IR (cm$^{-1}$): $f = 3461$, 3414, 3373, 2981, 1714, 1596, 1490, 1230, 1151, 760, 695. m/z HRMS (ESI) found [M+H]$^+$ 411.2058, $C_{27}H_{27}N_2O_2^+$ requires 411.2067.

tert-butyl (1-(3-aminophenyl)-6-methoxynaphthalen-2-yl)carbamate (1d)

This reaction was performed on 0.32 mmol scale of S2 according to method A. Purification by flash column chromatography (petroleum ether/EtOAc = 9: 1) gave the product 1d (78 mg, 67%).

$^1$H NMR (400 MHz, Chloroform-$d$) δ 8.30 (d, $J = 9.1$ Hz, 1H), 7.73 (d, $J = 9.0$ Hz, 1H), 7.40 – 7.27 (m, 2H), 7.12 (d, $J = 2.7$ Hz, 1H), 6.99 (dd, $J = 9.2$, 2.7 Hz, 1H), 6.80 (ddd, $J = 8.1$, 2.4, 1.0 Hz, 1H), 6.69 (dt, $J = 7.4$, 1.3 Hz, 1H), 6.61 (t, $J = 2.0$ Hz, 1H), 6.40 (s, 1H), 3.90 (s, 3H), 3.86 – 3.60 (m, 2H), 1.47 (s, 9H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 156.8, 153.5, 147.4, 137.3, 131.7, 131.4, 130.6, 128.5, 127.7, 127.2, 126.9, 121.0, 120.4, 119.0, 117.4, 115.2, 106.1, 80.7, 55.6, 28.7. IR (cm$^{-1}$): $f = 3475$, 3409, 3371, 2975, 1700, 1599, 1467, 1234, 1152, 853. m/z HRMS (ESI) found [M+H]$^+$ 365.1852, $C_{22}H_{25}N_2O_3^+$ requires 365.1860.

tert-butyl (1-(3-amino-4-methylphenyl)naphthalen-2-yl)carbamate (1e)
This reaction was performed on 0.94 mmol scale of S5 according to method B. Purification by flash column chromatography (petroleum ether/EtOAc = 9: 1) gave the product 1e (274 mg, 99%).

$^1$H NMR (400 MHz, Chloroform-$d$) δ 8.39 (d, $J = 9.1$ Hz, 1H), 7.88 – 7.74 (m, 2H), 7.38 (td, $J = 8.5, 1.5$ Hz, 1H), 7.35 – 7.27 (m, 2H), 7.23 (d, $J = 7.5$ Hz, 1H), 6.65 (dd, $J = 7.4, 1.7$ Hz, 1H), 6.62 (d, $J = 1.6$ Hz, 1H), 6.53 (s, 1H), 3.73 (s, 2H), 2.29 (s, 3H), 1.48 (s, 9H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 153.1, 145.4, 134.4, 133.5, 133.1, 131.6, 130.1, 128.2, 127.8, 126.1, 125.9, 124.2, 122.3, 120.9, 119.2, 117.1, 80.6, 28.5, 17.4. 17.6. IR (cm$^{-1}$): $f = 3475, 3413, 3366, 3010, 1717, 1700, 1490, 1235, 1156, 825, 746$. m/z HRMS (ESI) found [M+H]$^+$ 349.1902, C$_{22}$H$_{25}$N$_2$O$_2$ requires 349.1911.

**tert-butyl (1-(3-amino-4-methoxyphenyl)naphthalen-2-yl)carbamate (1f)**

This reaction was performed on 0.67 mmol scale of S5 according to method B. Purification by flash column chromatography (petroleum ether/EtOAc = 9: 1) gave the product 1f (202 mg, 88%).

$^1$H NMR (500 MHz, Chloroform-$d$) δ 8.40 (d, $J = 9.1$ Hz, 1H), 7.81 (dd, $J = 14.2, 8.5$ Hz, 2H), 7.39 (d, $J = 8.3$ Hz, 1H), 7.37 – 7.27 (m, 2H), 6.97 (d, $J = 7.9$ Hz, 1H), 6.67 (d, $J = 9.0$ Hz, 2H), 6.55 (s, 1H), 3.97 (s, 3H), 3.95 (s, 2H), 1.49 (s, 9H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 153.3, 147.4, 137.1, 134.0, 133.6, 130.2, 128.4, 128.3, 128.0, 126.3, 126.1, 126.0, 124.4, 120.9, 119.3, 117.4, 111.3, 80.8, 55.9, 28.7. IR (cm$^{-1}$): $f = 3468, 3395, 3373, 2988, 1698, 1500, 1227, 1155, 1027, 823$. m/z HRMS (ESI) found [M+H]$^+$ 365.1855, C$_{22}$H$_{25}$N$_2$O$_3$ requires 365.1860.

**tert-butyl (1-(3-amino-5-methylphenyl)naphthalen-2-yl)carbamate (1g)**

This reaction was performed on 0.91 mmol scale of S5 according to method B. Purification by flash column chromatography (petroleum ether/EtOAc = 9: 1) gave the product 1g (198 mg, 75%).
1H NMR (400 MHz, Chloroform-d) δ 8.38 (d, J = 9.1 Hz, 1H), 7.81 (dd, J = 11.3, 8.4 Hz, 2H), 7.40 (d, J = 8.1 Hz, 1H), 7.38 – 7.28 (m, 2H), 6.64 (s, 1H), 6.52 (d, J = 4.0 Hz, 2H), 6.44 (t, J = 1.8 Hz, 1H), 3.74 (s, 2H), 2.35 (s, 3H), 1.49 (s, 9H). 13C NMR (101 MHz, CDCl3) δ 153.2, 147.2, 140.4, 136.8, 133.4, 133.0, 131.7, 130.1, 128.2, 127.8, 126.1, 125.9, 124.2, 121.7, 119.3, 115.8, 114.5, 80.6, 28.5, 21.6. IR (cm⁻¹): f = 3463, 3405, 3375, 2974, 1731, 1595, 1499, 1249, 1145, 821, 747. m/z HRMS (ESI) found [M+H]+ 349.1901, C22H25N2O2+ requires 349.1911.

tert-butyl (1-(3-amino-5-methoxyphenyl)naphthalen-2-yl)carbamate (1h)

This reaction was performed on 0.63 mmol scale of S5 according to method B. Purification by flash column chromatography (petroleum ether/EtOAc = 9: 1) gave the product 1h (227 mg, 99%).

1H NMR (400 MHz, Chloroform-d) δ 8.39 (d, J = 9.0 Hz, 1H), 7.81 (dd, J = 13.2, 8.5 Hz, 2H), 7.43 (d, J = 8.1 Hz, 1H), 7.33 (t, J = 7.7 Hz, 2H), 6.54 (s, 1H), 6.37 (d, J = 2.1 Hz, 1H), 6.26 (d, J = 10.1 Hz, 2H), 3.81 (s, 2H), 3.79 (s, 3H), 1.49 (s, 9H). 13C NMR (101 MHz, CDCl3) δ 161.8, 153.3, 148.8, 138.2, 133.6, 133.0, 130.2, 128.5, 128.0, 126.4, 126.1, 126.0, 124.5, 119.5, 110.4, 106.4, 101.2, 80.9, 55.7, 28.7. IR (cm⁻¹): f = 3470, 3380, 2976, 1721, 1499, 1229, 1198, 1151, 1072, 814. m/z HRMS (ESI) found [M+H]+ 365.1854, C22H25N2O3+ requires 365.1860.

tert-butyl (3'-amino-6-methyl-[1,1'-biphenyl]-2-yl)carbamate (1i)

This reaction was performed on 2.42 mmol scale of S2 according to method A. Purification by flash column chromatography (petroleum ether/EtOAc = 9: 1) gave the product 1i (500 mg, 69%).

1H NMR (400 MHz, Chloroform-d) δ 8.06 (d, J = 8.3 Hz, 1H), 7.37 – 7.31 (m, 1H), 7.28 (t, J = 7.9 Hz, 1H), 7.00 (d, J = 7.5 Hz, 1H), 6.79 (ddd, J = 8.0, 2.5, 1.0 Hz, 1H), 6.64 (dt, J = 7.5, 1.3 Hz, 1H), 6.57 (t, J = 2.0 Hz, 1H), 6.29 (s, 1H), 3.83 (s, 2H), 2.09 (s, 3H), 1.51 (s, 9H). 13C NMR (101 MHz, CDCl3) δ 153.2, 147.4, 138.3, 138.8, 136.2, 131.2, 130.6, 128.0, 124.4, 120.1,
IR (cm⁻¹): f = 3441, 3419, 3353, 2985, 1704, 1507, 1233, 1154, 758. m/z HRMS (ESI) found [M+H]⁺ 299.1746, C₁₈H₂₃N₂O₂⁺ requires 299.1754.

tert-butyl (3'-amino-6-chloro-[1,1'-biphenyl]-2-yl)carbamate (1j)

This reaction was performed on 0.7 mmol scale of S2 according to method A. Purification by flash column chromatography (petroleum ether/EtOAc = 9: 1) gave the product 1j (181 mg, 82%).

¹H NMR (400 MHz, Chloroform-d) δ 8.12 (d, J = 8.4 Hz, 1H), 7.30 (t, J = 7.8 Hz, 1H), 7.23 (d, J = 8.2 Hz, 1H), 7.16 – 7.06 (m, 1H), 6.77 (dd, J = 8.3, 2.4 Hz, 1H), 6.67 – 6.60 (m, 1H), 6.56 (t, J = 2.0 Hz, 1H), 6.31 (s, 1H), 3.80 (s, 2H), 1.44 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 152.8, 147.4, 138.0, 136.2, 133.8, 130.6, 129.9, 129.2, 123.6, 120.1, 117.2, 116.7, 115.6, 81.1, 28.6. IR (cm⁻¹): f = 3476, 3397, 3380, 2988, 1709, 1573, 1507, 1420, 1147, 846, 776. m/z HRMS (ESI) found [M+H]⁺ 319.1198, C₁₇H₂₀ClN₂O₂⁺ requires 319.1208.

methyl 3'-amino-6-((tert-butoxycarbonyl)amino)-[1,1'-biphenyl]-2-carboxylate (1k)

This reaction was performed on 0.7 mmol scale of S2 according to method A. Purification by flash column chromatography (petroleum ether/EtOAc = 5: 1) gave the product 1k (100 mg, 42%).

¹H NMR (400 MHz, Chloroform-d) δ 8.34 (d, J = 8.3 Hz, 1H), 7.49 (dd, J = 7.8, 1.2 Hz, 1H), 7.37 (t, J = 8.0 Hz, 1H), 7.31 – 7.15 (m, 1H), 6.73 (dd, J = 8.0, 2.4 Hz, 1H), 6.65 – 6.58 (m, 1H), 6.52 (t, J = 2.0 Hz, 1H), 6.45 (s, 1H), 3.75 (s, 2H), 3.58 (s, 3H), 1.44 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 168.5, 153.0, 147.2, 137.5, 137.0, 130.2, 131.1, 130.2, 128.3, 123.8, 122.1, 119.7, 116.0, 115.2, 81.0, 52.3, 28.6. IR (cm⁻¹): f = 3473, 3404, 3383, 2972, 1731, 1712, 1515, 1218, 1146, 986, 754. m/z HRMS (ESI) found [M+H]⁺ 343.1640, C₁₉H₂₃N₂O₄⁺ requires 343.1652.

benzyl (1-(3-aminophenyl)naphthalen-2-yl)carbamate (1l)
This reaction was performed on 0.85 mmol scale of S2 according to method A. Purification by flash column chromatography (petroleum ether/EtOAc = 4: 1) gave the product 1l (218 mg, 70%).

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 8.41 (d, $J = 9.1$ Hz, 1H), 7.87 (d, $J = 9.1$ Hz, 1H), 7.85 – 7.79 (m, 1H), 7.47 – 7.28 (m, 9H), 6.79 (dd, $J = 8.1, 2.4$ Hz, 1H), 6.74 – 6.67 (m, 2H), 6.60 (t, $J = 1.9$ Hz, 1H), 5.17 (s, 2H), 3.75 (s, 2H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 153.6, 147.4, 136.6, 136.2, 132.8, 130.5, 130.3, 128.7, 128.5, 128.4, 127.9, 126.5, 126.3, 125.9, 124.5, 120.7, 119.2, 117.1, 115.1, 67.1. IR (cm$^{-1}$): $f = 3371, 3032, 2931, 1723, 1598, 1498, 1208, 1068, 743, 696$. m/z HRMS (ESI) found [M+H]$^+$ 369.1603, $C_{24}H_{21}N_{2}O_2$ requires 369.1598.

tert-butyl (1-(3-amino-2-chlorophenyl)naphthalen-2-yl)carbamate (1m)

This reaction was performed on 0.9 mmol scale of S5 according to method B. Purification by flash column chromatography (petroleum ether/EtOAc = 15: 1) gave the product 1m (141 mg, 54%).

$^1$H NMR (500 MHz, Chloroform-$d$) $\delta$ 8.36 (d, $J = 9.1$ Hz, 1H), 7.88 (d, $J = 9.1$ Hz, 1H), 7.82 (d, $J = 8.0$ Hz, 1H), 7.34 (dt, $J = 22.8, 7.1$ Hz, 2H), 7.29 – 7.18 (m, 2H), 6.93 (d, $J = 8.1$ Hz, 1H), 6.69 (d, $J = 7.4$ Hz, 1H), 6.25 (s, 1H), 4.25 (s, 2H), 1.48 (d, $J = 1.4$ Hz, 9H). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 153.3, 144.4, 135.4, 134.0, 132.6, 130.4, 129.1, 128.4, 128.2, 126.7, 125.4, 124.7, 122.0, 120.3, 119.9, 116.2, 115.3, 81.0, 28.7. IR (cm$^{-1}$): $f = 3465, 3407, 3364, 2997, 2963, 1717, 1499, 1229, 1146, 816$. m/z HRMS (ESI) found [M+H]$^+$ 369.1363, $C_{24}H_{32}ClN_{2}O_2$ requires 369.1364.

tert-butyl (1-(3-amino-2-methoxyphenyl)naphthalen-2-yl)carbamate (1n)
This reaction was performed on 0.85 mmol scale of S5 according to method B. Purification by flash column chromatography (petroleum ether/EtOAc = 10: 1) gave the product 1n (237 mg, 99%).

$^1$H NMR (500 MHz, Chloroform-$d$) $\delta$ 8.32 (d, $J = 9.1$ Hz, 1H), 7.87 (d, $J = 9.0$ Hz, 1H), 7.82 (d, $J = 7.8$ Hz, 1H), 7.43 (d, $J = 8.1$ Hz, 1H), 7.40 – 7.31 (m, 2H), 7.09 (t, $J = 7.7$ Hz, 1H), 6.91 (d, $J = 7.9$ Hz, 1H), 6.62 (s, 1H), 6.59 (d, $J = 7.5$ Hz, 1H), 4.00 (s, 2H), 3.25 (s, 3H), 1.47 (s, 9H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 153.3, 145.8, 140.8, 133.9, 132.9, 130.3, 128.6, 128.6, 128.0, 126.4, 125.8, 125.2, 124.4, 123.0, 122.0, 120.2, 116.2, 80.6, 60.0, 28.5. IR (cm$^{-1}$): $f = 3411, 3366, 2977, 2932, 1717, 1497, 1470, 1211, 1153, 745$. m/z HRMS (ESI) found [M+H]$^+$ 365.1854, C$_{22}$H$_{25}$N$_2$O$_3$ requires 365.1860.

tert-butyl (1-(3-amino-2-methylphenyl)naphthalen-2-yl)carbamate (1o)

This reaction was performed on 0.66 mmol scale of S5 according to method B. Purification by flash column chromatography (petroleum ether/EtOAc = 9: 1) gave the product 1o (120 mg, 69%).

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 8.41 (d, $J = 9.1$ Hz, 1H), 7.84 (dd, $J = 13.9, 8.5$ Hz, 2H), 7.39 – 7.32 (m, 1H), 7.32 – 7.27 (m, 1H), 7.21 (dd, $J = 8.6, 6.5$ Hz, 2H), 6.85 (d, $J = 7.9$ Hz, 1H), 6.65 (d, $J = 7.5$ Hz, 1H), 6.32 (s, 1H), 3.93 (s, 2H), 1.76 (s, 3H), 1.47 (s, 9H).$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 153.3, 145.8, 136.0, 133.9, 133.0, 130.3, 128.4, 128.2, 127.7, 126.5, 125.8, 125.4, 124.5, 122.6, 121.6, 119.4, 115.5, 80.9, 28.7, 13.9. IR (cm$^{-1}$): $f = 3470, 3399, 3373, 2978, 1712, 1496, 1228, 1157, 1066, 743$. m/z HRMS (ESI) found [M+H]$^+$ 349.1902, C$_{22}$H$_{25}$N$_2$O$_2$ requires 349.1911.

tert-butyl (1-(3-amino-2-(methoxymethyl)phenyl)naphthalen-2-yl)carbamate (1p)
This reaction was performed on 1.37 mmol scale of S5 according to method B. Purification by flash column chromatography (petroleum ether/EtOAc = 9: 1) gave the product 1p (200 mg, 50%).

$^1$H NMR (500 MHz, Chloroform-$d$) $\delta$ 8.35 (d, $J = 9.1$ Hz, 1H), 7.86 (d, $J = 9.0$ Hz, 1H), 7.82 (d, $J = 8.1$ Hz, 1H), 7.36 (t, $J = 7.5$ Hz, 1H), 7.29 (td, $J = 7.8$, 5.1 Hz, 2H), 7.21 (d, $J = 8.4$ Hz, 1H), 6.85 (d, $J = 7.9$ Hz, 1H), 6.60 (d, $J = 7.3$ Hz, 1H), 6.41 (s, 1H), 4.44 (s, 2H), 4.23 – 4.10 (m, 1H), 4.10 – 3.99 (m, 1H), 3.06 (s, 3H), 1.46 (s, 9H). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 153.3, 148.1, 136.2, 134.1, 133.4, 130.2, 128.6, 128.08, 126.6, 126.0, 124.8, 124.6, 122.2, 121.0, 119.8, 116.5, 80.8, 69.9, 58.0, 28.6. IR (cm$^{-1}$): $f =$ 3480, 3385, 2977, 2928, 1716, 1504, 1228, 1155, 1078, 740. m/z HRMS (ESI) found [M+H]$^+$ 379.2012, C$_{23}$H$_{27}$N$_2$O$_3$ requires 379.2016.

3-(2-methoxynaphthalen-1-yl)phenol (6a)

Yield = 98%. This reaction was performed on 3.0 mmol according to Method A. Purification by flash column chromatography (petroleum ether/EtOAc = 4: 1) gave the product 6a (782 mg, 98%) as white solid.

$^1$H NMR (500 MHz, Chloroform-$d$) $\delta$ 7.88 (d, $J = 9.0$ Hz, 1H), 7.82 (dd, $J = 6.3$, 3.2 Hz, 1H), 7.52 (dd, $J = 6.3$, 3.5 Hz, 1H), 7.40 – 7.32 (m, 4H), 6.94 (dt, $J = 7.5$, 1.2 Hz, 1H), 6.89 (dt, $J = 8.1$, 1.6 Hz, 1H), 6.83 (dd, $J = 2.6$, 1.4 Hz, 1H), 4.91 (s, 1H), 3.85 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 155.5, 153.7, 138.2, 133.6, 129.6, 129.3, 129.1, 127.9, 126.5, 125.4, 125.1, 123.7, 123.6, 118.1, 114.3, 113.9, 57.0. IR (cm$^{-1}$): $f =$ 3471, 1577, 1510, 1467, 1334, 1296, 1260, 1247, 1176, 1064, 886, 786, 741, 716, 683. m/z HRMS (ESI) found [M+H]$^+$ 251.1057, C$_{17}$H$_{15}$O$_2^+$ requires 251.1067.
**Scheme S4.** Synthesis of biaryl phenol, related to Scheme 4.

3-(2-(methoxymethoxy)naphthalen-1-yl)phenol (6b)

Compound S7 was synthesized according to the procedure reported by Katsuki and co-workers (Oguma and Katsuki, 2012).

Substrate 6b was synthesized according to the general procedure of Method A. This reaction was performed on 3.0 mmol scale, and purification by flash column chromatography (petroleum ether/EtOAc = 3:1) afforded the product 6b (826 mg, 98%) as white solid.

$^1$H NMR (500 MHz, Chloroform-d) δ 7.53 (dd, $J = 7.7$, 1.8 Hz, 1H), 7.46 (d, $J = 9.0$ Hz, 1H), 7.40 – 7.31 (m, 3H), 6.94 (dt, $J = 7.5$, 1.2 Hz, 1H), 6.89 (dt, $J = 8.3$, 1.7 Hz, 1H), 6.84 (dd, $J = 2.6$, 1.5 Hz, 1H), 5.29 (s, 1H), 5.11 (s, 2H), 3.34 (s, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 155.5, 151.3, 138.1, 133.6, 129.9, 129.5, 129.3, 127.9, 127.1, 126.4, 125.7, 124.3, 123.6, 118.0, 117.5, 114.3, 95.7, 56.3. IR (cm$^{-1}$): $\nu$ = 3487, 3415, 3150, 2944, 1590, 1504, 1239, 1143, 1040, 1017, 810, 746, 686. m/z HRMS (ESI) found [M+H]$^+$ 281.1173, $^{18}$C$_{18}$H$_{17}$O$_3^+$ requires 281.1172.

3-(2,4-dimethoxynaphthalen-1-yl)phenol (6c)

This reaction was performed on 2.34 mmol according to Method A. Purification by flash column chromatography (petroleum ether/EtOAc = 4:1) afforded the product 6c (450 mg, 69%) as white solid.

$^1$H NMR (400 MHz, Chloroform-d) δ 8.27 – 8.11 (m, 1H), 7.48 (dd, $J = 7.6$, 2.2 Hz, 1H), 7.39 – 7.29 (m, 3H), 6.92 (dt, $J = 7.5$, 1.2 Hz, 1H), 6.88 (dt, $J = 8.2$, 1.6 Hz, 1H), 6.82 (dd, $J = 2.7$, 1.4 Hz, 1H), 6.73 (s, 1H), 4.78 (s, 1H), 4.07 (s, 3H), 3.83 (s, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 156.4, 155.5, 154.1, 138.3, 134.1, 129.5, 127.2, 125.1, 124.1, 123.1, 121.9, 121.4, 118.5, 117.9, 114.1, 94.2, 57.4, 55.8. IR (cm$^{-1}$): $\nu$ = 3529, 3420, 3183, 2917, 2848, 1589, 1447, 1344, 1202, 1104, 862, 768, 714. m/z HRMS (ESI) found [M+H]$^+$ 281.1164, $^{18}$C$_{18}$H$_{17}$O$_3^+$ requires 281.1172.
Scheme S5. Synthesis of biaryl phenol substrates, related to Scheme 4.

3-(2,6-dimethoxynaphthalen-1-yl)phenol (6d)

Compound S9 was synthesized according to the procedure reported by Gu and co-workers (Pan et al., 2017).

Substrate 6d was synthesized according to the general procedure of Method A. This reaction was performed on 1.09 mmol scale. Purification by flash column chromatography (petroleum ether/EtOAc = 20: 1) afforded the product 6d (290 mg, 95%) as white solid.

$^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.76 (d, $J = 9.0$ Hz, 1H), 7.43 (d, $J = 9.3$ Hz, 1H), 7.39 – 7.29 (m, 2H), 7.12 (d, $J = 2.7$ Hz, 1H), 7.02 (dd, $J = 9.3$, 2.7 Hz, 1H), 6.96 – 6.86 (m, 2H), 6.84 – 6.80 (m, 1H), 4.78 (s, 1H), 3.91 (s, 3H), 3.81 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 156.1, 155.3, 152.2, 138.2, 129.9, 129.4, 128.9, 127.7, 126.9, 123.5, 119.2, 117.9, 114.6, 114.2, 105.7, 57.1, 55.3. IR (cm$^{-1}$): $\nu = 3481, 2935, 2838, 1576, 1458, 1339, 1250, 1179, 1111, 1065, 1025, 853, 798, 705, 668, 599$. m/z HRMS (ESI) found [M+H]$^+$ 281.1162, C$_{18}$H$_{17}$O$_3$ + requires 281.1172.

Scheme S6. Synthesis of biaryl phenol substrates, related to Scheme 4.

3-(2-methoxy-6-methylnaphthalen-1-yl)phenol (6e)

Compound S11 was synthesized referenced to the procedure reported by Pappo and co-workers (Narute et al., 2016).

Compound S12 was synthesized according to the procedure reported by Luan and co-workers (Zuo et al., 2017).

Substrate 6e was synthesized according to the general procedure Method A. This reaction was performed on 3.75 mmol scale, and purification by flash column chromatography (petroleum ether/EtOAc = 20: 1) afforded the product 6e (594 mg, 60%) as white solid.

$^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.78 (d, $J = 9.0$ Hz, 1H), 7.58 (s, 1H), 7.41 (d, $J = 8.7$ Hz, 1H), 7.38 – 7.30 (m, 2H), 7.17 (dd, $J = 8.7$, 1.8 Hz, 1H), 6.96 – 6.86 (m, 2H), 6.82 (dd, $J = 2.6$, 1.5 Hz, 1H), 4.77 (s, 1H), 3.82 (s, 3H), 2.46 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 155.4, 152.9, 138.2, 133.1, 131.6, 129.4, 129.2, 128.7, 128.4, 126.7, 125.2, 124.9, 123.5, 117.9, 114.1,
Scheme S7. Synthesis of biaryl phenol substrates, related to Scheme 4.

3-(2-methoxy-6-phenynaphthalen-1-yl)phenol (6f)

Substrate 6f was prepared by adopting the similar procedure for synthesizing 6e. The Suzuki coupling of S15 was carried out in 1.8 mmol scale, affording product 6f (346 mg, 59%) as white solid.

$^1$H NMR (400 MHz, Chloroform-d) $\delta$ 8.04 – 7.97 (m, 1H), 7.93 (d, $J = 9.0$ Hz, 1H), 7.72 – 7.66 (m, 2H), 7.63 – 7.58 (m, 2H), 7.47 (t, $J = 7.7$ Hz, 2H), 7.38 (td, $J = 7.9$, 3.0 Hz, 3H), 7.00 – 6.95 (m, 1H), 6.94 – 6.89 (m, 1H), 6.86 (dd, $J = 2.6$, 1.4 Hz, 1H), 4.81 (s, 1H), 3.86 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 155.4, 153.7, 141.0, 138.0, 136.2, 132.7, 129.5, 129.4, 128.8, 127.2, 127.1, 125.8, 125.7, 124.7, 117.9, 114.2, 114.2, 56.8. IR (cm$^{-1}$): $f = 3472, 2945,$

3-(2,7-dimethoxynaphthalen-1-yl)phenol (6g)

This reaction was performed on 1.8 mmol according to Method A. Purification by flash column chromatography (petroleum ether/EtOAc = 5: 1) afforded the product 6g (488 mg, 97%) as white solid.

$^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.78 (d, $J = 8.9$ Hz, 1H), 7.71 (d, $J = 8.9$ Hz, 1H), 7.36 (t, $J = 7.9$ Hz, 1H), 7.20 (d, $J = 9.0$ Hz, 1H), 7.00 (dt, $J = 9.0$, 2.2 Hz, 1H), 6.93 (dt, $J = 7.6$, 1.3 Hz, 1H), 6.88 (d, $J = 8.3$ Hz, 1H), 6.81 (dd, $J = 13.9$, 2.2 Hz, 2H), 4.81 (s, 1H), 3.82 (s, 3H), 3.70 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 158.1, 155.4, 154.2, 138.3, 134.8, 129.5, 129.4, 128.8, 124.5, 123.8, 123.4, 117.8, 116.2, 114.1, 111.1, 103.7, 56.6, 55.1. IR (cm$^{-1}$): $f = 3419, 2939,
1622, 1509, 1460, 1214, 1178, 1022, 827, 769, 706. m/z HRMS (ESI) found [M+H]\(^+\) 281.1165, C\(_{16}\)H\(_{17}\)O\(_3\) requires 281.1172.

**Asymmetric synthesis of products:**

**Scheme S8.** Asymmetric para-amination of biaryl aniline substrates, related to Scheme 2.

![Diagram](image)

**General procedure for the asymmetric synthesis of products 3a to 3p (expect 3g and 3h):**

To a solution of 1 (0.1 mmol), 2 (0.11 mmol) in CHCl\(_3\) (0.5 mL) was added 5 Å MS (30 mg) and (R)-A7 (5mg 0.005 mmol). After stirring at 40 °C for 16 h, the reaction was filtered through celite and the filtrate were concentrated under vacuum to afford a residue, which was purified by flash column chromatography to give the product 3.

*Most of the NMR spectra of the products show rotamers and therefore doubling the signal set or line broadening. Conducting NMR experiment of 3a at 45 °C in CDCl\(_3\) was attempted, which lead to some improvement of qualities of NMR spectra.*

For product 3g and 3h, a further catalytic hydrogenation step was conducted. To the solution of the above residue in MeOH (2 mL) was added 10% Pd/C (20 mg). The reaction was purged with H\(_2\) for 3 times and stirred under H\(_2\) atmosphere overnight. Then the reaction mixture was filtered through celite and the filtrate was concentrated under vacuum to give a residue, which was purified by flash column chromatography to give the products 3g and 3h.

dibenzy1(S)-1-(4-amino-2-(2-((tert-butoxycarbonyl)amino)naphthalen-1-yl)phenyl)hydrazine-1, 2-dicarboxylate (3a)

![Image](image)

55mg, 87% yield. \(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 8.36 – 7.95 (m, 1H), 7.92 – 7.57 (m, 3H), 7.27 (m, 6H), 7.15 – 6.07 (m, 11H), 5.04 (m, 4H), 3.86 (m, 2H), 1.53 – 1.34 (m, 9H). \(^1^3\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 155.4, 153.8, 153.0, 147.4, 135.9, 135.6, 135.1, 134.4, 133.9, 132.4,
131.8, 131.2, 130.8, 130.2, 129.0, 128.6, 128.5, 128.4, 128.1, 127.6, 127.3, 126.4, 125.5, 124.7, 120.0, 117.2, 116.0, 80.9, 68.1, 67.7, 28.4. \[\alpha\]D25 = 25.40 (c = 1.0, CHCl3). IR (cm⁻¹): \(\nu = 3369, 2962, 1715, 1497, 1223, 1153, 747, 695.\) m/z HRMS (ESI) found [M+H]+ 633.2697, \(\text{C}_{37}\text{H}_{37}\text{N}_{4}\text{O}_{6}\) requires 633.2708. HPLC: Chiralpak IA column, 75:25 hexanes/isopropanol, 1 ml/min; \(t_R = 13.6\) min (major), 15.2 min (minor); 98% ee.

dibenzyl(S)-1-(4-amino-2-(2-((tert-butoxycarbonyl)amino)-6-methylnaphthalen-1-yl)phenyl)hydrazine-1,2-dicarboxylate (3b)

\[
\begin{align*}
\text{Me} & \quad \text{NHBOC} \\
\text{H}_2\text{N} & \quad \text{N} - \text{NHCBz} \\
\text{C} & \quad \text{Cbz}
\end{align*}
\]

52 mg, 80% yield. \(^1\)H NMR (400 MHz, Chloroform-\(d\)) \(\delta 8.35 – 7.88\) (m, 1H), 7.85 – 7.46 (m, 3H), 7.28 (m, 5H), 7.21 – 6.57 (m, 9H), 6.59 – 6.11 (m, 2H), 5.26 – 4.73 (m, 4H), 3.86 (s, 2H), 2.43 (s, 3H), 1.56 – 1.31 (m, 9H). \(^{13}\)C NMR (101 MHz, CDCl3) \(\delta 155.7, 153.9, 153.1, 147.4, 135.9, 135.6, 134.3, 133.6, 133.1, 132.0, 131.9, 131.2, 130.8, 130.6, 128.6, 128.5, 128.4, 128.1, 127.6, 127.4, 127.1, 117.2, 117.0, 115.9, 80.8, 68.1, 67.7, 28.4, 21.5. \[\alpha\]D25 = 28.80 (c = 1.0, CHCl3). IR (cm⁻¹): \(\nu = 3368, 2966, 1715, 1497, 1225, 1153, 747, 695.\) m/z HRMS (ESI) found [M+H]+ 647.2851, \(\text{C}_{38}\text{H}_{39}\text{N}_{4}\text{O}_{6}\) requires 647.2864. HPLC: Chiralpak IA column, 75:25 hexanes/isopropanol, 1 ml/min; \(t_R = 13.7\) min (minor), 16.3 min (major); 98% ee.

dibenzyl(S)-1-(4-amino-2-((tert-butoxycarbonyl)amino)-6-phenylnaphthalen-1-yl)phenyl)hydrazine-1,2-dicarboxylate (3c)

\[
\begin{align*}
\text{Ph} & \quad \text{NHBOC} \\
\text{H}_2\text{N} & \quad \text{N} - \text{NHCBz} \\
\text{C} & \quad \text{Cbz}
\end{align*}
\]

69 mg, 79% yield. \(^1\)H NMR (400 MHz, Chloroform-\(d\)) \(\delta 8.38 – 8.08\) (m, 1H), 7.93 (m, 2H), 7.78 – 7.25 (m, 12H), 7.24 – 6.09 (m, 11H), 5.06 (m, 4H), 4.49 – 3.29 (m, 2H), 1.42 (m, 9H). \(^{13}\)C NMR (126 MHz, CDCl3) \(\delta 155.7, 153.8, 153.0, 147.4, 140.9, 137.3, 135.6, 134.1, 134.0, 132.2, 131.9, 131.6, 131.4, 131.0, 130.6, 130.4, 129.3, 129.0, 128.6, 128.4, 128.1, 127.6, 127.4, 127.4, 125.9, 123.3, 120.4, 117.2, 117.0, 116.1, 81.0, 68.2, 67.7, 28.5. \[\alpha\]D25 = 33.00 (c = 1.0, CHCl3). IR (cm⁻¹): \(\nu = 3369, 2962, 1715, 1490, 1224, 1152, 748, 695.\) m/z HRMS (ESI) found [M+H]+ 709.3004, \(\text{C}_{43}\text{H}_{41}\text{N}_{4}\text{O}_{6}\) requires 709.3021. HPLC: Chiralpak IA column, 75:25 hexanes/isopropanol, 1 ml/min; \(t_R = 16.7\) min (minor), 24.2 min (major); 98% ee.
dibenzyl(S)-1-(4-amino-2-(2-((tert-butoxycarbonyl)amino)naphthalen-1-yl)phenyl)hydrazine-1,2-dicarboxylate (3d)

\[
\text{MeO} \quad \text{NHBOc} \\
\begin{array}{c}
\text{H}_2\text{N} \\
\text{N} \quad \text{N-HNCbz} \\
\text{Cbz}
\end{array}
\]

53 mg, 80% yield. \(^1\)H NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 8.44 – 7.29 (m, 8H), 7.22 – 6.17 (m, 12H), 5.01 (m, 4H), 3.86 (s, 5H), 1.42 (m, 9H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 156.9, 154.0, 153.2, 147.4, 135.9, 135.6, 132.3, 131.8, 131.7, 131.4, 131.2, 130.8, 128.6, 128.5, 128.4, 128.1, 127.7, 127.6, 127.4, 127.1, 122.7, 120.9, 119.0, 117.1, 116.8, 115.9, 106.1, 80.7, 68.1, 67.7, 55.4, 28.4. \([\alpha]_{D}^{25}\) = 36.55 (c = 2.0, CHCl\(_3\)). IR (cm\(^{-1}\)): \(\nu\) = 3368, 2962, 2929, 1715, 1497, 1228, 1152, 1025, 749, 696. m/z HRMS (ESI) found [M+H\(^+\)] requires 663.2813.

HPLC: Chiralpak IA column, 75:25 hexanes/isopropanol, 1 ml/min; t\(_R\) = 17.3 min (minor), 20.8 min (major); 98% ee.

dibenzyl(S)-1-(4-amino-2-(2-((tert-butoxycarbonyl)amino)naphthalen-1-yl)-5-methoxyphenyl)hydrazine-1,2-dicarboxylate (3e)

\[
\text{Me} \quad \text{NHBOc} \\
\begin{array}{c}
\text{H}_2\text{N} \\
\text{N} \quad \text{N-HNCbz} \\
\text{Cbz}
\end{array}
\]

29 mg, 45% yield. \(^1\)H NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 8.47 – 7.29 (m, 10H), 7.17 – 5.74 (m, 10H), 5.21 – 4.77 (m, 4H), 3.78 (s, 2H), 2.26 (s, 3H), 1.43 (m, 9H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 155.4, 153.8, 153.0, 145.7, 135.9, 135.6, 134.5, 134.0, 132.6, 131.7, 130.2, 128.9, 128.7, 128.6, 128.5, 128.4, 128.3, 128.1, 127.6, 127.3, 126.4, 125.5, 124.6, 121.5, 119.8, 116.9, 116.7, 80.8, 68.1, 67.1, 28.4, 17.4. \([\alpha]_{D}^{25}\) = 25.60 (c = 1.0, CHCl\(_3\)). IR (cm\(^{-1}\)): \(\nu\) = 3369, 2964, 2928, 1715, 1497, 1224, 1149, 1027, 783, 695. m/z HRMS (ESI) found [M+H\(^+\)] requires 647.2844, C\(_{38}\)H\(_{38}\)N\(_4\)O\(_6\) requires 647.2864. HPLC: Chiralpak IA column, 75:25 hexanes/isopropanol, 1 ml/min; t\(_R\) = 12.8 min (major), 14.2 min (minor); 93% ee.

dibenzyl(S)-1-(4-amino-2-((tert-butoxycarbonyl)amino)naphthalen-1-yl)-5-methoxyphenyl)hydrazine-1,2-dicarboxylate (3f)
51 mg, 77% yield. \(^1\)H NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 8.50 – 7.59 (m, 3H), 7.47 – 6.59 (m, 15H), 6.37 (m, 2H), 5.44 – 4.48 (m, 4H), 4.13 – 3.67 (m, 5H), 1.44 (m, 9H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 155.4, 153.8, 153.0, 147.3, 137.4, 135.9, 135.6, 134.8, 134.3, 132.8, 131.5, 130.3, 130.2, 128.9, 128.6, 128.4, 128.0, 127.6, 126.3, 125.6, 124.6, 119.7, 116.2, 116.0, 112.0, 111.5, 80.8, 68.1, 67.7, 55.9, 28.4. \([\alpha]_D^{25}\) = 28.10 (c = 1.0, CHCl\(_3\)). IR (cm\(^{-1}\)):\(f\) = 3369, 2963, 1715, 1497, 1217, 1150, 1021, 745, 695. m/z HRMS (ESI) found [M+H]\(^+\) 663.2792, \(C_{38}H_{39}N_4O_7\) requires 663.2813.

HPLC: Chiralpak IA column, 75:25 hexanes/isopropanol, 1 ml/min; \(t_R\) = 10.8 min (major), 12.1 min (minor); 99% ee.

tert-butyl (S)-(1-(2,5-diamino-3-methylphenyl)naphthalen-2-yl)carbamate (3g)

20mg, 56% yield for two steps. \(^1\)H NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 8.42 (d, \(J\) = 9.1 Hz, 1H), 7.96 – 7.72 (m, 2H), 7.42 – 7.29 (m, 3H), 6.67 (d, \(J\) = 2.6 Hz, 1H), 6.59 (s, 1H), 6.38 (d, \(J\) = 2.6 Hz, 1H), 3.07 (s, 4H), 2.23 (s, 3H), 1.48 (s, 9H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 153.5, 138.6, 136.1, 134.8, 132.8, 130.6, 129.0, 128.3, 126.8, 125.7, 125.2, 124.7, 122.4, 121.2, 119.8, 119.4, 116.5, 80.9, 28.7, 18.4. \([\alpha]_D^{25}\) = 7.80 (c = 1.0, CHCl\(_3\)). IR (cm\(^{-1}\)):\(f\) = 3440, 3396, 2973, 2927, 1719, 1596, 1498, 1229, 1150, 1073, 828, 750. m/z HRMS (ESI) found [M+H]\(^+\) 364.2007, \(C_{22}H_{27}N_3O_2\) requires 364.2020.

HPLC: Chiralpak IC column, 80:20 hexanes/isopropanol, 1 ml/min; \(t_R\) = 10.2 min (major), 16.8 min (minor); 99% ee.

tert-butyl (S)-(1-(2,5-diamino-3-methoxyphenyl)naphthalen-2-yl)carbamate (3h)
21 mg, 55% yield for two steps. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 8.43 (d, $J = 9.1$ Hz, 1H), 7.93 – 7.66 (m, 2H), 7.46 – 7.29 (m, 3H), 6.69 (s, 1H), 6.42 (d, $J = 2.4$ Hz, 1H), 6.12 (d, $J = 2.4$ Hz, 1H), 3.91 (s, 3H), 3.23 (s, 4H), 1.48 (s, 9H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 153.5, 149.2, 138.9, 134.7, 132.6, 129.0, 128.7, 128.6, 128.2, 127.7, 127.6, 125.7, 125.6, 121.9, 119.8, 109.9, 100.5, 80.9, 55.9, 28.7. 

$\left[\alpha\right]_{D}^25 = 8.20$ (c = 1.0, CHCl$_3$).

IR (cm$^{-1}$): $\nu = 3439, 3396, 2982, 1715, 1499, 1481, 1230, 1150, 820, 750$.

m/z HRMS (ESI) found [M+H]$^+$ 380.1956, $C_{22}H_{26}N_3O_3$ requires 380.1969.

HPLC: Chiralpak IA column, 75:25 hexanes/isopropanol, 1 ml/min; $t_R = 8.2$ min (minor), 9.9 min (major); 99% ee.

dibenzy1(S)-1-(5-amino-2'-(tert-butoxycarbonyl)amino)-6'-methyl-[1,1'-biphenyl]-2-yl)hydrazine-1,2-dicarboxylate (3i)

44 mg, 74% yield. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 8.09 – 7.43 (m, 2H), 7.36 – 7.26 (m, 6H), 7.25 – 7.09 (m, 5H), 5.07 (m, 4H), 3.85 (s, 2H), 1.37 (m, 9H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 155.6, 153.3, 152.8, 147.2, 136.9, 135.9, 135.6, 131.2, 130.7, 128.7, 128.6, 128.5, 128.2, 127.7, 127.5, 124.9, 124.7, 118.1, 117.1, 116.5, 116.3, 115.8, 115.6, 80.5, 68.3, 67.9, 28.4, 20.5. 

$\left[\alpha\right]_{D}^25 = -1.50$ (c = 1.0, CHCl$_3$). IR (cm$^{-1}$): $f = 3439, 3396, 2982, 1715, 1497, 1455, 1154, 1016, 784, 749, 695$. m/z HRMS (ESI) found [M+H]$^+$ 597.2708, $C_{34}H_{37}N_4O_6$ requires 597.2693.

HPLC: Chiralpak IA column, 75:25 hexanes/isopropanol, 1 ml/min; $t_R = 12.0$ min (major), 13.4 min (minor); 98% ee.

dibenzy1(R)-1-(5-amino-2'-(tert-butoxycarbonyl)amino)-6'-chloro-[1,1'-biphenyl]-2-yl)hydrazine-1,2-dicarboxylate (3j)

51 mg, 83% yield. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 8.09 – 7.44 (m, 2H), 7.40 – 7.26 (m, 7H), 7.16 m, 5H), 6.89 – 6.22 (m, 4H), 5.04 (m, 4H), 3.85 (s, 2H), 1.40 (m, 9H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 155.9, 155.5, 153.5, 147.2, 138.6, 138.0, 135.9, 135.6, 134.6, 130.9, 129.9, 129.6, 129.3, 128.7, 128.6, 128.5, 128.2, 127.7, 127.4, 124.1, 120.5, 118.0, 116.4, 81.1, 68.3, 67.9, 28.4. 

$\left[\alpha\right]_{D}^25 = 29.20$ (c = 1.0, CHCl$_3$). IR (cm$^{-1}$): $f = 3374, 2963, 2928, 1715, 1506, 1218, 1150, 1055, 749, 695$. m/z HRMS (ESI) found [M+H]$^+$ 617.2143, $C_{33}H_{36}ClN_4O_6$ requires
HPLC: Chiralpak IA column, 75:25 hexanes/isopropanol, 1 ml/min; t<sub>R</sub> = 15.0 min (minor), 15.8 min (major); 99% ee.

dibenzyl(S)-1-(5-amino-2'-((tert-butoxycarbonyl)amino)-6'-{(methoxycarbonyl)}-1,1'-biphenyl-2'-yl)hydrazine-1,2-dicarboxylate (3k)

Scheme S9. Kinetic resolution of biaryl anilines via asymmetric para-aminations, related to Scheme 3.
General procedure for the asymmetric synthesis of products 3m to 3o via kinetic resolution: To a solution of 1 (0.1 mmol), 2 (0.06 mmol) in DCM (0.5 mL) was 5 Å MS (30 mg) and (R)-A6 (4 mg, 0.01 mmol). After stirring at room temperature for 16 h, the reaction was filtered through celite and the filtrate was concentrated under vacuum to give a residue, which was purified by flash column chromatography to give the product 3 and recovered (S)-1.

(S)-tert-butyl (1-(3-amino-2-chlorophenyl)naphthalen-2-yl)carbamate (1m)

17 mg, 47% yield. HPLC: Chiralpak IA column, 85:15 hexanes/isopropanol, 1 ml/min; t_R = 6.8 min (major), 7.6 min (minor); 95% ee. [α]_D^{25} = 4.40 (c = 0.5, CHCl_3)

(S)-tert-butyl (1-(3-amino-2-methoxyphenyl)naphthalen-2-yl)carbamate (1n)

17 mg, 47% yield. HPLC: Chiralpak IA column, 85:15 hexanes/isopropanol, 1 ml/min; t_R = 6.3 min (major), 7.5 min (minor); 89% ee. [α]_D^{25} = 34.40 (c = 0.5, CHCl_3)

(S)-tert-butyl (1-(3-amino-2-methylphenyl)naphthalen-2-yl)carbamate (1o)
16 mg, 45% yield. HPLC: Chiralpak IA column, 85:15 hexanes/isopropanol, 1 ml/min; \( t_R = 6.4 \) min (major), 7.5 min (minor); 88% ee. \([\alpha]_D^{25} = -10.00 \) (c = 0.5, CHCl\(_3\))

(S)-\text{tert-butyl (1-(3-amino-2-(methoxymethyl)phenyl)naphthalen-2-yl)carbamate(1p)}

14 mg, 37% yield. HPLC: Chiralpak IA column, 85:15 hexanes/isopropanol, 1 ml/min; \( t_R = 6.0 \) min (major), 6.3 min (minor); 93% ee. \([\alpha]_D^{25} = -4.00 \) (c = 0.2, CHCl\(_3\))

\text{Dibenzyl-}(R)-1-(4-amino-2-(((\text{tert-butoxycarbonyl})amino)naphthalen-1-yl)-3-chlorophenyl)hydrazine-1,2-dicarboxylate (3m)

33 mg, 50% yield. \(^1\)H NMR (400 MHz, Chloroform-\(d\)) \( \delta \) 8.31 – 7.56 (m, 4H), 7.43 – 7.27 (m, 6H), 7.25 – 5.99 (m, 10H), 5.34 – 4.71 (m, 4H), 4.35 (s, 2H), 1.43 (m, 9H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 155.2, 153.7, 153.2, 144.5, 135.9, 135.7, 135.0, 132.4, 131.7, 130.6, 129.7, 129.3, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 127.7, 127.6, 126.8, 125.1, 124.8, 122.1, 120.8, 119.5, 116.2, 80.6, 68.3, 67.8, 28.5. \([\alpha]_D^{25} = 14.30 \) (c = 1.0, CHCl\(_3\)). IR (cm\(^{-1}\)):\( f = 3368, 2962, 1714, 1485, 1223, 1153, 1059, 748, 695. \) m/z HRMS (ESI) found [M+H]\(^+\) 667.2296, \( \text{C}_{37}\text{H}_{50}\text{ClN}_{10}\text{O}_{6}^+ \) requires 667.2318. HPLC: Chiralpak IA column, 75:25 hexanes/isopropanol, 1 ml/min; \( t_R = 10.2 \) min (major), 11.9 min (minor); 97% ee.

\text{Dibenzyl-}(R)-1-(4-amino-2-(((\text{tert-butoxycarbonyl})amino)naphthalen-1-yl)-3-methoxyphenyl)hydrazine-1,2-dicarboxylate (3n)
35 mg, 53% yield. $^1$H NMR (400 MHz, Chloroform-\textit{d}) $\delta$ 8.21 – 7.33 (m, 4H), 7.21 (s, 6H), 7.18 – 5.88 (m, 10H), 4.97 (m, 4H), 3.98 (s, 2H), 3.14 (s, 3H), 1.34 (m, 9H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 155.4, 153.7, 153.1, 145.1, 143.5, 141.1, 135.9, 135.6, 132.4, 131.6, 130.4, 129.3, 129.0, 128.6, 128.4, 128.2, 128.1, 128.1, 127.7, 127.4, 126.5, 125.2, 124.9, 122.0, 120.7, 80.4, 68.1, 67.2, 59.8, 28.4. [\textalpha] D$^25$ = 21.60 (c = 1.0, CHCl$_3$). IR (cm$^{-1}$): $\nu$ = 3368, 2963, 1714, 1487, 1222, 1154, 747, 695. m/z HRMS (ESI) found [M+H]$^+$ 663.2789, C$_{38}$H$_{39}$N$_4$O$_7$ requires 663.2813.

HPLC: Chiralpak IA column, 75:25 hexanes/isopropanol, 1 ml/min; $t_R$ = 10.2 min (major), 11.9 min (minor); 93% ee.

Dibenzyl-(S)-1-(4-amino-2-(2-((tert-butoxycarbonyl)amino)naphthalen-1-yl)-3-methylphenyl)hydrazine-1,2-dicarboxylate (3o)

![](image)

32 mg, 50% yield. $^1$H NMR (400 MHz, Chloroform-\textit{d}) $\delta$ 8.37 – 7.99 (m, 1H), 7.82 (m, 2H), 7.70 – 7.44 (m, 6H), 7.22 – 5.87 (m, 10H), 5.31 – 4.66 (m, 4H), 4.14 – 3.53 (m, 2H), 1.66 (s, 3H), 1.53 – 1.32 (m, 9H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 155.6, 153.7, 153.0, 145.7, 136.0, 135.7, 134.8, 134.1, 132.0, 130.5, 130.4, 129.0, 128.7, 128.6, 128.3, 128.2, 128.0, 127.6, 127.3, 126.5, 125.1, 124.9, 122.4, 122.0, 120.2, 115.9, 115.7, 80.8, 68.0, 28.4, 28.4, 13.8. [\textalpha] D$^25$ = 22.90 (c = 1.0, CHCl$_3$). IR (cm$^{-1}$): $\nu$ = 3378, 2962, 1714, 1484, 1218, 1154, 1072, 747, 695. m/z HRMS (ESI) found [M+H]$^+$ 647.2862, C$_{38}$H$_{39}$N$_4$O$_6$ requires 647.2864.

HPLC: Chiralpak IB column, 80:20 hexanes/isopropanol, 1 ml/min; $t_R$ = 11.4 min (major), 13.0 min (minor); 92% ee.

Dibenzyl-(S)-1-(4-amino-2-(2-((tert-butoxycarbonyl)amino)naphthalen-1-yl)-3-methylphenyl)hydrazine-1,2-dicarboxylate (3p)

![](image)

27 mg, 40% yield. $^1$H NMR (400 MHz, Chloroform-\textit{d}) $\delta$ 8.36 – 7.35 (m, 10H), 7.21 – 5.91 (m, 10H), 5.29 – 4.77 (m, 4H), 4.57 (s, 1H), 4.12 – 3.82 (m, 1H), 2.99 (m, 2H), 1.41 (m, 9H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 154.4, 152.5, 151.9, 146.9, 134.8, 134.5, 133.8, 133.3, 131.2, 130.2, 129.4, 129.3, 128.1, 127.6, 127.4, 127.2, 127.0, 126.9, 126.5, 126.2, 125.4, 124.2, 123.8, 121.1, 119.5, 115.7, 115.6, 79.6, 68.5, 66.9, 56.4, 28.7, 27.3. [\textalpha] D$^25$ = 35.20 (c = 1.0, CHCl$_3$). IR (cm$^{-1}$): $\nu$ = 3369, 2927, 1715, 1484, 1217, 1154, 1073, 747, 695. m/z HRMS (ESI) found
[M+H]+ 677.2974, C_{39}H_{41}N_{4}O_{7} requires 677.2970. HPLC: Chiralpak IA column, 75:25 hexanes/isopropanol, 1 mL/min, t_{R} = 10.0 min (major), 13.5 min (minor); 94% ee.

dibenzyl-3-(3-(tert-butoxycarbonyl)amino)naphthalen-1-yl)phenyl)triazene-1,2-dicarboxylate (4a)

\[
\begin{align*}
\text{CbzHN} & \quad \text{NHboc} \\
\text{Cbz} & \quad \text{N} \\
\text{H} & \quad \text{N}
\end{align*}
\]

^1H NMR (400 MHz, Chloroform-d) 8.33 (d, J = 9.1 Hz, 1H), 7.83 (dd, J = 13.8, 8.5 Hz, 2H), 7.58 (s, 1H), 7.43 (t, J = 7.8 Hz, 1H), 7.39 – 7.21 (m, 13H), 7.00 – 6.70 (m, 4H), 6.40 (s, 1H), 5.18 (m, 4H), 1.45 (s, 9H). ^13C NMR (101 MHz, Chloroform-d) 8.5 156.7, 155.8, 153.2, 146.5, 137.1, 135.3, 135.2, 132.8, 130.5, 130.2, 128.7, 128.5, 128.4, 128.1, 127.9, 127.8, 127.1, 126.4, 125.6, 124.4, 123.8, 119.8, 115.7, 113.6, 80.9, 69.5, 68.3, 28.4. HRMS (ESI) found [M+H]+ 633.2682, C_{37}H_{37}N_{4}O_{6}+ requires 633.2708.

Scheme S10. Asymmetric para-aminations of biaryl phenols, related to Scheme 4.

General procedure for synthesis of 7a to 7g: To a solution of 6 (0.1 mmol), 2 (0.3 mmol) in CHCl₃ (1 mL) was added 5 Å MS (50 mg) and (R)-cat-A8 (0.01 mmol). After stirring at room temperature for 36 h, the reaction mixture was filtered through celite and concentrated under vacuum to give a residue, which was purified by flash column chromatography to give the products 7.

Dibenzylic-3-S)-1-(4-hydroxy-2-(2-methoxynaphthalen-1-yl)phenyl)hydrazine-1,2-dicarboxylate (7a)
31 mg, 56% yield. $^1$H NMR (500 MHz, Chloroform-δ) δ 7.85 (dd, $J = 9.1, 3.5$ Hz, 1H), 7.77 (d, $J = 8.1$ Hz, 1H), 7.66 – 7.27 (m, 7H), 7.24 – 6.65 (m, 9H), 6.37 (m, 1H), 5.40 – 4.16 (m, 4H), 3.66 (d, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 155.9, 153.5, 135.9, 135.7, 135.6, 133.7, 133.3, 130.3, 130.2, 129.3, 128.6, 128.4, 128.3, 128.1, 127.9, 127.4, 126.9, 126.6, 125.4, 124.0, 118.6, 115.7, 113.8, 67.9, 67.7, 56.8. IR (cm$^{-1}$): 3018, 1214, 1005, 928, 746, 668. $[\alpha]_{D}^{25} = 5.05$ (c = 2.0, CHCl$_3$). m/z HRMS (ESI) found [M+H$^+$] 549.2011, C$_{33}$H$_{29}$N$_2$O$_6$+ requires 549.2020. HPLC: Chiralpak IA column, 70:30 hexanes/isopropanol, 1 ml/min; $t_R$ = 11.1 min (major), 13.0 min (minor); 86% ee.

Dibenzyl-(S)-1-(4-hydroxy-2-(2-(methoxymethoxy)naphthalen-1-yl)phenyl)hydrazine-1,2-dicarboxylate (7b)

27 mg, 84% yield. $^1$H NMR (400 MHz, Chloroform-δ) δ 7.85 – 7.73 (m, 2H), 7.71 – 7.27 (m, 8H), 7.23 – 6.77 (m, 8H), 6.71 (d, $J = 3.1$ Hz, 1H), 5.85 (m, 1H), 5.24 – 4.79 (m, 6H), 3.34 – 3.08 (m, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 155.8, 155.4, 135.8, 135.6, 134.0, 133.0, 130.2, 130.1, 129.9, 128.5, 128.3, 128.1, 127.7, 127.5, 127.2, 126.4, 125.6, 124.4, 123.3, 118.4, 117.2, 116.8, 115.6, 95.9, 67.7, 67.6, 56.1. IR (cm$^{-1}$): 3018, 1214, 1003, 928, 746, 668, 623. $[\alpha]_{D}^{25} = 17.20$ (c = 1.0, CHCl$_3$). m/z HRMS (ESI) found [M+H$^+$]$^+$ 579.2112, C$_{34}$H$_{31}$N$_2$O$_7$+ requires 579.2126. HPLC: Chiralpak IA column, 80:20 hexanes/isopropanol, 1 ml/min; $t_R$ = 20.2 min (minor), 21.6 min (major); 84% ee.

Dibenzyl-(S)-1-(2-(2,4-dimethoxynaphthalen-1-yl)-4-hydroxyphenyl)hydrazine-1,2-dicarboxylate (7c)

39 mg, 68% yield. $^1$H NMR (400 MHz, Chloroform-δ) δ 8.17 (d, $J = 8.5$ Hz, 1H), 7.45 (dd, 6H), 7.23 – 6.46 (m, 12H), 5.85 (d, 1H), 5.35 – 4.72 (m, 4H), 4.02 (s, 3H), 3.65 (d, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 157.1, 155.9, 155.6, 154.0, 135.9, 135.8, 134.3, 133.7, 130.5, 130.4, 128.6, 128.4, 128.1, 127.9, 127.8, 127.7, 127.3, 125.1, 123.4, 122.0, 121.8, 121.6, 119.3, 119.1, 115.5, 93.9, 67.8, 67.6, 55.7, 55.7. IR (cm$^{-1}$): 3018, 1214, 1004, 928, 746, 668, 608. $[\alpha]_{D}^{25} = -0.70$ (c = 1.0, CHCl$_3$). m/z HRMS (ESI) found [M+H$^+$]$^+$ 579.2113, C$_{34}$H$_{31}$N$_2$O$_7$+ requires
Dibenzyl-(S)-1-(2-(2,6-dimethoxynaphthalen-1-yl)-4-hydroxyphenyl)hydrazine-1,2-dicarboxylate (7d)

35 mg, 61% yield. $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.72 (dd, $J$ = 9.0, 2.2 Hz, 1H), 7.66 – 7.26 (m, 5H), 7.24 – 6.64 (m, 12H), 6.07 (d, 1H), 5.40 – 4.68 (m, 4H), 3.87 (d, 3H), 3.63 (d, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 156.2, 155.8, 155.7, 152.1, 135.8, 133.8, 130.3, 128.7, 128.6, 128.4, 128.1, 127.9, 127.6, 127.4, 127.0, 119.4, 118.6, 115.7, 114.6, 105.8, 67.9, 67.7, 57.1, 55.4. IR (cm$^{-1}$): $\nu$ = 3018, 1214, 1006, 928, 746, 668, 608. $[\alpha]_{D}^{25}$ = 9.40 (c = 1.0, CHCl$_3$).

m/z HRMS (ESI) found [M+H]$^+$ 579.2114, C$_{34}$H$_{31}$N$_2$O$_7$ requires 579.2126. HPLC: Chiralpak IB column, 80:20 hexanes/isopropanol, 1 ml/min; $t_R$ = 9.2 min (major), 11.0 min (minor); 87% ee.

Dibenzyl-(S)-1-(4-hydroxy-2-(2-methoxy-6-methylnaphthalen-1-yl)phenyl)hydrazine-1,2-dicarboxylate (7e)

37 mg, 66% yield. $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.75 (dd, $J$ = 9.1, 4.9 Hz, 1H), 7.63 (d, $J$ = 8.0 Hz, 1H), 7.53 (d, $J$ = 7.9 Hz, 1H), 7.29 (m, $J$ = 6.9 Hz, 3H), 7.24 – 6.60 (m, 12H), 5.98 (d, 1H), 5.31 – 4.81 (m, 4H), 3.64 (d, 3H), 3.40 (d, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 155.7, 152.9, 135.9, 135.8, 135.7, 133.9, 133.4, 131.4, 130.3, 129.5, 129.4, 128.9, 128.6, 128.4, 128.1, 127.8, 127.6, 127.4, 126.8, 125.2, 67.9, 67.7, 56.9, 21.4. IR (cm$^{-1}$): $f$ = 3018, 1214, 1006, 747, 668. $[\alpha]_{D}^{25}$ = 15.00 (c = 1.0, CHCl$_3$). m/z HRMS (ESI) found [M+H]$^+$ 563.2160, C$_{34}$H$_{31}$N$_2$O$_6$ requires 563.2177. HPLC: Chiralpak IA column, 70:30 hexanes/isopropanol, 1 ml/min; $t_R$ = 6.9 min (major), 13.7 min (minor); 89% ee.

Dibenzyl-(S)-1-(4-hydroxy-2-(2-methoxy-6-phenylnaphthalen-1-yl)phenyl)hydrazine-1,2-dicarboxylate (7f)
Gram-scale preparation of 3a:

Scheme S11. Gram-scale preparation of 3a, related to Scheme 6.
To a solution of 1 (1.002g, 3 mmol), 2 (1.03g, 3.45mmol) and 5 Å MS (300 mg) in CHCl₃ (15 mL) was added (R)-A7 (60 mg, 0.06 mmol). After stirring at 40 °C overnight, the reaction mixture was filtered through celite and the filtrate was concentrated under vacuum to give a residue, which was purified by flash column chromatography (petroleum ether/THF = 5: 1) to give the product 3a (1.326 g, 70%, 99% ee).

**Derivatizations of chiral products:**

**Scheme S12.** Transformations of the amino group in product, related to **Scheme 6**.

To a solution of p-TsOH·H₂O (180mg, 0.95 mmol) in MeCN (4 mL) was added 3a (200 mg, 0.31 mmol). The resulting suspension of amine salt was cooled to 5-10 °C and to this was gradually added a solution of NaNO₂ (44 mg, 0.63mmol) and NaI (118 mg, 0.8 mmol) in H₂O (0.3 mL). The reaction mixture was stirred for 10 min then allowed to warm to 20 °C. After stirring for 30 min, the reaction mixture was then added H₂O (2 mL), NaHCO₃ (1 M; until pH = 9-10) and Na₂S₂O₃ (2 M, 1 mL). The mixture was extracted with EtOAc for 3 times. The combined organic layer was dried over Na₂SO₄ and concentrated under vacuum to afford a residue, which was purified by column chromatography (petroleum ether/EtOAc = 10:1) as eluent to give the product 8a (115 mg, 50% yield). ¹H NMR (400 MHz, Chloroform-δ) δ 8.10 (s, 1H), 7.86 (m, 3H), 7.74 – 7.52 (m, 2H), 7.31 (s, 7H), 7.24 – 6.92 (m, 6H), 6.78 – 5.91 (m, 2H), 5.04 (m, 4H), 1.48 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 155.8, 154.7, 153.6, 141.1, 140.7, 139.0, 135.6, 135.4, 135.3, 132.7, 132.0, 131.3, 130.4, 130.0, 129.4, 128.6, 128.6, 128.5, 128.3, 128.2, 128.1, 127.6, 126.8, 125.0, 124.8, 122.3, 94.7, 80.8, 68.4, 68.0, 28.4. [α]D₂₅ = 33.55 (c = 2.0, CHCl₃). IR (cm⁻¹): f = 3307, 2973, 1716, 1496, 1222, 1153, 1023, 746, 695. m/z HRMS (ESI) found [M+H]⁺ 744.1561, C₃₇H₃₅IN₃O₆⁺ requires 744.1565. HPLC: Chiralpak IB column, 95:05 hexanes/isopropanol, 1 ml/min; tₙ = 9.8 min (major), 11.2 min (minor); 99% ee.
dibenzyl(S)-1-(3-(2-((tert-butoxycarbonyl)amino)naphthalen-1-yl)-1',1'-biphenyl-4-yl)hydrazine-1,2-dicarboxylate (9a)

A mixture of 8a (110 mg, 0.15 mmol), phenylboronic acid (27 mg, 0.22 mmol), Pd₂dba₃ (9.6 mg, 0.01 mmol), S-Phos (8.6 mg, 0.02 mmol) and K₂PO₄ were suspended in dry toluene (10 mL). The mixture was purged with N₂ for 3 times and then heated to 105 °C. After stirring at this temperature overnight, the reaction mixture was cooled to room temperature and filtered through celite. The filtrate was concentrated under vacuum to give a residue, which was purified by flash column chromatography (petroleum ether/EtOAc = 10:1) to give the product 9a (83 mg, 81%). ¹H NMR (500 MHz, Chloroform-d) δ 8.49 – 7.96 (m, 2H), 7.87 (m, 3H), 7.65 (d, J = 7.6 Hz, 2H), 7.56 (s, 1H), 7.51 – 5.94 (m, 18H), 5.32 – 4.78 (m, 4H), 1.45 (m, 9H). ¹³C NMR (126 MHz, CDCl₃) δ 155.9, 155.1, 153.7, 145.6, 142.2, 140.3, 139.6, 135.6, 135.4, 134.5, 134.1, 132.3, 130.5, 129.8, 129.0, 128.9, 128.6, 128.4, 128.2, 128.1, 127.6, 127.2, 126.6, 125.1, 124.9, 124.5, 122.1, 120.4, 109.6, 80.5, 68.3, 67.9, 28.4. [α]D₂⁵ = 28.70 (c = 2.0, CHCl₃). m/z HRMS (ESI) found [M+H]⁺ 694.2903, C₄₃H₄₀N₃O₆⁺ requires 694.2912. HPLC: Chiralpak IB column, 95:05 hexanes/isopropanol, 1 ml/min; tR = 11.6 min (major), 13.2 min (minor); 99% ee.

(S)-4-amino-3-(2-methoxynaphthalen-1-yl)phenol (10a)

Scheme S13. Hydrogenation of products 7a, related to Scheme 6.

![Scheme S13](image)

To a solution of 7a (27 mg, 86% ee, 0.05 mmol) in MeOH (1 ml) was added Pd/C (10 mg, 10 % Pd, 55% w/w water). After stirring under H₂ atmosphere (1 atm) overnight, the reaction mixture was filtered through celite and concentrated under vacuum to give a residue, which was purified by flash column chromatography (Petroleum ether/EtOAc = 1:1) to give the product 10a (12 mg, 90% yield). ¹H NMR (400 MHz, Chloroform-d) δ 7.91 (d, J = 9.0 Hz, 1H), 7.85 – 7.77 (m, 1H), 7.49 – 7.43 (m, 1H), 7.40 – 7.32 (m, 3H), 6.79 (d, J = 2.5 Hz, 2H), 6.63 (dd, J = 2.2, 1.0 Hz, 1H), 3.88 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 154.3, 148.1, 138.5, 133.2, 129.7, 129.2, 127.9, 126.8, 124.9, 123.8, 123.4, 121.0, 118.4, 117.0, 115.8, 113.8, 56.8. IR (cm⁻¹): f = 3018, 2975, 1662, 1568, 1454, 1378, 1322, 1292, 1244, 1151, 698. [α]D₂⁵ = -6.00 (c = 0.25, CHCl₃). m/z HRMS (ESI) found [M+H]⁺ 266.1165, C₁₇H₉₂N₂O⁺ requires 266.1176. HPLC: Chiralpak IA column, 80:20 hexanes/isopropanol, 1 ml/min; tR = 12.6 min (major), 17.5 min (minor); 86% ee

(R)-2-(2-aminonaphthalen-1-yl)-3-methoxybenzene-1,4-diamine (11n)

Scheme S14. Hydrogenation of product 3n, related to Scheme 6.
To a solution of 3n (158 mg, 0.24 mmol) in MeOH (4 mL) was added 10% Pd/C (15 mg). After stirring under H₂ atmosphere (1 atm) overnight at room temperature, the reaction mixture was filtered through celite and concentrated under vacuum to give a residue, which was then dissolved in HCl/EA solution (2.0 M, 4 mL). After stirring for 1 h at room temperature, the reaction was quenched by adding saturated NaHCO₃ solution. The mixture was extracted with EtOAc for three times and the combined organic layers were dried over Na₂SO₄ and concentrated under vacuum to give a residue, which was purified by flash column chromatography (petroleum ether/EtOAc = 1:3) to give the product 11n (55 mg, 82%).

**Scheme S15.** Preparation of amine-thiourea catalyst from 3a, related to Scheme 6.

Tert-butyl (S)-(1-(5-acetamido-2-aminophenyl)naphthalen-2-yl)carbamate (12a)
To a solution of 3a (400 mg, 0.63 mmol) in dry DCM (10 mL) was added acetic anhydride (65 μL, 0.7 mmol) at room temperature. After stirring for 3 h, the solvent was removed under vacuum to give a residue, which was purified by flash column chromatography (petroleum ether/EtOAc = 2:1) to give the product.

To a solution of above product in MeOH (4 mL) was added 10% Pd/C (60 mg). After stirring under H₂ atmosphere (1 atm) overnight at 50 °C, the reaction mixture was filtered through celite and concentrated under vacuum to give a residue, which was purified by flash column chromatography (petroleum ether/EtOAc = 2:1) to give the product 12a (136 mg, 55%).
8.6 Hz, 1H), 6.58 (s, 1H), 3.40 (s, 2H), 2.04 (s, 3H), 1.45 (s, 9H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 168.6, 153.3, 141.8, 134.4, 132.5, 130.5, 129.9, 129.0, 128.1, 125.2, 124.7, 123.7, 122.9, 121.5, 120.2, 120.0, 116.4, 80.9, 28.4, 24.3.

$[\alpha]_D^{25}$ = 19.60 (c = 0.5, CHCl$_3$).

IR (cm$^{-1}$): $\nu$ = 3307, 2976, 1716, 1597, 1496, 1227, 1151, 1072, 820, 747. m/z HRMS (ESI) found [M+H]$^+$ 392.1957, C$_{23}$H$_{26}$N$_3$O$_3$ requires 392.1969. HPLC: Chiralpak IA column, 90:10 hexanes/isopropanol, 1 ml/min; t$_R$ = 16.3 min (minor), 17.3 min (major); 99% ee.

(S)-N-(3-(2-aminophthalen-1-yl)-4-(3,5-bis(trifluoromethyl)phenyl)thioureido)phenyl)acetamide (13a)

To a solution of 12a (99 mg, 0.25 mmol) in THF (2mL) was added 3,5-bis(trifluoromethyl)phenyl isothiocyanate (51 $\mu$L, 0.28 mmol) at rt. After stirring overnight at this temperature, the solvent was removed under vacuum to give a residue, which was purified by flash column chromatography (petroleum ether/EtOAc = 2:1) to afford the product.

The above product was dissolved in HCl/EA solution (2.0 M, 4mL) at 0°C. After stirring for 1h at this temperature, the reaction mixture was quenched by adding saturated NaHCO$_3$ solution. The mixture was extracted with EtOAc for three times and the combined organic layer was dried over Na$_2$SO$_4$ and concentrated under vacuum to give a residue, which was purified by flash column chromatography (petroleum ether/EtOAc = 1:1) to give the product 13a (87mg, 61%). $^1$H NMR (500 MHz, Acetone-d$_6$) $\delta$ 9.32 (s, 1H), 9.16 (s, 1H), 8.57 (s, 1H), 7.91 (s, 2H), 7.78 (dd, $J$ = 8.8, 2.5 Hz, 1H), 7.66 (d, $J$ = 8.8 Hz, 1H), 7.60 (d, $J$ = 8.8 Hz, 2H), 7.57 – 7.50 (m, 2H), 7.20 (d, $J$ = 8.4 Hz, 1H), 7.08 (ddd, $J$ = 8.3, 6.6, 1.4 Hz, 1H), 7.06 - 6.97 (m, 2H), 4.67 (s, 2H), 2.01 (s, 3H). $^{13}$C NMR (126 MHz, Acetone-d$_6$) $\delta$ 181.8, 169.3, 144.3, 142.8, 140.1, 135.3, 134.6, 133.0, 131.6 (q, $J$ = 33.2 Hz), 130.2 (d, $J$ = 2.2 Hz), 129.0, 128.6, 127.3, 125.5, 124.8, 124.4, 123.7, 123.4, 122.5, 120.2, 119.5, 118.0 (q, $J$ = 3.9 Hz), 114.8, 24.4. $[\alpha]_D^{25}$ = 13.10 (c = 1, CHCl$_3$). IR (cm$^{-1}$): $\nu$ = 3297, 2962, 1615, 1514, 1273, 1120, 812, 750, 678. m/z HRMS (ESI) found [M+H]$^+$ 563.1327, C$_{27}$H$_{21}$F$_6$N$_4$OS requires 563.1335. HPLC: Chiralpak IA column, 80:20 hexanes/isopropanol, 1 ml/min; t$_R$ = 7.3 min (minor), 15.6 min (major); 99% ee.

Application of amine-thiourea catalyst 13a:

Scheme S16. Application of amine-thiourea catalyst 13a, related to Scheme 6.

The procedure was adopted from the reported literature (Galzerano et al., 2009) by using the catalyst 13a.

3-(3-hydroxy-1-phenylpropyl)-3-methylindolin-2-one (16)
53%, 6:1 dr. The major diastereomers: $^1$H NMR (400 MHz, Chloroform-$d$) δ 7.97 (s, 1H), 7.30 (d, $J = 7.3$ Hz, 1H), 7.24 – 7.15 (m, 1H), 7.12 – 6.99 (m, 4H), 6.87 – 6.79 (m, 2H), 6.70 (d, $J = 7.7$ Hz, 1H), 3.45 (ddd, $J = 11.4$, 7.3, 4.3 Hz, 1H), 3.32 (ddd, $J = 10.7$, 8.2, 6.4 Hz, 1H), 3.21 (dd, $J = 12.6$, 2.8 Hz, 1H), 2.30 (ddt, $J = 15.7$, 7.8, 3.8 Hz, 1H), 2.09 (ddddd, $J = 12.9$, 8.5, 6.4, 3.2 Hz, 1H), 1.46 (s, 3H). [$\alpha$]$_{D}^{25} = -25.80$ (c = 1.0, CHCl$_3$). HPLC: Chiralpak IB column, 90:10 hexanes/isopropanol, 1 ml/min; $t_R$ = 9.6 min (major), 11.2 min (minor); 73% ee.
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