Enantioselective Copper-Catalyzed Cyanation of Remote C(sp³)-H Bonds Enabled by 1,5-Hydrogen Atom Transfer

**HIGHLIGHTS**
- Remote C-H functionalization
- Enantioselective cyanation
- High ee & excellent yields
- Low catalysts loading

![Enantioselective Cyanation of Remote C(sp³)-H Bonds](image)
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SUMMARY
The direct functionalization of C(sp³)-H bonds has led to the development of methods to access molecules or intermediates from basic chemicals in an atom- and step-economic fashion. Nevertheless, achieving high levels of chemo-, regio-, and enantioselectivity in these reactions remains challenging due to the ubiquity and low reactivity of C(sp³)-H bonds. Herein, we report an unprecedented protocol for enantioselective cyanation of remote C(sp³)-H bonds. With chiral Box-Cu complex as the catalyst, the reaction of N-fluorosulfonamide furnishes the corresponding products in excellent yields and high enantiomeric excess (ee) under mild reaction conditions. A radical relay pathway involving 1,5-hydrogen atom transfer (1,5-HAT) of N-center radicals followed by enantioselective cyanation of the in situ-formed benzyl radicals is proposed. This enantioselective copper-catalyzed cyanation thus offers insights into an efficient way for the synthesis of bioactive molecules for drug discovery.

INTRODUCTION
Synthesizing functional molecules in a rapid, efficient, and convenient manner still represents a significant challenge in organic synthesis (McMurry et al., 2011; Gutekunst and Baran, 2011; Yamaguchi et al., 2012; Karimov and Hartwig, 2018). The past several decades have witnessed the renaissance of C-H bond functionalization, which thus offers a unique solution for facile synthesis of functional molecules from basic chemicals (Giri et al., 2009; Colby et al., 2010; Lyons and Sanford, 2010; Newhouse and Baran, 2011; Sun et al., 2011; Wencel-Delord et al., 2011; Wendlandt et al., 2011; Liu et al., 2015; Davies and Morton, 2016; Rao and Shi, 2016; Liang and Jiao, 2017; Yang et al., 2017; Dong et al., 2017; Gensch et al., 2018). Specifically, the direct functionalization of C(sp³)-H bonds has led to the development of methods to access molecules or intermediates from simple starting materials in an atom- and step-economic fashion (Zhang et al., 2011; Baudoin, 2011; Rouquet and Chatani, 2013; Xie et al., 2014; Liu and Groves, 2015; He et al., 2016, 2017; Hartwig, 2016; Yi et al., 2017; Saint-Denis et al., 2018). Nevertheless, achieving high levels of chemo-, regio-, and enantioselectivity in these reactions remains challenging due to the ubiquity and low reactivity of C(sp³)-H bonds. To date, one efficient approach to asymmetric C(sp³)-H functionalization was the enantioselective insertion of chiral metallocarbene (Davies and Beckwith, 2003; Doyle et al., 2010; Davies and Morton, 2011; Davies and Manning, 2008; Lu and Zhang, 2011; Zheng and You, 2014; Schafer and Blakey, 2015; Newton et al., 2017) or metallonitrene (Davies and Manning, 2008; Lu and Zhang, 2011; Zheng and You, 2014; Schafer and Blakey, 2015; Newton et al., 2017; Müller and Fruit, 2003; Collet et al., 2011) species in situ generated into C-H bonds. The other known approach was transition-metal-catalyzed C(sp³)-H activation, which involves a stereocontrolled C-H cleavage to generate an enantioenriched organometallic intermediate for further functionalization (Saint-Denis et al., 2018). Despite recent advances in both approaches, the efficient and practical methods for enantioselective functionalization of remote C(sp³)-H bonds are still less developed.

As an alternative tactic, hydrogen-atom abstraction via radical pathway has long been used as a powerful tool to activate the C(sp³)-H bonds. Of note is a radical relay strategy for enantioselective functionalization of allylic (Zhou and Andrus, 2002) and benzylic (Zhang et al., 2016, 2019a, 2019b; Wang et al., 2018) C-H bonds has recently been developed, in which a benzylic or allylic radical generated by hydrogen-atom abstraction underwent asymmetric functionalization by a chiral copper catalysis. Although inert C(sp³)-H bonds are almost impossible to distinguish from other aliphatic C-H bonds on the alkyl side chain, 1-n-hydrogen-atom transfer strategy offers us a reliable solution to selectively cleave the remote C(sp³)-H bonds in a high chemo- and regioselective path. Starting from the pioneering work of Hofmann (Hofmann, 1817),...
1883), known as Hofmann–Löffler–Freytag (HLF) reaction with N-haloamines used as precursors to generate N-centered radical (Hofmann, 1883; Löffler and Freytag, 1909; Wolff, 1963; Neale, 1971; Mackiewicz and Furstoff, 1978), the selective cleavage of remote C(sp³)-H bonds via 1,5-HAT process is well documented (Robertson et al., 2001; Čeković, 2003; Chiba and Chen, 2014; Stateman et al., 2018; Chu and Rovis, 2016, 2018; Martínez and Muñiz, 2015; Wappes et al., 2016; Choi et al., 2016; Xia et al., 2018; Na and Alexanian, 2018). Although the early examples utilize transition metal to facilitate electron transfer, to further expand the scope of this remote C(sp³)-H functionalization process, many domino processes involving a metal-catalyzed cross-coupling pathway have developed (Scheme 1A) (Zhou and Andrus, 2002; Zhang et al., 2016, 2019a, 2019b, 2019c; Wang et al., 2018; Groendyke et al., 2016; Li et al., 2018; Liu et al., 2019; Bao et al., 2019). With the generation of N-centered radical initiating remote hydrogen transfer, the following cross-coupling reactions enabled by the recapture of in situ-generated carbon radical could be achieved with transition metals (Groendyke et al., 2016; Li et al., 2017, 2018; Liu et al., 2019; Bao et al., 2019; Zhang et al., 2019a, 2019b, 2019c; Yu et al., 2014). As our continuous efforts on selective cleavage of remote aliphatic C(sp³)-H via a 1,5-HAT process (Scheme 1B) (Wang et al., 2017a, 2017b), we envisioned that the recapture of in situ-generated carbon radical of 1,5-HAT by chiral metal catalyst, followed by reductive elimination from the chiral metal complex would realize enantioselective C(sp³)-H functionalizations, thus providing a convenient entry to optically pure α-cyano amines and their pharmaceutical derivatives (Figure 1) (Sugimoto et al., 2000; van de Waterbeemd et al., 2001; Abdel-Rahman et al., 2002). More recently, the remote C(sp³)-H functionalization was accomplished by the groups of Zhu (Bao et al., 2019) and Nagib (Zhang et al., 2019a, 2019b; 2019c), whereas the enantioselective remote C(sp³)-H cyanation reaction of excellent yield and high ee still remains as an unsolved problem.

Herein, we described the first example of N-radical initiated enantioselective copper-catalyzed cyanation of remote C(sp³)-H bonds with excellent yield and high enantioselectivity (up to 95% ee). This asymmetric

Scheme 1. Enantioselective C(sp³)-H Functionalization via Reductive Elimination from Chiral Transition-Metal Catalyst

(A) Previous work: copper-catalyzed benzylic or allylic C-H functionalizations.
(B) This work: copper-catalyzed remote C(sp³)-H cyanation enabled by 1,5-HAT.
(C) Proposed mechanism.
reaction has demonstrated high catalytic reactivity, excellent regio- and enantioselective control, low catalyst loading, mild conditions, and broad scope. The key to success is the recapture of the alkyl radical generated by selective cleavage of C(sp3)-H bond via 1,5-HAT with Box-Cu catalyst resulting in chiral copper cyanide for stereoselective reductive elimination (Wang et al., 2018). This radical relay strategy will offer a solution for regio- and enantioselective functionalization of remote C(sp3)-H bonds and provides an efficient way for facile synthesis of chiral \( \delta \)-cyano amines and their pharmaceutical derivatives.

**RESULTS AND DISCUSSION**

**Optimization of the Enantioselective Copper-Catalyzed Cyanation**

Our initial investigation commenced with N-fluorosulfonamide 1a used as the pilot substrate, along with trimethylsilyl cyanide (TMSCN) used as the coupling partner in the presence of a catalytic amount of Cu(MeCN)4PF6 (3 mol%) at room temperature. To our delight, the desired cyanation product 2a was obtained in 62% yield and 78% ee when chiral bis(oxazoline) ligand L1 was used (Entry 1, Table 1). To improve the enantioselectivity of this reaction, various chiral bis(oxazoline) ligands were next investigated. Gratifyingly, indanyl amino alcohol-derived bis(oxazoline) ligands (L2-L7) could afford almost the same good ee and normally satisfactory yield, whereas Pybox (L8) gave only trace amount of 2a (Entries 2–8). Lowering the reaction temperature to 10°C could further improve the ee to 90%, albeit with a relatively lower yield (52%, Entry 9). A careful investigation of various copper salts with the optimal bis(oxazoline) ligand (L6) were next performed, which indicated that a variety of Cu(I) and Cu(II) sources (Entries 10–12) gave higher ee, but with a low overall yield. Although a majority of H-abstraction byproduct of nitrogen was found after the reaction had run for 24 h, we proposed decreasing catalyst loading might improve the mass balance by reducing the amount of H-abstraction byproducts and allowing for a higher yield (Shu et al., 2017). As expected, lower catalyst loading to 1 mol% remarkably increased the yield to about 80% without a decline in ee (Entries 13–14).

To further improve the yield of this transformation, solvent effect was next studied with 1 mol% of CuSCN used as the catalyst, which showed DCE was the optimal solvent with excellent yield and a slightly lower ee (99% yield, 90% ee, Entry 17). Interestingly, a lower concentration and an enhancement of the ratio of ligand to copper salts (2/1) could slightly improve the ee to 92% (Entries 19–21), whereas further reducing the reaction temperature to 0°C resulted in an obvious drop in yield and 29% of 1a recovered from the reaction system (Entry 22). The absolute configuration of product 2a was assigned as (R) by single crystal X-ray diffraction.

**Scope of the Enantioselective Copper-Catalyzed Cyanation**

With the optimal reaction conditions in hand, we next explored the scope of this enantioselective cyanation of remote C(sp3)-H bonds (Figure 2). First, with respect to substituted benzenesulfonyl protecting groups (ArSO2), both electron-donating (1b-1c) and electron-withdrawing (1d-1e) substituents (R1) at para-position of the aryl rings gave the desired product in good to excellent yield along with excellent ee, among
| Entry | Cu cat.       | Ligand | Solvent | Yield (%) | ee (%) |
|-------|---------------|--------|---------|-----------|--------|
| 1     | Cu(MeCN)4PF6  | L1     | DCM     | 62        | 78     |
| 2     | Cu(MeCN)4PF6  | L2     | DCM     | 75        | 86     |
| 3     | Cu(MeCN)4PF6  | L3     | DCM     | 33        | 87     |
| 4     | Cu(MeCN)4PF6  | L4     | DCM     | 58        | 86     |
| 5     | Cu(MeCN)4PF6  | L5     | DCM     | 70        | 87     |
| 6     | Cu(MeCN)4PF6  | L6     | DCM     | 73        | 89     |
| 7     | Cu(MeCN)4PF6  | L7     | DCM     | 33        | 87     |
| 8     | Cu(MeCN)4PF6  | L8     | DCM     | trace     | –      |
| 9a    | Cu(MeCN)4PF6  | L6     | DCM     | 52        | 90     |
| 10a   | CuSCN         | L6     | DCM     | 43        | 92     |
| 11a   | Cu(OAc)2      | L6     | DCM     | 43        | 92     |
| 12a   | CuI           | L6     | DCM     | 30        | 92     |
| 13a,b | CuSCN         | L6     | DCM     | 81        | 91     |
| 14a,b | Cu(OAc)2      | L6     | DCM     | 78        | 92     |
| 15a,b | CuSCN         | L6     | MeCN    | 39        | 81     |
| 16a,b | CuSCN         | L6     | PhCl    | 84        | 88     |
| 17a,b | CuSCN         | L6     | DCE     | 99        | 90     |
| 18a,b | Cu(OAc)2      | L6     | DCE     | 91        | 90     |
| 19a,b,c | CuSCN   | L6     | DCE     | 92        | 91     |
| 20a,c,d | CuSCN   | L6     | DCE     | 98        | 91     |
| 21a,b,e | CuSCN   | L6     | DCE     | 99        | 92     |
| 22a,f | CuSCN         | L6     | DCE     | 64        | 92     |

Table 1. Optimization of Reaction Conditions
Reaction conditions: 1a (0.1 mmol, 1.0 equiv), TMSCN (1.2 equiv), Cu cat. (3 mol%), L (3.6 mol%), solvent (1.0 mL), rt, 2 d, Ar. Yields were determined by 1H NMR analysis using CH2Br2 as internal standard. The ee values were determined by HPLC analysis on a chiral stationary phase. DCM, dichloromethane; THF, tetrahydrofuran; DCE, 1,2-dichloroethane; Ac, acetyl.

*1°C, 3 days.
**Cu cat. (1 mol%), L6 (1.2 mol%).
***Solvent (2.0 mL).
****CuSCN (1 mol%), L6 (1.5 mol%).
*****CuSCN (1 mol%), L6 (2 mol%).
******O°C.
which para-CF$_3$ substituted substrate performed best with 97% yield and 93% ee. Considering the common availability and low cost, benzenesulfonyl group was selected as the N-protecting group to investigate the substituent effect (R2) of the aromatic ring linked to the alkyl chain. A variety of N-fluorosulfonamides 1 installed with ortho-, meta-, and para-substituents on the aryl rings were smoothly cyanated on the benzylic position in this asymmetric catalytic system, furnishing the corresponding products 2 with satisfactory yields and high ee (up to 95%). Both electron-donating, including Me (2f, 2o, 2s), "C$_6$H$_{11}$" (2h), "Bu (2g), PhO (2j), and MeO (2p), and electron-withdrawing groups, including F (2t), Cl (2i, 2q), Br (2m), and CF$_3$ (2n, 2r, 2u), were well compatible with the optimized conditions. Notably, Br (2m) as well as inert halides including F and Cl on the aromatic ring offered the synthetic potential for further transformations through transition-metal-catalyzed cross-coupling methods. Moreover, polycyclic arenes, such as naphthalene (2w-2x), and heteroaromatic ring, such as thiophene (2y), were well tolerated in this reaction with high ee and good yield. To our surprise, the incorporation of two methyl groups to the alkyl chain to induce the Thorpe-Ingold effect failed to give higher ee (2z), possibly because the increased steric hindrance of the methyl groups hampered the stereo control of chiral copper catalyst.

Mechanistic Studies
To gain some insights into the mechanism of this asymmetric cyanation of remote C(sp$^3$)-H bonds, we next carried out a series of control experiments. Firstly, the addition of 2.0 equiv of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) into the standard conditions completely inhibited the reaction, and 1a was
100% recovered from the reaction system (Scheme 2A), which was consistent with our previously noted hypothesis that this reaction may proceed via a radical path (Scheme 1). Although the coupling product of TEMPO and 1a was not isolated, compounds 4 and 6 had been designed and synthesized to trap the corresponding radicals. Accordingly, the subjection of alkene 4 into the reaction system afforded 5-exo cyclization product 5 in 62% yield, indicating an N-centered radical was involved in the catalytic cycle (Scheme 2B). Meanwhile, a radical clock experiment with 6 furnished the ring-opening product 7 in 73% yield, which suggested a carbon-centered radical generated via N-radical initiated 1,5-HAT (Scheme 2C). Secondly, competition experiments had been performed using N-fluorosulfonamide substrates with different substituents on respective aryl ring. Indeed, a competition experiment between 1c and 1e with para-OMe or CF3 groups on the aryl rings in the arylsulfonyl protecting groups showed that trifluoromethylated substrate reacted faster than methoxylated substrate (16% yield to 9% yield). On the other hand, the competition experiment between 1j and 1n with para-OPh or CF3 groups on the alkylated aryl rings afforded the desired products 2j and 2n in almost the same yields (15% and 17%, Scheme 2D). All these results indicated that a copper-involved single electron transfer process for the cleavage of N-F bond might be the rate-determining step (Zhang et al., 2016, 2019a; Shu et al., 2017; Shekhar et al., 2018, 2019b, 2019c). It should be noted that besides our proposed mechanism as shown in Scheme 1C, an alternative

Scheme 2. Mechanistic Studies
(A) The radical trapping experiment with TEMPO.
(B) N-radical trapping experiment.
(C) Radical clock experiment.
(D) Competition experiments.
mechanism involving the direct cyano group enantioselective transfer from chiral copper cyanide could not be excluded at this stage (Liu et al., 2018; Xiao et al., 2019).

Conclusion
In summary, we have developed a nitrogen-centered radical-initiated enantioselective copper-catalyzed cyanation of remote C(sp³)-H bonds with high yield and enantioselectivity (up to 95% ee). This method has demonstrated high catalytic reactivity, excellent regio- and enantioselective control, low catalyst loading, mild conditions, and broad scope. This radical relay strategy will offer a solution for region- and enantioselective functionalization of remote C(sp³)-H bonds and provides an efficient way for facile synthesis of chiral α-cyano amines and their pharmaceutical derivatives. Mechanistic studies indicate that this transformation undergoes a radical relay pathway involving a 1,5-HAT process. Further exploration on enantioselective functionalizations of remote C(sp³)-H bonds are currently ongoing in our laboratory.

Limitations of the Study
Starting materials were cyanated only on the benzylic position under the current reaction conditions.

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

DATA AND CODE AVAILABILITY
The structures of 2a reported in this article have been deposited in the Cambridge Crystallographic Data Center under accession numbers CCDC: 1911620.

SUPPLEMENTAL INFORMATION
Supplemental Information can be found online at https://doi.org/10.1016/j.isci.2019.10.048.

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AUTHOR CONTRIBUTIONS
C.-Y. W. and Z.-Y. Q. designed and performed the experiments. Y.-L. H., R.-X. J., and Q. L. helped to complete the experiments. X.-S. W. directed the project and wrote the manuscript. All authors interpreted the results on the manuscript.

DECLARATION OF INTERESTS
The authors declare no competing interests.

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Supplemental Information

Enantioselective Copper-Catalyzed Cyanation of Remote C(sp³)-H Bonds Enabled by 1,5-Hydrogen Atom Transfer

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Transparent Methods

I. General Information

NMR spectra were recorded on Bruker-400 MHz NMR spectrometer (400 MHz for $^1$H; 101 MHz for $^{13}$C and 376 MHz for $^{19}$F { $^1$H, $^{13}$C decoupled}). $^1$H NMR spectra were referenced relative to internal Si(Me)$_4$ (TMS) at δ 0.00 ppm. $^{13}$C NMR spectra were recorded at ambient temperature on Bruker-400 (100 MHz) spectrometers and are referenced relative to CDCl$_3$ at δ 77.16 ppm. The $^{13}$C NMR spectra were obtained with $^1$H decoupling. Data for $^1$H, $^{13}$C, $^{19}$F NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, q = quartet, quint = quintet, br = broad), integration, and coupling constant (Hz). High resolution mass spectra were recorded on P-SIMS-Gly of BrukerDaltonics Inc. using ESI-TOF (electrospray ionization-time of flight). High performance liquid chromatography was performed on shimadzu Series HPLC, using AD-H, OD-H, AS-H chiral column eluted with a mixture of hexane and isopropyl alcohol. TMSCN was purchased from energy-chemical, CuSCN was purchased from TCI. And DCE was purchased from J&K Chemical Reagent Co., Ltd.
### II. Tables of the Optimization of Reaction Conditions of Enantioselective Copper-catalyzed Cyanation

Table S1. Solvent Screening$^{[a]}$, related to Table 1.

| Entry | Solvent | $2a^{[b]}$ | $3a^{[b]}$ | $ee^{[c]}$ |
|-------|---------|------------|------------|-----------|
| 1     | MeCN    | 39%        | 40%        | 81%       |
| 2     | DCE     | 99%        | 8%         | 90%       |
| 3     | THF     | 20%        | 78%        | 89%       |
| 4     | PhCl    | 84%        | 15%        | 88%       |
| 5     | PhCF$_3$| 84%        | 14%        | 87%       |
| 6     | DCM     | 78%        | 26%        | 91%       |

$^{[a]}$ Reaction conditions: 1a (0.1 mmol, 1.0 equiv), CuSCN (1 mol%), L6 (1.2 mol%), TMSCN (1.2 equiv), solvent (1.0 mL), Ar, 10 °C, 3 d.
$^{[b]}$ Yields detected by crude $^1$H NMR with CH$_3$Br$_2$ as internal standard.
$^{[c]}$ Enantiomeric excess ($ee$) values detected by HPLC on a chiral stationary phase.

Table S2. Catalyst Screening$^{[a]}$, related to Table 1.

| Entry | Solvent | Cu cat. (1 mol%) | L6 (1.2 mol%) | $2a^{[b]}$ | $3a^{[b]}$ | $ee^{[c]}$ |
|-------|---------|-----------------|---------------|------------|------------|-----------|
| 1     | CuI     | 69%             | 23%           | 90%        |
| 2     | CuCN    | 51%             | 32%           | 88%        |
| 3     | Cu(MeCN)$_2$PF$_6$ | trace     | 0%           | -          |
| 4     | Cu(OAc)$_2$ | 91%         | 13%          | 90%        |
| 5     | Cu(acac)$_2$ | 70%          | 21%          | 90%        |
| 6     | Cu(OTf)$_2$ | 0%          | 0%           | -          |

$^{[a]}$ Reaction conditions: 1a (0.1 mmol, 1.0 equiv), Cu cat. (1 mol%), L6 (1.2 mol%), TMSCN (1.2 equiv), DCE (1.0 mL), Ar, 10 °C, 3 d.
$^{[b]}$ Yields detected by crude $^1$H NMR with CH$_3$Br$_2$ as internal standard.
$^{[c]}$ Enantiomeric excess ($ee$) values detected by HPLC on a chiral stationary phase.

Table S3. Loading of Catalyst Screening$^{[a]}$, related to Table 1.

| Entry | X | $2a^{[b]}$ | $3a^{[b]}$ | $ee^{[c]}$ |
|-------|---|------------|------------|-----------|
| 1     | 0.5 | 86%        | 11%        | 89%       |
| 2     | 1.5 | 60%        | 30%        | 90%       |
| 3     | 2.0 | 55%        | 20%        | 91%       |

$^{[a]}$ Reaction conditions: 1a (0.1 mmol, 1.0 equiv), CuSCN (X mol%), L6 (1.2X mol%), TMSCN (1.2 equiv), DCE (1.0 mL), Ar, 10 °C, 3 d.
$^{[b]}$ Yields detected by crude $^1$H NMR with CH$_3$Br$_2$ as internal standard.
$^{[c]}$ Enantiomeric excess ($ee$) values detected by HPLC on a chiral stationary phase.
Table S4. Concentration Screening$^{[a]}$, related to Table 1.

| Entry | Y   | 1a$^{[h]}$ | 2a$^{[h]}$ | 3a$^{[h]}$ | ee$^{[i]}$ |
|-------|-----|-----------|-----------|-----------|-----------|
| 1     | 0.05| 0%        | 92%       | 13%       | 91%       |
| 2     | 0.2 | 45%       | 22%       | 12%       | 90%       |

[a] Reaction conditions: 1a (0.1 mmol, 1.0 equiv), CuSCN (1 mol%), L6 (1.2 mol%), TMSCN (1.2 equiv), Ar, 10 °C, 3 d.
[b] Yields detected by crude $^1$H NMR with CH$_2$Br$_2$ as internal standard.
[c] Enantiomeric excess (ee) values detected by HPLC on a chiral stationary phase.

Table S5. Ligand Screening$^{[a]}$, related to Table 1.

| Entry | Ligand | 2a$^{[h]}$ | 3a$^{[h]}$ | ee$^{[i]}$ |
|-------|--------|-----------|-----------|-----------|
| 1     | L2     | 92%       | 16%       | 88%       |
| 2     | L3     | 72%       | 5%        | 87%       |
| 3     | L4     | 98%       | 4%        | 87%       |
| 4     | L5     | 89%       | 15%       | 91%       |
| 5     | L7     | 74%       | 25%       | 82%       |

[a] Reaction conditions: 1a (0.1 mmol, 1.0 equiv), CuSCN (1 mol%), ligand (1.2 mol%), TMSCN (1.2 equiv), Ar, DCE (2.0 mL), 10 °C, 3 d.
[b] Yields detected by crude $^1$H NMR with CH$_2$Br$_2$ as internal standard.
[c] Enantiomeric excess (ee) values detected by HPLC on a chiral stationary phase.

Table S6. Loading of Ligand Screening$^{[a]}$, related to Table 1.

| Entry | Z    | 2a$^{[h]}$ | 3a$^{[h]}$ | ee$^{[i]}$ |
|-------|------|-----------|-----------|-----------|
| 1     | 1.5  | 98%       | 4%        | 91%       |
| 2     | 2.0  | 99%       | 5%        | 92%       |

[a] Reaction conditions: 1a (0.1 mmol, 1.0 equiv), CuSCN (1 mol%), L6 (2 mol%), TMSCN (1.2 equiv), Ar, DCE (2.0 mL), 10 °C, 3 d.
[b] Yields detected by crude $^1$H NMR with CH$_2$Br$_2$ as internal standard.
[c] Enantiomeric excess (ee) values detected by HPLC on a chiral stationary phase.

Table S7. Temperature Screening$^{[a]}$, related to Table 1.

| Entry | 1a$^{[h]}$ | 2a$^{[h]}$ | 3a$^{[h]}$ | ee$^{[i]}$ |
|-------|------------|-----------|-----------|-----------|
| 1     | 29%        | 64%       | 4%        | 92%       |

[a] Reaction conditions: 1a (0.1 mmol, 1.0 equiv), CuSCN (1 mol%), L6 (2 mol%), TMSCN (1.2 equiv), Ar, DCE (2.0 mL), 0 °C, 3 d.
[b] Yields detected by crude $^1$H NMR with CH$_2$Br$_2$ as internal standard.
[c] Enantiomeric excess (ee) values detected by HPLC on a chiral stationary phase.

Table S8. Controlling Experiments$^{[a]}$, related to Table 1.
| Entry | Reaction conditions | 2a<sup>[a]</sup> | 3a<sup>[b]</sup> | ee<sup>[c]</sup> |
|-------|---------------------|-----------------|-----------------|-----------------|
| 1     | w/o CuSCN           | 0%              | 0%              | -               |
| 2     | w/o L6              | trace           | 0%              | -               |

[a] Reaction conditions: 1a (0.1 mmol, 1.0 equiv), CuSCN (1 mol%), L6 (2 mol%), TMSCN (1.2 equiv), Ar, DCE (2.0 mL), 0 °C, 3 d.
[b] Yields detected by crude $^1$H NMR with CH$_3$Br$_2$ as internal standard.
[c] Enantiomeric excess (ee) values detected by HPLC on a chiral stationary phase.
III. Experimental procedures and data

1. Synthesis of Starting Materials

**General Procedure A – N-F sulfonamides**

![Chemical Structure](image)

Synthesized according to a reported procedure (Wang et al., 2017): In a 100 mL round-bottomed flask, to a stirred suspension of NaH (6 mmol, 60 wt% in mineral oil) in anhydrous CH<sub>2</sub>Cl<sub>2</sub> (24 mL), a solution of sulfonamide (3 mmol) in anhydrous CH<sub>2</sub>Cl<sub>2</sub> (6 mL) was slowly added at room temperature under an N<sub>2</sub> atmosphere. After stirring for 30 min, N-fluorobenzenesulfonimide (NFSI, 5.67 g, 18 mmol) was added. The reaction mixture was stirred for another 6 h. Upon completion, the reaction was quenched by the addition of water. The mixture was extracted with DCM (3 × 30 mL) and the organic layers were combined, washed with brine, and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. The crude mixture was filtered through celite and concentrated. The resulting residue was purified by column chromatography on silica gel with a gradient eluent of petroleum ether and ethyl acetate.

![Chemical Structure](image)

Synthesized according to a reported procedure (Zhang et al., 2019). To a clean, dry round bottom flask was added a magnetic stir bar and primary amine (1 equiv) under nitrogen at RT. The substrate was dissolved in DCM [0.2 M], followed by addition of freshly distilled triethylamine (1.5 equiv), 4-Dimethylaminopyridine (0.1 equiv) and p-toluenesulfonyl chloride (1.1 equiv) were subsequently added. The reaction was allowed to stir at room temperature overnight. H<sub>2</sub>O was added to the reaction and the aqueous layer was extracted DCM (3 × 100 mL). The combined organic layers were washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated in vacuo. The crude material was purified by silica gel chromatography.

![Chemical Structure](image)

Synthesized according to a reported procedure (Zhang et al., 2019). To a clean, dry round bottom flask was added a magnetic stir bar, the starting carboxylic acid (1.0 equiv), 4-Dimethylaminopyridine (1.5 equiv) and benzenesulfonamide (1.0 equiv) under nitrogen at room temperature. The mixture was
dissolved in DCM, followed by addition of EDCI (1.5 equiv). The reaction was allowed to stir at room temperature overnight. Upon completion, 4N HCl was added, the organic phase was collected, and the aqueous layer was extracted three times with DCM. The combined organic phase was washed with brine, dried over Na₂SO₄, and concentrated in vacuo. The crude mixture was then taken onto the reduction step.

To a dry round bottom flask, was added a magnetic stir bar, the starting amide (1.0 equiv), and lithium aluminum hydride (2.0 equiv) under nitrogen. Reaction was cooled to 0 °C and slowly dissolved in THF. The reaction was monitored by TLC and upon consumption of starting material, the mixture was cooled to 0 °C and quenched carefully by addition of a 1 M solution of sodium hydroxide. The reaction was allowed to warm to room temperature and stirred for 20 minutes. The mixture was filtered through celite and the resulting clear solution was dried over Na₂SO₄ and concentrated in vacuo. Final substrates were purified by silica gel chromatography.

2. Synthesis of Products

**General Procedure B** – Enantioselective 1,5-HAT cyanation

**Preparation of catalyst solution A.** To a 25 mL sealed tube, CuSCN (1.1 mg, 0.009 mmol), chiral bisoxazoline ligand (IR, 2S) – L₆ (6.9 mg, 0.018 mmol) were added in degassed DCE (18.0 mL) under Ar atmosphere. The tube was sealed with a Teflon-lined cap, then the mixture was stirred at room temperature for 30 minutes. The solution A was used immediately.

To a sealed tube, solution A (4.0 mL), TMSCN (23.8 mg, 30 µL, 0.24 mmol, 1.2 equiv) and substrate were sequentially added under Ar atmosphere. The tube was sealed with a Teflon-lined cap, and the mixture was stirred at 10 °C for three days. After the reaction was completed, the mixture was concentrated. Then the residue was purified by silica gel chromatography with petroleumether and ethylacetate (PE/EA = 5:1) to afford the product.
3. Analytical data for compounds

1. N-F sulfonamides:

N-fluoro-N-(4-phenylbutyl)benzenesulfonamide (1a)

Prepared following general procedure A the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 19/1 as the eluent) as a yellow solid (664 mg, 72% yield). $^1$H NMR (400 MHz, Chloroform-$d$) δ 7.99 – 7.88 (m, 2H), 7.78 – 7.69 (m, 1H), 7.65 – 7.56 (m, 2H), 7.31 – 7.23 (m, 2H), 7.22 – 7.11 (m, 3H), 3.23 (dt, $J = 40.7$, 6.4 Hz, 2H), 2.63 (t, $J = 7.0$ Hz, 2H), 1.83 – 1.66 (m, 4H). $^{13}$C NMR (101 MHz, Chloroform-$d$) δ 141.80, 135.00, 132.11, 130.04, 129.40, 128.49, 126.03, 53.60 (d, $J = 12.5$ Hz), 35.41, 28.41, 25.97. $^{19}$F NMR (376 MHz, Chloroform-$d$) δ -49.82 (t, $J = 40.6$ Hz). HRMS (ESI) ($m/z$): [M+Na]$^+$ calcld. for C$_{16}$H$_{18}$FNO$_2$SNa: 330.0940, found: 330.0914.

N-fluoro-4-methyl-N-(4-phenylbutyl)benzenesulfonamide (1b)

Prepared following general procedure A the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 19/1 as the eluent) as a light yellow solid (571 mg, 59% yield). The NMR spectra were identical to the reference.

N-fluoro-4-methoxy-N-(4-phenylbutyl)benzenesulfonamide (1c)

Prepared following general procedure A the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 19/1 as the eluent) as a yellow solid (597 mg, 62% yield). The NMR spectra were identical to the reference.

4-chloro-N-fluoro-N-(4-phenylbutyl)benzenesulfonamide (1d)

Prepared following general procedure A the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 19/1 as the eluent) as a light yellow solid (655 mg, 64% yield). $^1$H NMR (400 MHz, Chloroform-$d$) δ 7.84 – 7.75 (m, 2H), 7.55 – 7.46 (m, 2H), 7.25 – 7.16 (m, 2H), 7.15 – 7.03 (m, 3H), 3.17 (dt, $J = 40.5$, 5.6 Hz, 2H), 2.56 (t, $J = 6.2$ Hz, 2H), 1.77 – 1.56 (m, 4H). $^{13}$C NMR (101 MHz, Chloroform-$d$) δ 142.01, 141.74, 131.39, 130.62, 129.81, 128.51, 128.48, 126.06, 53.50 (d, $J = 12.5$ Hz), 35.40, 28.37, 25.93. $^{19}$F NMR (376 MHz, Chloroform-$d$) δ -49.50 (t, $J = 40.5$ Hz). HRMS (ESI) ($m/z$): [M+Na]$^+$ calcld. for C$_{16}$H$_7$ClFNO$_2$SNa: 364.0550, found: 364.0524.

N-fluoro-N-(4-phenylbutyl)-4-(trifluoromethyl)benzenesulfonamide (1e)

Prepared following general procedure A the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 19/1 as the eluent) as a light yellow solid (617 mg, 55% yield). $^1$H NMR (400 MHz, Chloroform-$d$) δ 8.07 (d, $J = 8.2$ Hz, 2H), 7.87 (d, $J = 8.3$ Hz, 2H), 7.31 – 7.25 (m, 2H), 7.22 – 7.12 (m, 3H), 3.28 (dt, $J = 40.3$, 6.5 Hz, 2H), 2.64 (t, $J = 7.0$ Hz, 2H), 1.83 – 1.70 (m, 4H). $^{13}$C NMR (101 MHz, Chloroform-$d$) δ 141.70, 136.54 (q, $J = 33.3$ Hz), 136.00, 130.61, 128.54, 128.50, 126.55 (q, $J = 3.6$ Hz), 126.10, 123.08 (q, $J = 273.2$ Hz), 53.39 (d, $J = 12.6$ Hz), 35.40, 28.35,
25.93. $^{19}$F NMR (376 MHz, Chloroform-$d$) $\delta$ -49.57 (t, $J = 40.3$ Hz), -63.36 (s). HRMS (ESI) ($m/z$): [M+N+] calcd. for $C_{17}H_{17}F_2NO_2SNa$: 398.0814, found: 398.0790.

N-fluoro-N-(4-(p-tolyl)butyl)benzenesulfonamide (1f)

Prepared following general procedure A the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 19/1 as the eluent) as a light yellow oil (439 mg, 46% yield). $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.98 - 7.89 (m, 2H), 7.78 - 7.70 (m, 1H), 7.65 - 7.57 (m, 2H), 7.12 - 7.01 (m, 4H), 3.23 (dt, $J = 40.7$, 6.5 Hz, 2H), 2.59 (t, $J = 7.0$ Hz, 2H), 2.31 (s, 3H), 1.79 - 1.67 (m, 4H). $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 138.72, 135.48, 134.99, 132.16, 130.05, 129.39, 129.18, 128.37, 53.61 (d, $J = 12.5$ Hz), 34.96, 28.53, 25.97, 21.13. $^{19}$F NMR (376 MHz, Chloroform-$d$) $\delta$ -49.86 (t, $J = 40.7$ Hz). HRMS (ESI) ($m/z$): [M+N+] calcd. for $C_{17}H_{20}FNO_2SNa$: 344.1096, found: 344.1086.

N-(4-(4-(tert-butyl)phenyl)butyl)-N-fluorobenzenesulfonamide (1g)

Prepared following general procedure A the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 19/1 as the eluent) as a light yellow oil (373 mg, 34% yield). $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.99 - 7.90 (m, 2H), 7.78 - 7.70 (m, 1H), 7.65 - 7.56 (m, 2H), 7.29 (d, $J = 8.3$ Hz, 2H), 7.09 (d, $J = 8.2$ Hz, 2H), 3.24 (dt, $J = 40.7$, 6.4 Hz, 2H), 2.60 (t, $J = 7.1$ Hz, 2H), 1.83 - 1.67 (m, 4H), 1.30 (s, 9H). $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 148.83, 138.73, 135.00, 132.17, 130.06, 129.40, 128.14, 125.38, 53.62 (d, $J = 12.5$ Hz), 34.86, 34.49, 31.54, 28.42, 26.06. $^{19}$F NMR (376 MHz, Chloroform-$d$) $\delta$ -49.79 (t, $J = 40.7$ Hz). HRMS (ESI) ($m/z$): [M+N+] calcd. for $C_{20}H_{26}FNO_2SNa$: 386.1566, found: 386.1570.

N-fluoro-N-(4-(4-pentylphenyl)butyl)benzenesulfonamide (1h)

Prepared following general procedure A the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 19/1 as the eluent) as a white solid (581 mg, 51% yield). $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 8.00 - 7.85 (m, 2H), 7.78 - 7.68 (m, 1H), 7.66 - 7.54 (m, 2H), 7.14 - 6.96 (m, 4H), 3.23 (dt, $J = 40.7$, 6.0 Hz, 2H), 2.67 - 2.47 (m, 4H), 1.82 - 1.66 (m, 4H), 1.65 - 1.52 (m, 2H), 1.40 - 1.23 (m, 4H), 0.88 (t, $J = 6.3$ Hz, 3H). $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 140.62, 138.92, 134.99, 132.16, 130.05, 129.39, 128.51, 128.34, 53.63 (d, $J = 12.5$ Hz), 35.65, 35.00, 31.69, 31.40, 28.49, 26.01, 22.69, 14.18. $^{19}$F NMR (376 MHz, Chloroform-$d$) $\delta$ -49.83 (t, $J = 40.7$ Hz). HRMS (ESI) ($m/z$): [M+N+] calcd. for $C_{21}H_{28}FNO_2SNa$: 400.1722, found: 400.1714.

N-(4-(1,1'-biphenyl)-4-yl)butyl]-N-fluorobenzenesulfonamide (1i)

Prepared following general procedure A the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 19/1 as the eluent) as a white solid (520 mg, 45% yield). $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.98 - 7.90 (m, 2H), 7.77 - 7.71 (m, 1H), 7.64 - 7.55 (m, 4H), 7.51 (d, $J = 8.0$ Hz, 2H), 7.46 - 7.39 (m, 2H), 7.35 - 7.29 (m, 1H), 7.23 (d, $J = 8.0$ Hz, 2H), 3.26 (dt, $J = 40.7$, 6.2 Hz, 2H), 2.68 (t, $J = 6.8$ Hz, 2H), 1.83 - 1.75 (m, 4H). $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 141.14, 140.94, 139.03, 135.02, 132.15, 130.06, 129.41, 128.93, 128.86, 127.25, 127.18, 127.12, 53.60 (d, $J = 12.5$ Hz), 35.05, 28.39, 26.02. $^{19}$F NMR (376 MHz, Chloroform-$d$) $\delta$ -
N-fluoro-N-(4-(4-phenoxypbenyl)butyl)benzenesulfonamide (1j)

Prepared following general procedure A the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 19/1 as the eluent) as a light yellow oil (332 mg, 28% yield). $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 8.02 – 7.87 (m, 2H), 7.80 – 7.69 (m, 1H), 7.68 – 7.56 (m, 2H), 7.36 – 7.29 (m, 2H), 7.15 – 7.04 (m, 3H), 7.03 – 6.96 (m, 2H), 6.96 – 6.88 (m, 2H), 3.25 (dt, $J = 40.7$, 6.3 Hz, 2H), 2.62 (t, $J = 6.9$ Hz, 2H), 1.86 – 1.64 (m, 4H). $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 157.70, 155.34, 136.80, 135.03, 132.15, 130.07, 129.81, 129.70, 129.42, 123.08, 119.17, 118.66, 53.59 (d, $J = 12.5$ Hz), 34.71, 28.55, 25.96. $^{19}$F NMR (376 MHz, Chloroform-$d$) $\delta$ -49.81 (t, $J = 40.6$ Hz). HRMS (ESI) (m/z): [M+Na]$^+$ calcd. for C$_{22}$H$_{23}$FNO$_2$SNa: 406.1253, found: 406.1250.

N-fluoro-N-(4-(4-(trifluoromethoxy)phenyl)butyl)benzenesulfonamide (1k)

Prepared following general procedure A the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 19/1 as the eluent) as a colourless oil (835 mg, 71% yield). $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.98 – 7.90 (m, 2H), 7.79 – 7.70 (m, 1H), 7.66 – 7.58 (m, 2H), 7.17 (d, $J = 8.7$ Hz, 2H), 7.11 (d, $J = 8.2$ Hz, 2H), 3.24 (dt, $J = 40.6$, 6.0 Hz, 2H), 2.64 (t, $J = 6.8$ Hz, 2H), 1.82 – 1.66 (m, 4H). $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 147.56, 140.55, 135.07, 132.05, 130.04, 129.71, 129.43, 121.09, 120.62 (q, $J = 256.5$ Hz), 53.52 (d, $J = 12.5$ Hz), 34.72, 28.32, 25.89. $^{19}$F NMR (376 MHz, Chloroform-$d$) $\delta$ -49.82 (t, $J = 40.6$ Hz), -57.92 (s). HRMS (ESI) (m/z): [M+Na]$^+$ calcd. for C$_{17}$H$_{19}$FNO$_3$SNa: 414.0763, found: 414.0773.

N-(4-(4-chlorophenyl)butyl)-N-fluorobenzenesulfonamide (1l)

Prepared following general procedure A the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 19/1 as the eluent) as a light yellow oil (483 mg, 47% yield). $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 8.00 – 7.88 (m, 2H), 7.79 – 7.70 (m, 1H), 7.67 – 7.56 (m, 2H), 7.23 (d, $J = 8.4$ Hz, 2H), 7.08 (d, $J = 8.4$ Hz, 2H), 3.23 (dt, $J = 40.6$, 6.3 Hz, 2H), 2.60 (t, $J = 7.0$ Hz, 2H), 1.81 – 1.65 (m, 4H). $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 140.22, 135.05, 132.06, 131.73, 130.03, 129.83, 129.42, 128.58, 53.51 (d, $J = 12.5$ Hz), 34.74, 28.27, 25.86. $^{19}$F NMR (376 MHz, Chloroform-$d$) $\delta$ -49.81 (t, $J = 40.6$ Hz). HRMS (ESI) (m/z): [M+Na]$^+$ calcd. for C$_{16}$H$_{17}$ClFNO$_2$SNa: 364.0550, found: 364.0548.

N-(4-(4-bromophenyl)butyl)-N-fluorobenzenesulfonamide (1m)

Prepared following general procedure A the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 19/1 as the eluent) as a light yellow oil (243 mg, 21% yield). $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.98 – 7.88 (m, 2H), 7.79 – 7.70 (m, 1H), 7.67 – 7.58 (m, 2H), 7.38 (d, $J = 8.4$ Hz, 2H), 7.03 (d, $J = 8.4$ Hz, 2H), 3.23 (dt, $J = 40.6$, 6.4 Hz, 2H), 2.59 (t, $J = 7.0$ Hz, 2H), 1.81 – 1.65 (m, 4H). $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 140.74, 135.05, 132.10, 131.55, 130.26, 130.04, 129.42, 119.77, 53.49 (d, $J = 12.5$ Hz), 34.81, 28.21, 25.87. $^{19}$F NMR (376 MHz,
Chloroform-\(d\) \(\delta\) -49.75 (t, \(J = 40.5\) Hz). HRMS (ESI) (\(m/z\)): [M+Na]\(^+\) calcd. for \(C_{16}H_{17}BrFNO_2SNa\): 408.0045, found: 408.0040.

N-fluoro-N-(4-(4-(trifluoromethyl)phenyl)butyl)benzenesulfonamide (1n)

Prepared following general procedure A the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 19/1 as the eluent) as a colourless oil (474 mg, 42% yield). \(^1\)H NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 8.01 – 7.85 (m, 2H), 7.79 – 7.71 (m, 1H), 7.65 – 7.58 (m, 2H), 7.53 (d, \(J = 8.0\) Hz, 2H), 7.27 (d, \(J = 7.4\) Hz, 2H), 3.25 (dt, \(J = 40.5, 5.8\) Hz, 2H), 2.70 (t, \(J = 6.6\) Hz, 2H), 1.89 – 1.63 (m, 4H). \(^{13}\)C NMR (101 MHz, Chloroform-\(d\)) \(\delta\) 145.92, 135.08, 132.06, 130.04, 129.44, 128.80, 128.44 (q, \(J = 32.3\) Hz), 125.44 (q, \(J = 3.8\) Hz), 124.44 (q, \(J = 271.8\) Hz), 53.45 (d, \(J = 12.4\) Hz), 35.24, 28.10, 25.89. \(^{19}\)F NMR (376 MHz, Chloroform-\(d\)) \(\delta\) -49.81 (t, \(J = 40.5\) Hz), -62.30 (s). HRMS (ESI) (\(m/z\)): [M+Na]\(^+\) calcd. for \(C_{16}H_{17}F_2NO_2SNa\): 398.0814, found: 398.0815.

N-fluoro-N-(4-(m-tolyloxy)butyl)benzenesulfonamide (1o)

Prepared following general procedure A the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 19/1 as the eluent) as a light yellow oil (447 mg, 46% yield). \(^1\)H NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 8.00 – 7.86 (m, 2H), 7.78 – 7.69 (m, 1H), 7.67 – 7.54 (m, 2H), 7.16 (t, \(J = 7.5\) Hz, 1H), 7.07 – 6.88 (m, 3H), 3.23 (dt, \(J = 40.7, 5.9\) Hz, 2H), 2.59 (t, \(J = 6.6\) Hz, 2H), 2.31 (s, 3H), 1.81 – 1.66 (m, 4H). \(^{13}\)C NMR (101 MHz, Chloroform-\(d\)) \(\delta\) 141.74, 138.02, 134.99, 132.09, 130.02 (d, \(J = 0.6\) Hz), 129.39, 129.30, 128.37, 126.75, 125.48, 53.63 (d, \(J = 12.7\) Hz), 35.33, 28.42, 26.01, 21.51. \(^{19}\)F NMR (376 MHz, Chloroform-\(d\)) \(\delta\) -49.83 (t, \(J = 40.7\) Hz). HRMS (ESI) (\(m/z\)): [M+Na]\(^+\) calcd. for \(C_{17}H_{20}FNO_2SNa\): 344.1096, found: 344.1092.

N-fluoro-N-(4-(3-methoxyphenyl)butyl)benzenesulfonamide (1p)

Prepared following general procedure A the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 19/1 as the eluent) as a light yellow oil (476 mg, 47% yield). \(^1\)H NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 8.00 – 7.90 (m, 2H), 7.78 – 7.70 (m, 1H), 7.66 – 7.56 (m, 2H), 7.19 (t, \(J = 7.8\) Hz, 1H), 6.82 – 6.64 (m, 3H), 3.79 (s, 3H), 3.23 (dt, \(J = 40.7, 6.3\) Hz, 2H), 2.61 (t, \(J = 6.9\) Hz, 2H), 1.80 – 1.68 (m, 4H). \(^{13}\)C NMR (101 MHz, Chloroform-\(d\)) \(\delta\) 159.75, 143.43, 135.00, 132.08, 130.02 (d, \(J = 0.5\) Hz), 129.45, 129.39, 120.90, 114.23, 111.30, 55.25, 53.60 (d, \(J = 12.7\) Hz), 35.43, 28.26, 25.95. \(^{19}\)F NMR (376 MHz, Chloroform-\(d\)) \(\delta\) -49.82 (t, \(J = 40.7\) Hz). HRMS (ESI) (\(m/z\)): [M+Na]\(^+\) calcd. for \(C_{17}H_{20}FNO_3SNa\): 360.1046, found: 360.1053.

N-(4-(3-chlorophenyl)butyl)-N-fluorobenzenesulfonamide (1q)

Prepared following general procedure A the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 19/1 as the eluent) as a light yellow oil (498 mg, 49% yield). \(^1\)H NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 8.00 – 7.90 (m, 2H), 7.78 – 7.71 (m, 1H), 7.67 – 7.57 (m, 2H), 7.23 – 7.12 (m, 3H), 7.09 – 7.00 (m, 1H), 3.23 (dt, \(J = 40.6, 6.1\) Hz, 2H), 2.61 (t, \(J = 6.9\) Hz, 2H), 1.81 – 1.67 (m, 4H). \(^{13}\)C NMR (101 MHz, Chloroform-\(d\)) \(\delta\) 143.83, 135.05, 134.22, 132.05, 130.04, 129.76, 129.42, 128.58, 126.71, 126.25, 53.50 (d, \(J = 12.7\) Hz), 35.08, 28.14, 25.88. \(^{19}\)F NMR (376 MHz, Chloroform-\(d\)) \(\delta\) -49.78 (t, \(J = 40.6\) Hz). HRMS (ESI) (\(m/z\)): [M+Na]\(^+\) calcd. for
C_{18}H_{17}ClFNO_{2}SNa: 364.0550, found: 364.0555.

N-fluoro-N-(4-(3-(trifluoromethyl)phenyl)butyl)benzenesulfonamide (1r)

Prepared following general procedure A the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 19/1 as the eluent) as a light yellow oil (588 mg, 52% yield). \(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 8.01 – 7.88 (m, 2H), 7.79 – 7.71 (m, 1H), 7.66 – 7.58 (m, 2H), 7.50 – 7.29 (m, 4H), 3.25 (dt, \(J = 40.5, 6.2\) Hz, 2H), 2.70 (t, \(J = 7.1\) Hz, 2H), 1.86 – 1.67 (m, 4H). \(^{13}\)C NMR (101 MHz, Chloroform-d) \(\delta\) 142.69, 135.08, 132.04, 131.91 (d, \(J = 1.1\) Hz), 130.78 (q, \(J = 32.0\) Hz), 130.05, 129.44, 128.94, 125.13 (q, \(J = 3.8\) Hz), 124.34 (q, \(J = 273.3\) Hz), 122.98 (q, \(J = 3.8\) Hz), 53.48 (d, \(J = 12.5\) Hz), 35.25, 28.23, 25.93. \(^{19}\)F NMR (376 MHz, Chloroform-d) \(\delta\) -49.77 (t, \(J = 40.5\) Hz), -62.54 (s). HRMS (ESI) (m/z): [M+Na]^+ calcd. for C_{17}H_{15}F_{4}NO_{2}SNa: 398.0814, found: 398.0812.

N-fluoro-N-(4-(o-tolyl)butyl)benzenesulfonamide (1s)

Prepared following general procedure A the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 19/1 as the eluent) as a light yellow oil (580 mg, 60% yield). \(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 7.98 – 7.90 (m, 2H), 7.78 – 7.71 (m, 1H), 7.66 – 7.57 (m, 2H), 7.16 – 7.06 (m, 4H), 3.26 (dt, \(J = 40.7, 6.7\) Hz, 2H), 2.62 (t, \(J = 7.7\) Hz, 2H), 2.29 (s, 3H), 1.85 – 1.75 (m, 2H), 1.74 – 1.65 (m, 2H). \(^{13}\)C NMR (101 MHz, Chloroform-d) \(\delta\) 140.02, 135.93, 135.01, 132.15, 130.35, 130.05, 129.40, 128.91, 126.17, 126.07, 53.60 (d, \(J = 12.5\) Hz), 32.78, 27.24, 26.32, 19.41. \(^{19}\)F NMR (376 MHz, Chloroform-d) \(\delta\) -49.83 (t, \(J = 40.7\) Hz). HRMS (ESI) (m/z): [M+Na]^+ calcd. for C_{17}H_{20}FNO_{2}SNa: 344.1096, found: 344.1090.

N-fluoro-N-(4-(2-fluorophenyl)butyl)benzenesulfonamide (1t)

Prepared following general procedure A the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 19/1 as the eluent) as a light yellow oil (529 mg, 54% yield). \(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 8.00 – 7.87 (m, 2H), 7.78 – 7.70 (m, 1H), 7.66 – 7.56 (m, 2H), 7.20 – 7.12 (m, 2H), 7.09 – 6.93 (m, 2H), 3.25 (dt, \(J = 40.6, 6.4\) Hz, 2H), 2.66 (t, \(J = 6.7\) Hz, 2H), 1.81 – 1.68 (m, 4H). \(^{13}\)C NMR (101 MHz, Chloroform-d) \(\delta\) 161.21 (d, \(J = 244.5\) Hz), 135.02, 132.11, 130.71 (d, \(J = 5.1\) Hz), 130.05, 129.41, 128.57 (d, \(J = 15.9\) Hz), 127.80 (d, \(J = 8.1\) Hz), 124.11 (d, \(J = 3.5\) Hz), 115.34 (d, \(J = 22.2\) Hz), 53.54 (d, \(J = 12.5\) Hz), 28.55 (d, \(J = 2.3\) Hz), 27.21, 25.99. \(^{19}\)F NMR (376 MHz, Chloroform-d) \(\delta\) -49.77 (t, \(J = 40.9\) Hz), -118.70 – -119.10 (m). HRMS (ESI) (m/z): [M+Na]^+ calcd. for C_{16}H_{17}F_{2}NO_{2}SNa: 348.0846, found: 348.0852.

N-fluoro-N-(4-(2-(trifluoromethyl)phenyl)butyl)benzenesulfonamide (1u)

Prepared following general procedure A the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 19/1 as the eluent) as a light yellow oil (563 mg, 50% yield). \(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 8.02 – 7.87 (m, 2H), 7.78 – 7.71 (m, 1H), 7.69 – 7.55 (m, 3H), 7.50 – 7.41 (m, 1H), 7.34 – 7.26 (m, 2H), 3.26 (dt, \(J = 40.6, 6.5\) Hz, 2H), 2.79 (t, \(J = 7.5\) Hz, 2H), 1.89 – 1.67 (m, 4H). \(^{13}\)C NMR (101 MHz, Chloroform-d) \(\delta\) 140.67, 135.06, 132.03, 131.91, 131.04, 130.05, 129.43, 128.45 (q, \(J = 29.7\) Hz), 126.17, 126.05 (q, \(J = 5.8\) Hz), 124.72 (q, \(J = 274.8\) Hz), 53.57 (d, \(J = 12.5\) Hz),
Prepared following general procedure A the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 19/1 as the eluent) as a yellow solid (752 mg, 70% yield). $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.99 (d, $J = 8.1$ Hz, 1H), 7.91 (d, $J = 7.4$ Hz, 2H), 7.86 – 7.81 (m, 1H), 7.73 – 7.66 (m, 2H), 7.57 (t, $J = 7.8$ Hz, 2H), 7.52 – 7.43 (m, 2H), 7.37 (t, $J = 7.6$ Hz, 1H), 7.28 (d, $J = 6.8$ Hz, 1H), 3.24 (dt, $J = 40.7$, 6.3 Hz, 2H), 3.08 (t, $J = 7.1$ Hz, 2H), 1.94 – 1.73 (m, 4H). $^{13}$C NMR (101 MHz, Chloroform-d) $\delta$ 137.85, 135.00, 133.99, 132.03, 131.82, 130.00, 129.38, 128.91, 126.86, 126.13, 125.94, 125.61, 125.59, 123.76, 53.60 (d, $J = 12.5$ Hz), 32.55, 27.72, 26.38. $^{19}$F NMR (376 MHz, Chloroform-d) $\delta$ -49.67 (t, $J = 40.7$ Hz). HRMS (ESI) ($m/z$): [M+Na]$^+$ calcd. for C$_{20}$H$_{20}$FNO$_2$SNa: 380.1096, found: 380.1091.

N-fluoro-N-(4-(naphthalen-2-yl)butyl)benzenesulfonylamine (1w)

Prepared following general procedure A the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 19/1 as the eluent) as a yellow solid (834 mg, 78% yield). $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.91 (d, $J = 7.5$ Hz, 2H), 7.81 – 7.73 (m, 3H), 7.71 (t, $J = 7.5$ Hz, 1H), 7.63 – 7.53 (m, 3H), 7.49 – 7.38 (m, 2H), 7.33 – 7.26 (m, 1H), 3.24 (dt, $J = 40.6$, 6.5 Hz, 2H), 2.79 (t, $J = 7.1$ Hz, 2H), 1.90 – 1.68 (m, 4H). $^{13}$C NMR (101 MHz, Chloroform-d) $\delta$ 139.29, 134.99, 133.68, 132.13, 132.06, 130.01, 129.38, 128.08, 127.72, 127.53, 127.28, 126.54, 126.06, 125.31, 53.62 (d, $J = 12.5$ Hz), 35.53, 28.22, 25.99. $^{19}$F NMR (376 MHz, Chloroform-d) $\delta$ -49.82 (t, $J = 40.6$ Hz). HRMS (ESI) ($m/z$): [M+Na]$^+$ calcd. for C$_{20}$H$_{20}$FNO$_2$SNa: 380.1096, found: 380.1093.

N-fluoro-N-(4-(thiophen-2-yl)butyl)benzenesulfonylamine (1y)

Prepared following general procedure A the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 19/1 as the eluent) as a yellow oil (417 mg, 42% yield). $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.94 (d, $J = 7.8$ Hz, 2H), 7.74 (t, $J = 7.5$ Hz, 1H), 7.61 (t, $J = 7.8$ Hz, 2H), 7.11 (d, $J = 5.1$ Hz, 1H), 6.97 – 6.83 (m, 1H), 6.77 (d, $J = 3.3$ Hz, 1H), 3.24 (dt, $J = 40.5$, 6.0 Hz, 2H), 2.85 (t, $J = 6.6$ Hz, 2H), 1.90 – 1.68 (m, 4H). $^{13}$C NMR (101 MHz, Chloroform-d) $\delta$ 144.52, 135.03, 132.03, 130.03, 129.41, 126.87, 124.46, 123.23, 53.46 (d, $J = 12.5$ Hz), 29.41, 28.73, 25.76. $^{19}$F NMR (376 MHz, Chloroform-d) $\delta$ -
N-(2,2-dimethyl-4-phenylbutyl)-N-fluorobenzenesulfonamide (1z)

Prepared following general procedure A the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 19/1 as the eluent) as a white solid (653 mg, 65% yield). $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.99 – 7.90 (m, 2H), 7.78 – 7.71 (m, 1H), 7.66 – 7.58 (m, 2H), 7.30 – 7.25 (m, 2H), 7.21 – 7.13 (m, 3H), 3.10 (d, $J = 44.2$ Hz, 2H), 2.60 – 2.52 (m, 2H), 1.68 – 1.61 (m, 2H), 1.05 (s, 6H). $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 142.69, 134.96, 132.68, 129.92, 129.44, 128.52, 128.46, 125.88, 62.85 (d, $J = 10.6$ Hz), 42.42, 34.69, 30.44, 25.76. $^{19}$F NMR (376 MHz, Chloroform-$d$) $\delta$ -36.35 (t, $J = 44.2$ Hz). HRMS (ESI) ($m/z$): [M+Na]$^+$ calced. for $C_{12}H_{18}FNO_2SNa$: 358.1253, found: 358.1242.

N-fluoro-N-((pent-4-en-1-yl)benzenesulfonamide (4)

Prepared following general procedure A the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 19/1 as the eluent) as a yellow oil (565 mg, 77% yield). $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 8.00 – 7.90 (m, 2H), 7.79 – 7.71 (m, 1H), 7.67 – 7.57 (m, 2H), 5.87 – 5.66 (m, 1H), 5.12 – 4.96 (m, 2H), 3.25 (dt, $J = 40.5$, 6.9 Hz, 2H), 2.18 (q, $J = 7.0$ Hz, 2H), 1.82 (quint, $J = 7.3$ Hz, 2H). $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 136.97, 135.02, 132.18, 130.05, 129.41, 116.09, 53.02 (d, $J = 12.5$ Hz), 30.59, 25.53. $^{19}$F NMR (376 MHz, Chloroform-$d$) $\delta$ -49.87 (t, $J = 40.6$ Hz). HRMS (ESI) ($m/z$): [M+Na]$^+$ calced. for $C_{13}H_{14}FNO_2SNa$: 266.0627, found: 266.0616.

N-fluoro-N-((4-(2-phenylcyclopropyl)butyl)benzenesulfonamide (6)

Prepared following general procedure A (1.1 mmol scale) the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 19/1 as the eluent) as a light yellow oil (214 mg, 56% yield). $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 8.00 – 7.87 (m, 2H), 7.78 – 7.69 (m, 1H), 7.66 – 7.57 (m, 2H), 7.26 – 7.20 (m, 2H), 7.16 – 7.09 (m, 1H), 7.07 – 6.96 (m, 2H), 3.23 (dt, $J = 40.6$, 6.9 Hz, 2H), 1.83 – 1.70 (m, 2H), 1.64 – 1.50 (m, 3H), 1.45 – 1.37 (m, 2H), 1.05 – 0.93 (m, 1H), 0.92 – 0.84 (m, 1H), 0.79 – 0.70 (m, 1H). $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 143.80, 134.99, 132.18, 130.06, 129.40, 128.38, 125.88, 125.38, 53.78 (d, $J = 12.5$ Hz), 33.96, 26.55, 26.20, 23.55, 23.36, 16.23. $^{19}$F NMR (376 MHz, Chloroform-$d$) $\delta$ -49.85 (t, $J = 40.6$ Hz). HRMS (ESI) ($m/z$): [M+Na]$^+$ calced. for $C_{19}H_{22}FNO_3SNa$: 370.1253, found: 370.1248.

2. Products:

(R)-N-(4-cyano-4-phenylbutyl)benzenesulfonamide (2a)

Prepared following general procedure B the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 5/1 as the eluent) to afford the product 2a (58.0 mg, 92% yield, 92% ee) as a white solid. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.88 – 7.80 (m, 2H), 7.62 – 7.55 (m, 1H), 7.55 – 7.47 (m, 2H), 7.40 – 7.30 (m, 3H), 7.30 – 7.26 (m, 2H), 4.95 – 4.55 (m, 1H), 3.80 (t, $J = 7.3$ Hz, 1H), 3.07 – 2.91 (m, 2H), 2.00 – 1.85 (m, 2H), 1.71 – 1.58 (m, 2H). $^{13}$C NMR (101 MHz, Chloroform-
mL/min, detection at 214 nm) retention time = 20.62 min (minor) and 22.13 min (major).

(R)-N-(4-cyano-4-phenylbutyl)-4-methylbenzenesulfonamide (2b)

Prepared following general procedure B the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 5/1 as the eluent) to afford the product 2b (47.5 mg, 72% yield, 91% ee) as a white solid. ¹H NMR (400 MHz, Chloroform-d) δ 7.77 (d, J = 9.0 Hz, 2H), 7.39 – 7.30 (m, 3H), 7.30 – 7.26 (m, 2H), 6.97 (d, J = 9.0 Hz, 2H), 4.76 (t, J = 6.4 Hz, 1H), 3.86 (s, 3H), 3.80 (t, J = 7.4 Hz, 1H), 3.02 – 2.89 (m, 2H), 1.98 – 1.83 (m, 2H), 1.68 – 1.58 (m, 2H). ¹³C NMR (101 MHz, Chloroform-d) δ 163.04, 135.39, 131.29, 129.22, 128.27, 127.28, 120.61, 114.45, 55.74, 42.28, 36.80, 32.71, 26.98. HRMS (ESI) (m/z): [M+Na]⁺ calcd. for C₁₈H₂₀N₂O₃SNa: 351.1143, found: 351.1151.

[R]ᵈ⁺ = 10.08 (c 0.57, CHCl₃). HPLC (OD-H, 0.46*25 cm, 5 μm, hexane/isopropanol = 7/3, flow 0.5 mL/min, detection at 214 nm) retention time = 20.17 min (minor) and 21.88 min (major).

(R)-N-(4-cyano-4-phenylbutyl)-4-methoxybenzenesulfonamide (2c)

Prepared following general procedure B the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 5/1 to 3/1 as the eluent) to afford the product 2c (63.5 mg, 92% yield, 90% ee) as a yellow solid. ¹H NMR (400 MHz, Chloroform-d) δ 7.39 – 7.30 (m, 3H), 7.30 – 7.26 (m, 2H), 6.97 (d, J = 9.0 Hz, 2H), 4.76 (t, J = 6.4 Hz, 1H), 3.86 (s, 3H), 3.80 (t, J = 7.4 Hz, 1H), 3.02 – 2.89 (m, 2H), 1.98 – 1.83 (m, 2H), 1.68 – 1.58 (m, 2H). ¹³C NMR (101 MHz, Chloroform-d) δ 163.04, 135.39, 131.29, 129.22, 128.27, 127.28, 120.61, 114.45, 55.74, 42.28, 36.80, 32.71, 26.98. HRMS (ESI) (m/z): [M+Na]⁺ calcd. for C₁₈H₂₀N₂O₃SNa: 367.1092, found: 367.1082.

[R]ᵈ⁺ = 21.03 (c 0.50, CHCl₃). HPLC (OD-H, 0.46*25 cm, 5 μm, hexane/isopropanol = 7/3, flow 0.5 mL/min, detection at 214 nm) retention time = 27.64 min (minor) and 29.80 min (major).

(R)-4-chloro-N-(4-cyano-4-phenylbutyl)benzenesulfonamide (2d)

Prepared following general procedure B the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 5/1 as the eluent) to afford the product 2d (51.7 mg, 74% yield, 91% ee) as a white solid. ¹H NMR (400 MHz, Chloroform-d) δ 7.77 (d, J = 8.7 Hz, 2H), 7.47 (d, J = 8.7 Hz, 2H), 7.40 – 7.31 (m, 3H), 7.30 – 7.26 (m, 2H), 4.84 (t, J = 6.4 Hz, 1H), 3.82 (t, J = 7.3 Hz, 1H), 3.05 – 2.92 (m, 2H), 1.99 – 1.85 (m, 2H), 1.73 – 1.58 (m, 2H). ¹³C NMR (101 MHz, Chloroform-d) δ 139.42, 138.34, 135.24, 129.64, 129.30, 128.55, 128.39, 127.27, 120.54, 42.44, 36.85, 32.69, 27.07. HRMS (ESI) (m/z): [M+Na]⁺ calcd. for C₁₇H₁₇ClN₂O₃SNa: 371.0597, found: 371.0591.

[R]ᵈ⁺ = 13.10 (c 1.0, CHCl₃). HPLC (OD-H, 0.46*25 cm, 5 μm, hexane/isopropanol = 7/3, flow 0.5 mL/min, detection at 214 nm) retention time = 20.62 min (minor) and 22.13 min (major).
(R)-N-(4-cyano-4-phenylbutyl)-4-(trifluoromethyl)benzenesulfonamide (2e)

Prepared following general procedure B the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 5/1 as the eluent) to afford the product 2e (74.1 mg, 97% yield, 93% ee) as a colourless oil. \(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 7.96 (d, \(J = 8.2\) Hz, 2H), 7.77 (d, \(J = 8.2\) Hz, 2H), 7.40 – 7.31 (m, 3H), 7.30 – 7.26 (m, 2H), 4.92 (t, \(J = 6.3\) Hz, 1H), 3.83 (t, \(J = 7.3\) Hz, 1H), 3.10 – 2.93 (m, 2H), 1.99 – 1.89 (m, 2H), 1.73 – 1.62 (m, 2H). \(^1^3\)C NMR (101 MHz, Chloroform-d) \(\delta\) 143.47, 135.20, 139.78, 138.10, 132.87, 132.31, 129.87, 129.31, 127.15, 127.04, 120.76, 42.39, 36.40, 32.68, 27.13.

HRMS (ESI) \((\text{m}/\text{z})\): [M+Na]\(^+\) calcd. for C\(_{18}\)H\(_{17}\)F\(_3\)N\(_2\)O\(_2\)SNa: 405.0861, found: 405.0871. \([\alpha]_D^{20.0} = 11.51\) (c 1.0, CHCl\(_3\)). HPLC (AS-H, 0.46*25 cm, 5 \(\mu\)m, hexane/isopropanol = 8/2, flow 0.5 mL/min, detection at 214 nm) retention time = 56.98 min (major) and 69.90 min (minor).

(R)-N-(4-cyano-4-(p-tolyl)butyl)benzenesulfonamide (2f)

Prepared following general procedure B the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 5/1 as the eluent) to afford the product 2f (62.4 mg, 95% yield, 84% ee) as a white solid. \(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 7.89 – 7.79 (m, 2H), 7.62 – 7.54 (m, 1H), 7.54 – 7.46 (m, 2H), 7.20 – 7.11 (m, 4H), 5.02 – 4.86 (m, 1H), 3.74 (t, \(J = 7.3\) Hz, 1H), 3.06 – 2.86 (m, 2H), 2.34 (s, 3H), 1.94 – 1.83 (m, 2H), 1.68 – 1.56 (m, 2H). \(^1^3\)C NMR (101 MHz, Chloroform-d) \(\delta\) 139.78, 138.10, 132.87, 132.31, 129.87, 129.31, 127.15, 127.04, 120.76, 42.39, 36.40, 32.66, 27.01, 21.16. HRMS (ESI) \((\text{m}/\text{z})\): [M+Na]\(^+\) calcd. for C\(_{18}\)H\(_{20}\)N\(_2\)O\(_2\)SNa: 351.1143, found: 351.1140.

\([\alpha]_D^{20.0} = 14.60\) (c 0.70, CHCl\(_3\)). HPLC (AD-H, 0.46*25 cm, 5 \(\mu\)m, hexane/isopropanol = 8/2, flow 0.5 mL/min, detection at 214 nm) retention time = 30.62 min (minor) and 34.30 min (major).

(R)-N-(4-(4-(tert-butyl)phenyl)-4-cyano-butyl)benzenesulfonamide (2g)

Prepared following general procedure B the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 5/1 as the eluent) to afford the product 2g (67.2 mg, 91% yield, 86% ee) as a white solid. \(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 7.89 – 7.82 (m, 2H), 7.60 – 7.55 (m, 1H), 7.54 – 7.47 (m, 2H), 7.37 (d, \(J = 8.3\) Hz, 2H), 7.20 (d, \(J = 8.3\) Hz, 2H), 4.87 (t, \(J = 6.0\) Hz, 1H), 3.76 (t, \(J = 7.3\) Hz, 1H), 3.06 – 2.90 (m, 2H), 2.00 – 1.81 (m, 2H), 1.70 – 1.58 (m, 2H), 1.31 (s, 9H). \(^1^3\)C NMR (101 MHz, Chloroform-d) \(\delta\) 151.36, 139.81, 132.89, 132.26, 129.33, 127.06, 126.98, 126.17, 120.74, 42.44, 36.38, 34.68, 32.66, 31.38, 27.09. HRMS (ESI) \((\text{m}/\text{z})\): [M+Na]\(^+\) calcd. for C\(_{31}\)H\(_{36}\)N\(_2\)O\(_2\)SNa: 393.1613, found: 393.1609.

\([\alpha]_D^{20.0} = 13.20\) (c 0.61, CHCl\(_3\)). HPLC (OD-H, 0.46*25 cm, 5 \(\mu\)m, hexane/isopropanol = 8/2, flow 0.5 mL/min, detection at 214 nm) retention time = 19.71 min (minor) and 22.73 min (major).

(R)-N-(4-cyano-4-(4-pentylphenyl)butyl)benzenesulfonamide (2h)

Prepared following general procedure B the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 5/1 as the eluent) to afford the product 2h (70.8 mg, 92% yield, 86% ee) as a white solid. \(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 7.88 – 7.81
Prepared following general procedure B the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 5/1 as the eluent) to afford the product 2i (71.4 mg, 91% yield, 91% ee) as a white solid. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.89 – 7.81 (m, 2H), 7.61 – 7.54 (m, 5H), 7.53 – 7.42 (m, 4H), 7.40 – 7.32 (m, 3H), 4.80 (t, $J = 6.2$ Hz, 1H), 3.85 (t, $J = 7.3$ Hz, 1H), 3.08 – 2.93 (m, 2H), 2.07 – 1.86 (m, 2H), 1.76 – 1.59 (m, 2H). $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 141.32, 140.26, 139.80, 134.28, 132.93, 129.35, 129.01, 127.94, 127.78, 127.75, 127.18, 127.07, 120.52, 42.41, 36.51, 32.67, 27.10. HRMS (ESI) ($m/z$): [M+Na]$^+$ calcd. for C$_{23}$H$_{27}$N$_2$O$_3$SNa: 413.1300, found: 413.1292.

$[\alpha]_{D}^{20.0}$ = 11.58 (c 0.60, CHCl$_3$). HPLC (OD-H, 0.46*25 cm, 5 µm, hexane/isopropanol = 8/2, flow 0.5 mL/min, detection at 214 nm) retention time = 20.22 min (minor) and 21.85 min (major).

(R)-N-(4-[[1,1'-biphenyl]-4-yl]-4-cyanobutyl)benzenesulfonamide (2j)

Prepared following general procedure B the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 5/1 as the eluent) to afford the product 2j (34.5 mg, 42% yield, 86% ee) as a yellow oil. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.88 – 7.81 (m, 2H), 7.59 (t, $J = 7.0$ Hz, 1H), 7.52 (t, $J = 7.7$ Hz, 2H), 7.36 (t, $J = 7.7$ Hz, 2H), 7.23 (d, $J = 8.5$ Hz, 2H), 7.14 (t, $J = 7.4$ Hz, 1H), 6.99 (dd, $J = 15.0$, 8.4 Hz, 4H), 4.73 (t, $J = 6.3$ Hz, 1H), 3.78 (t, $J = 7.4$ Hz, 1H), 3.07 – 2.93 (m, 2H), 1.92 (t, $J = 7.7$ Hz, 2H), 1.73 – 1.57 (m, 2H). $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 157.53, 156.72, 139.85, 132.95, 130.01, 129.86, 129.37, 128.74, 127.08, 123.90, 120.59, 119.36, 119.21, 42.42, 36.19, 32.76, 27.14. HRMS (ESI) ($m/z$): [M+Na]$^+$ calcd. for C$_{23}$H$_{27}$N$_2$O$_3$SNa: 429.1249, found: 429.1248.

$[\alpha]_{D}^{20.0}$ = 7.03 (c 0.34, CHCl$_3$). HPLC (OD-H, 0.46*25 cm, 5 µm, hexane/isopropanol = 8/2, flow 0.5 mL/min, detection at 214 nm) retention time = 46.47 min (major) and 54.01 min (minor).

(R)-N-(4-cyano-4-(4-phenoxyphenyl)butyl)benzenesulfonamide (2k)

Prepared following general procedure B the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 5/1 as the eluent) to afford the product 2k (66.5 mg, 83% yield, 88% ee) as a white solid. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.91 – 7.78 (m, 2H), 7.63 – 7.55 (m, 1H), 7.55 – 7.47 (m, 2H), 7.33 (d, $J = 8.3$ Hz, 2H), 7.21 (d, $J = 8.2$ Hz, 2H), 5.03 – 4.71 (m, 1H), 3.85 (t, $J = 7.3$ Hz, 1H), 3.11 – 2.91 (m, 2H), 2.03 – 1.83 (m, 2H), 1.75 – 1.58 (m, 2H). $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 148.96, 139.64, 134.00, 132.87, 129.26, 128.75, 126.93, 121.62, 120.19 (q,
Prepared following general procedure B the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 5:1 as the eluent) to afford the product 2I (59.5 mg, 85% yield, 90% ee) as a white solid. ¹H NMR (400 MHz, Chloroform-d) δ 7.88 – 7.80 (m, 2H), 7.62 – 7.56 (m, 1H), 7.54 – 7.47 (m, 2H), 7.32 (d, J = 8.4 Hz, 2H), 7.22 (d, J = 8.4 Hz, 2H), 5.05 (s, 1H), 3.80 (t, J = 7.4 Hz, 1H), 3.04 – 2.92 (m, 2H), 1.96 – 1.84 (m, 2H), 1.69 – 1.57 (m, 2H). ¹³C NMR (101 MHz, Chloroform-d) δ 139.71, 134.27, 133.89, 132.95, 129.42, 129.35, 128.69, 127.01, 120.17, 42.24, 36.20, 32.55, 26.95. HRMS (ESI) (m/z): [M+Na]+ calcd. for C₁₇H₁₇F₂N₂O₄SnA: 415.0092, found: 415.0092.

Prepared following general procedure B the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 5:1 as the eluent) to afford the product 2m (74.1 mg, 94% yield, 89% ee) as a white solid. ¹H NMR (400 MHz, Chloroform-d) δ 7.90 – 7.80 (m, 2H), 7.62 – 7.56 (m, 1H), 7.55 – 7.44 (m, 4H), 7.16 (d, J = 8.4 Hz, 2H), 4.98 (s, 1H), 3.79 (t, J = 7.4 Hz, 1H), 3.06 – 2.91 (m, 2H), 2.00 – 1.80 (m, 2H), 1.70 – 1.56 (m, 2H). ¹³C NMR (101 MHz, Chloroform-d) δ 139.72, 134.41, 132.97, 132.40, 129.36, 129.01, 127.02, 122.36, 120.07, 42.25, 36.28, 32.51, 26.97. HRMS (ESI) (m/z): [M+Na]+ calcd. for C₁₇H₁₇BrN₂O₄SnA: 415.0092, found: 415.0092.

Prepared following general procedure B the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 5:1 as the eluent) to afford the product 2n (63.0 mg, 82% yield, 87% ee) as a yellow solid. ¹H NMR (400 MHz, Chloroform-d) δ 7.89 – 7.81 (m, 2H), 7.65 – 7.55 (m, 3H), 7.54 – 7.48 (m, 2H), 7.43 (d, J = 8.1 Hz, 2H), 5.04 (s, 1H), 3.91 (dd, J = 8.5, 6.3 Hz, 1H), 3.10 – 2.91 (m, 2H), 2.05 – 1.86 (m, 2H), 1.72 – 1.61 (m, 2H). ¹³C NMR (101 MHz, Chloroform-d) δ 139.70, 139.40, 133.00, 130.69 (q, J = 32.8 Hz), 129.38, 127.81, 127.02, 126.27 (q, J = 3.7 Hz), 123.87 (q, J = 273.1 Hz), 119.82, 42.20, 36.62, 32.53, 27.01. ¹⁹F NMR (376 MHz, Chloroform-d) δ -62.68 (s). HRMS (ESI) (m/z): [M+Na]+ calcd. for C₁₇H₁₇F₃N₂O₂SnA: 405.0861, found: 405.0862.

Prepared following general procedure B the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 5:1 as the eluent) to afford the product 2n (63.0 mg, 82% yield, 87% ee) as a yellow solid. ¹H NMR (400 MHz, Chloroform-d) δ 7.89 – 7.81 (m, 2H), 7.65 – 7.55 (m, 3H), 7.54 – 7.48 (m, 2H), 7.43 (d, J = 8.1 Hz, 2H), 5.04 (s, 1H), 3.91 (dd, J = 8.5, 6.3 Hz, 1H), 3.10 – 2.91 (m, 2H), 2.05 – 1.86 (m, 2H), 1.72 – 1.61 (m, 2H). ¹³C NMR (101 MHz, Chloroform-d) δ 139.70, 139.40, 133.00, 130.69 (q, J = 32.8 Hz), 129.38, 127.81, 127.02, 126.27 (q, J = 3.7 Hz), 123.87 (q, J = 273.1 Hz), 119.82, 42.20, 36.62, 32.53, 27.01. ¹⁹F NMR (376 MHz, Chloroform-d) δ -62.68 (s). HRMS (ESI) (m/z): [M+Na]+ calcd. for C₁₇H₁₇F₃N₂O₂SnA: 405.0861, found: 405.0862.
(R)-N-(4-cyano-4-(m-tolyl)butyl)benzenesulfonamide (2o)

Prepared following general procedure B the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 5/1 as the eluent) to afford the product 2o (50.1 mg, 76% yield, 90% ee) as a yellow oil. $^1$H NMR (400 MHz, Chloroform-d) δ 7.87 – 7.81 (m, 2H), 7.61 – 7.55 (m, 1H), 7.54 – 7.47 (m, 2H), 7.24 (t, J = 7.6 Hz, 1H), 7.15 – 7.03 (m, 3H), 4.80 (s, 1H), 3.74 (t, J = 7.3 Hz, 1H), 3.04 – 2.93 (m, 2H), 2.35 (s, 3H), 1.96 – 1.85 (m, 2H), 1.70 – 1.59 (m, 2H). $^{13}$C NMR (101 MHz, Chloroform-d) δ 139.84, 139.12, 135.26, 132.90, 129.33, 129.12, 129.07, 127.95, 127.07, 124.35, 120.67, 42.44, 36.78, 32.71, 27.12, 21.49. HRMS (ESI) (m/z): [M+Na]$^+$ calcd. for C$_{18}$H$_{20}$N$_2$O$_2$SNa: 351.1143, found: 351.1142.

[α]$_D^{20.0}$ = 14.95 (c 0.60, CHCl$_3$). HPLC (OD-H, 0.46*25 cm, 5 μm, hexane/isopropanol = 8/2, flow 0.5 mL/min, detection at 214 nm) retention time = 23.46 min (minor) and 26.59 min (major).

(R)-N-(4-cyano-4-(3-methoxyphenyl)butyl)benzenesulfonamide (2p)

Prepared following general procedure B the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 5/1 to 3/1 as the eluent) to afford the product 2p (60.5 mg, 88% yield, 93% ee) as a yellow oil. $^1$H NMR (400 MHz, Chloroform-d) δ 7.87 – 7.81 (m, 2H), 7.60 – 7.55 (m, 1H), 7.54 – 7.47 (m, 2H), 7.26 (t, J = 7.9 Hz, 1H), 6.87 – 6.80 (m, 3H), 4.85 (t, J = 5.8 Hz, 1H), 3.81 (s, 3H), 3.76 (t, J = 7.36 Hz, 1H), 3.03 – 2.93 (m, 2H), 1.95 – 1.87 (m, 2H), 1.68 – 1.59 (m, 2H). $^{13}$C NMR (101 MHz, Chloroform-d) δ 139.01, 139.83, 136.80, 132.90, 130.32, 129.33, 127.05, 124.35, 119.54, 113.69, 113.13, 55.46, 42.40, 36.80, 32.59, 27.07. HRMS (ESI) (m/z): [M+Na]$^+$ calcd. for C$_{18}$H$_{20}$N$_2$O$_2$SNa: 367.1092, found: 367.1102.

[α]$_D^{20.0}$ = 11.36 (c 0.80, CHCl$_3$). HPLC (OD-H, 0.46*25 cm, 5 μm, hexane/isopropanol = 8/2, flow 0.5 mL/min, detection at 214 nm) retention time = 39.34 min (minor) and 45.54 min (major).

(R)-N-(4-(3-chlorophenyl)-4-cyanobutyl)benzenesulfonamide (2q)

Prepared following general procedure B the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 5/1 as the eluent) to afford the product 2q (51.6 mg, 74% yield, 93% ee) as a yellow oil. $^1$H NMR (400 MHz, Chloroform-d) δ 7.90 – 7.80 (m, 2H), 7.63 – 7.56 (m, 1H), 7.56 – 7.47 (m, 2H), 7.33 – 7.27 (m, 3H), 7.22 – 7.15 (m, 1H), 4.86 (t, J = 6.3 Hz, 1H), 3.80 (dd, J = 8.4, 6.4 Hz, 1H), 3.11 – 2.91 (m, 2H), 2.00 – 1.82 (m, 2H), 1.74 – 1.56 (m, 2H). $^{13}$C NMR (101 MHz, Chloroform-d) δ 139.75, 137.30, 135.12, 132.99, 130.58, 129.38, 128.64, 127.51, 127.05, 125.55, 119.93, 42.29, 36.48, 32.55, 27.05. HRMS (ESI) (m/z): [M+Na]$^+$ calcd. for C$_{17}$H$_{17}$ClN$_2$O$_2$SNa: 371.0597, found: 371.0601.

[α]$_D^{20.0}$ = 13.75 (c 0.70, CHCl$_3$). HPLC (OD-H, 0.46*25 cm, 5 μm, hexane/isopropanol = 8/2, flow 0.5 mL/min, detection at 214 nm) retention time = 27.74 min (minor) and 32.43 min (major).

(R)-N-(4-cyano-4-(3-(trifluoromethyl)phenyl)butyl)benzenesulfonamide (2r)

Prepared following general procedure B the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 5/1 as the eluent) to afford the product 2r (54.1 mg, 71% yield, 90% ee) as a yellow oil. $^1$H NMR (400 MHz, Chloroform-d) δ 7.89 – 7.81 (m, 2H), 7.62 – 7.56
Prepared following general procedure B the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 5/1 as the eluent) to afford the product 2s (51.5 mg, 78% yield, 90% ee) as a light yellow solid.

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.88 – 7.80 (m, 2H), 7.60 – 7.54 (m, 1H), 7.54 – 7.47 (m, 2H), 7.38 – 7.31 (m, 1H), 7.25 – 7.19 (m, 2H), 7.19 – 7.14 (m, 1H), 4.88 (t, $J = 6.2$ Hz, 1H), 3.94 (t, $J = 7.3$ Hz, 1H), 3.11 – 2.91 (m, 2H), 2.31 (s, 3H), 2.00 – 1.82 (m, 2H), 1.74 – 1.56 (m, 2H). $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 139.72, 135.07, 133.67, 132.91, 131.20, 129.89, 128.35, 127.43, 127.05, 126.97, 120.84, 42.50, 33.73, 31.27, 27.26, 19.24. HRMS (ESI) (m/z): [M+Na]$^+$ calcd. for C$_{18}$H$_{17}$F$_3$N$_2$O$_2$SNa: 405.0861, found: 405.0859.

[$\alpha$]$_{D}^{20.0}$ = 4.48 (c 0.60, CHCl$_3$). HPLC (OD-H, 0.46*25 cm, 5 µm, hexane/isopropanol = 8/2, flow 0.5 mL/min, detection at 214 nm) retention time = 20.85 min (minor) and 23.16 min (major).

(R)-N-(4-cyano-4-(o-tolyl)butyl)benzenesulfonamide (2s)

Prepared following general procedure B the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 5/1 as the eluent) to afford the product 2t (42.9 mg, 65% yield, 94% ee) as a yellow oil.

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.89 – 7.81 (m, 2H), 7.62 – 7.55 (m, 1H), 7.55 – 7.48 (m, 2H), 7.44 – 7.37 (m, 1H), 7.37 – 7.29 (m, 1H), 7.22 – 7.14 (m, 1H), 7.12 – 7.04 (m, 1H), 4.63 (t, $J = 6.3$ Hz, 1H), 4.07 (t, $J = 7.3$ Hz, 1H), 3.01 (q, $J = 6.7$ Hz, 2H), 1.98 – 1.87 (m, 2H), 1.74 – 1.58 (m, 2H). $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 159.80 (d, $J = 247.6$ Hz), 139.85, 132.91, 130.36 (d, $J = 8.3$ Hz), 129.34, 129.01 (d, $J = 3.1$ Hz), 127.08, 125.01 (d, $J = 3.7$ Hz), 122.61 (d, $J = 14.0$ Hz), 119.71, 116.06 (d, $J = 21.4$ Hz), 42.44, 31.27, 30.79 (d, $J = 3.3$ Hz), 27.20. $^{19}$F NMR (376 MHz, Chloroform-$d$) $\delta$ -118.14 – -118.34 (m). HRMS (ESI) (m/z): [M+Na]$^+$ calcd. for C$_{18}$H$_{20}$F$_3$N$_2$O$_2$SNa: 355.1143, found: 355.1148.

[$\alpha$]$_{D}^{20.0}$ = 32.73 (c 0.60, CHCl$_3$). HPLC (OD-H, 0.46*25 cm, 5 µm, hexane/isopropanol = 8/2, flow 0.5 mL/min, detection at 214 nm) retention time = 30.22 min (minor) and 34.51 min (major).

(R)-N-(4-cyano-4-(2-fluorophenyl)butyl)benzenesulfonamide (2t)

Prepared following general procedure B the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 5/1 as the eluent) to afford the product 2u (55.6 mg, 73% yield, 95% ee) as a yellow oil.

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.88 – 7.82 (m, 2H), 7.70 – 7.65 (m, 1H), 7.64 – 7.54 (m, 3H), 7.54 – 7.42 (m, 3H), 4.77 (s, 1H), 4.08 (dd, $J = 9.1, 5.7$ Hz, 1H), 3.06 – 2.97 (m, 2H), 1.98 – 1.84 (m, 2H), 1.84 – 1.72 (m, 1H), 1.70 – 1.58 (m, 1H). $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 139.84, 134.37, 133.04, 132.92, 129.59, 129.34, 128.68, 127.71 (q, $J = 30.4$ Hz), 127.09, 126.67 (q, $J =$
5.5 Hz), 124.01 (q, J = 273.8 Hz), 120.18, 42.49, 33.47 (q, J = 2.3 Hz), 33.32, 27.67. $^{19}$F NMR (376 MHz, Chloroform-d) δ -58.82 (s). HRMS (ESI) (m/z): [M+Na]$^+$ calcd. for C$_{18}$H$_{17}$F$_2$N$_2$O$_2$SNa: 405.0861, found: 405.0855.

[$\alpha$]$_D$$_{20.0}^{19}$ = 18.90 (c 0.71, CHCl$_3$). HPLC (AD-H, 0.46×25 cm, 5 µm, hexane/isopropanol = 8/2, flow 0.5 mL/min, detection at 214 nm) retention time = 20.36 min (minor) and 23.87 min (major).

(R)-N-(4-(4-chloro-2-methylphenyl)-4-cyanobutyl)benzenesulfonamide (2v)

Prepared following general procedure B the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 5/1 as the eluent) to afford the product 2v (47.3 mg, 65% yield, 85% ee) as a yellow oil. $^1$H NMR (400 MHz, Chloroform-d) δ 7.95 – 7.80 (m, 2H), 7.65 – 7.47 (m, 3H), 7.35 – 7.15 (m, 3H), 4.90 (s, 1H), 3.92 (t, J = 7.3 Hz, 1H), 3.12 – 2.90 (m, 2H), 2.29 (s, 3H), 1.96 – 1.78 (m, 2H), 1.78 – 1.60 (m, 2H). $^{13}$C NMR (101 MHz, Chloroform-d) δ 139.74, 137.10, 134.03, 132.95, 132.28, 131.07, 129.35, 128.83, 127.05, 120.40, 42.42, 33.30, 31.15, 27.19, 19.16. HRMS (ESI) (m/z): [M+Na]$^+$ calcd. for C$_{18}$H$_{17}$F$_2$N$_2$O$_2$SNa: 385.0753, found: 385.0753.

[$\alpha$]$_D$$_{20.0}^{19}$ = 19.91 (c 0.67, CHCl$_3$). HPLC (OD-H, 0.46×25 cm, 5 µm, hexane/isopropanol = 8/2, flow 0.5 mL/min, detection at 214 nm) retention time = 30.23 min (minor) and 32.25 min (major).

(R)-N-(4-cyano-4-(naphthalen-1-yl)butyl)benzenesulfonamide (2w)

Prepared following general procedure B the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 5/1 as the eluent) to afford the product 2w (49.4 mg, 68% yield, 90% ee) as a yellow oil. $^1$H NMR (400 MHz, Chloroform-d) δ 7.92 – 7.87 (m, 2H), 7.85 – 7.79 (m, 3H), 7.63 – 7.50 (m, 4H), 7.50 – 7.42 (m, 3H), 4.73 (t, J = 6.3 Hz, 1H), 4.56 (dd, J = 8.8, 5.3 Hz, 1H), 3.08 – 2.92 (m, 2H), 2.16 – 1.92 (m, 2H), 1.81 – 1.66 (m, 2H). $^{13}$C NMR (101 MHz, Chloroform-d) δ 139.71, 134.12, 132.89, 130.99, 129.94, 129.44, 129.30, 129.23, 127.22, 127.05, 126.34, 125.63, 125.52, 122.17, 120.80, 42.49, 33.90, 31.55, 27.34. HRMS (ESI) (m/z): [M+Na]$^+$ calcd. for C$_{21}$H$_{20}$N$_2$O$_2$SNa: 387.1143, found: 387.1139.

[$\alpha$]$_D$$_{20.0}^{19}$ = 52.21 (c 0.50, CHCl$_3$). HPLC (AD-H, 0.46×25 cm, 5 µm, hexane/isopropanol = 8/2, flow 0.5 mL/min, detection at 214 nm) retention time = 48.28 min (major) and 64.37 min (minor).

(R)-N-(4-cyano-4-(naphthalen-2-yl)butyl)benzenesulfonamide (2x)

Prepared following general procedure B the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 5/1 as the eluent) to afford the product 2x (60.1 mg, 82% yield, 90% ee) as a white solid. $^1$H NMR (400 MHz, Chloroform-d) δ 7.86 – 7.78 (m, 5H), 7.77 – 7.73 (m, 1H), 7.55 – 7.48 (m, 3H), 7.48 – 7.41 (m, 2H), 7.33 (dd, J = 8.5, 1.8 Hz, 1H), 4.90 (t, J = 6.2 Hz, 1H), 3.95 (t, J = 7.2 Hz, 1H), 3.05 – 2.91 (m, 2H), 2.05 – 1.93 (m, 2H), 1.69 – 1.60 (m, 2H). $^{13}$C NMR (101 MHz, Chloroform-d) δ 139.75, 133.31, 132.91, 132.87, 132.57, 129.29, 129.27, 127.97, 127.82, 127.01, 126.88, 126.69, 126.42, 124.72, 120.58, 42.38, 36.92, 32.49, 27.02. HRMS (ESI) (m/z): [M+Na]$^+$ calcd. for C$_{21}$H$_{20}$N$_2$O$_2$SNa: 387.1143, found: 387.1140.

[$\alpha$]$_D$$_{20.0}^{19}$ = 15.25 (c 0.67, CHCl$_3$). HPLC (OD-H, 0.46×25 cm, 5 µm, hexane/isopropanol = 8/2, flow 0.5 mL/min, detection at 214 nm) retention time = 48.95 min (minor) and 55.55 min (major).

(S)-N-(4-cyano-4-(thiophen-2-yl)butyl)benzenesulfonamide (2y)

S21
Prepared following general procedure B the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 5/1 as the eluent) to afford the product 2y (36.2 mg, 56% yield, 93% ee) as a yellow oil. \(^1\)H NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 7.88 – 7.83 (m, 2H), 7.62 – 7.56 (m, 1H), 7.56 – 7.48 (m, 2H), 7.28 – 7.24 (m, 1H), 7.05 – 7.00 (m, 1H), 6.99 – 6.93 (m, 1H), 4.83 (t, \(J = 5.9\) Hz, 1H), 4.08 (t, \(J = 7.2\) Hz, 1H), 3.82 (dd, \(J = 10.6, 3.8\) Hz, 1H), 2.85 (dd, \(J = 13.1, 8.2\) Hz, 1H), 2.71 (dd, \(J = 13.1, 6.3\) Hz, 1H), 1.98 (dd, \(J = 14.4, 10.6\) Hz, 1H), 1.75 (dd, \(J = 14.5, 3.9\) Hz, 1H), 1.05 (s, 3H), 1.00 (s, 3H). \(^13\)C NMR (101 MHz, Chloroform-\(d\)) \(\delta\) 139.76, 137.17, 132.93, 129.37, 128.20, 127.35, 127.04, 122.04, 52.64, 45.38, 34.77, 32.64, 25.69, 25.13. HRMS (ESI) (m/z): [M+Na]\(^{+}\) calcd. for C\(_{19}\)H\(_{22}\)N\(_2\)O\(_2\)S\(_2\)Na: 365.1300, found: 365.1302. 

\([\alpha]_D^{20.0} = 18.59\) (c 0.30, CHCl\(_3\)). HPLC (AD-H, 0.46*25 cm, 5 µm, hexane/isopropanol = 8/2, flow 0.5 mL/min, detection at 214 nm) retention time = 37.54 min (minor) and 41.14 min (major). 

(R)-N-(4-cyano-2,2-dimethyl-4-phenylbutyl)benzenesulfonamide (2z) Prepared following general procedure B the reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate = 5/1 as the eluent) to afford the product 2z (68.5 mg, 92% yield, 86% ee) as a white solid. \(^1\)H NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 7.90 – 7.81 (m, 2H), 7.61 – 7.55 (m, 1H), 7.54 – 7.48 (m, 2H), 7.39 – 7.29 (m, 5H), 4.91 (t, \(J = 7.2\) Hz, 1H), 3.82 (dd, \(J = 10.6, 3.8\) Hz, 1H), 2.85 (dd, \(J = 13.1, 8.2\) Hz, 1H), 2.71 (dd, \(J = 13.1, 6.3\) Hz, 1H), 1.98 (dd, \(J = 14.4, 10.6\) Hz, 1H), 1.75 (dd, \(J = 14.5, 3.9\) Hz, 1H), 1.05 (s, 3H), 1.00 (s, 3H). \(^13\)C NMR (101 MHz, Chloroform-\(d\)) \(\delta\) 139.76, 137.17, 132.93, 129.37, 128.20, 127.35, 127.04, 122.04, 52.64, 45.38, 34.77, 32.64, 25.69, 25.13. HRMS (ESI) (m/z): [M+Na]\(^{+}\) calcd. for C\(_{19}\)H\(_{22}\)N\(_2\)O\(_2\)S\(_2\)Na: 365.1300, found: 365.1302. 

\([\alpha]_D^{20.0} = 12.35\) (c 0.50, CHCl\(_3\)). HPLC (OD-H, 0.46*25 cm, 5 µm, hexane/isopropanol = 7/3, flow 0.5 mL/min, detection at 214 nm) retention time = 13.26 min (minor) and 17.62 min (major).
Mechanistic Studies

1. Procedure of the radical trapping experiment with TEMPO:

![Scheme S1](image)

Scheme S1. The radical trapping experiment with TEMPO, related to Scheme 2.

To a sealed tube containing TEMPO, solution A (2.0 mL), TMSCN (11.9 mg, 15 µL, 0.12 mmol, 1.2 equiv) and 1a (0.1 mmol, 1.0 equiv) were sequentially added under Ar atmosphere. The tube was sealed with a Teflon-lined cap, and the mixture was stirred at 10 °C for three days. After the reaction was completed, the mixture was concentrated. Then the residue was purified by silica gel chromatography with petroleum ether and ethyl acetate (PE/EA = 5:1) to afford the product.

2. Procedure of competition experiments:

![Scheme S2](image)

Scheme S2. Competitive experiments, related to Scheme 2.

To a sealed tube, solution A (2.0 mL), TMSCN (9.9 mg, 12.5 µL, 0.10 mmol, 1.0 equiv), 1c (0.1 mmol, 1.0 equiv) and 1e (0.1 mmol, 1.0 equiv) were sequentially added under Ar atmosphere. The tube was sealed with a Teflon-lined cap, and the mixture was stirred at 10 °C for 12 h. After the reaction was completed, the mixture was concentrated. Then the residue was purified by silica gel chromatography with petroleum ether and ethyl acetate (PE/EA = 5:1) to afford the product.

To a sealed tube, solution A (2.0 mL), TMSCN (9.9 mg, 12.5 µL, 0.10 mmol, 1.0 equiv), 1j (0.1 mmol, 1.0 equiv) and 1n (0.1 mmol, 1.0 equiv) were sequentially added under Ar atmosphere. The tube was sealed with a Teflon-lined cap, and the mixture was stirred at 10 °C for 8 h. After the reaction was completed, the mixture was concentrated. Then the residue was purified by silica gel chromatography with petroleum ether and ethyl acetate (PE/EA = 5:1) to afford the product.
Figure S1. $^1$H NMR spectrum of the mixture of 2j and 2n, related to Scheme 2.

3. Procedure of 5-exo cyclization reaction:

Scheme S3. 5-exo cyclization reaction, related to Scheme 2.

To a sealed tube, solution A (4.0 mL), TMSCN (23.8 mg, 30.0 uL, 0.24 mmol, 1.2 equiv), 4 (0.2 mmol, 1.0 equiv) were sequentially added under Ar atmosphere. The tube was sealed with a Teflon-lined cap, and the mixture was stirred at room temperature for two days. After the reaction was completed, the mixture was concentrated. Then the residue was purified by silica gel chromatography with petroleumether and ethylacetate (PE/EA = 5:1) to afford the product.

2-(1-(phenylsulfonyl)pyrrolidin-2-yl)acetonitrile (5)

$^1$H NMR (400 MHz, Chloroform-d) δ 7.89 – 7.82 (m, 2H), 7.69 – 7.62 (m, 1H), 7.61 – 7.54 (m, 2H), 3.90 – 3.78 (m, 1H), 3.52 (dt, $J = 10.2, 5.9$ Hz, 1H), 3.19 (dt, $J = 10.1, 7.1$ Hz, 1H), 2.90 (dd, $J = 16.8, 3.6$ Hz, 1H), 2.81 (dd, $J = 16.8, 7.9$ Hz, 1H), 2.03 – 1.93 (m, 1H), 1.90 (q, $J = 7.0$ Hz, 2H), 1.66 – 1.58 (m, 1H). $^{13}$C NMR (101 MHz, Chloroform-d) δ 136.77, 133.34, 129.46, 127.61, 117.52, 56.11, 49.72, 31.37, 25.40, 24.02. HRMS (ESI) (m/z): [M+Na]$^+$ calcd. for C$_{12}$H$_{14}$N$_2$O$_2$SNa: 273.0674, found: 273.0675.

4. Procedure of radical clock experiment:
Scheme S4. Radical clock experiment, related to Scheme 2.

To a sealed tube solution A (3.0 mL), TMSCN (17.9 mg, 22.5 µL, 0.18 mmol, 1.2 equiv) and 6 (0.15 mmol, 1.0 equiv) were sequentially added under Ar atmosphere. The tube was sealed with a Teflon-lined cap, and the mixture was stirred at 10 °C for three days. After the reaction was completed, the mixture was concentrated. Then the residue was purified by silica gel chromatography with petroleum ether and ethyl acetate (PE/EA = 5:1) to afford the product.

(R)-N-(7-cyano-7-phenylhept-4-en-1-yl)benzenesulfonamide (7)

\( ^1 \)H NMR (400 MHz, Chloroform-\( d \)) \( \delta 7.92 - 7.82 \) (m, 2H), \( 7.63 - 7.56 \) (m, 1H), \( 7.56 - 7.49 \) (m, 2H), \( 7.40 - 7.28 \) (m, 5H), \( 5.55 - 5.32 \) (m, 2H), \( 4.59 \) (s, 1H), \( 3.80 \) (t, \( J = 7.2 \) Hz, 1H), \( 3.01 - 2.84 \) (m, 2H), \( 2.53 \) (t, \( J = 6.9 \) Hz, 2H), \( 2.03 \) (q, \( J = 6.6 \) Hz, 2H), 1.59 – 1.45 (m, 2H). \( ^{13} \)C NMR (101 MHz, Chloroform-\( d \)) \( \delta 140.08, 135.37, 134.10, 132.74, 129.25, 129.16, 128.23, 127.42, 127.14, 125.56, 120.59, 42.54, 38.93, 38.10, 29.35, 29.10. HRMS (ESI) (m/z): [M+Na]\(^+\) calcd. for C\(_{20}\)H\(_{22}\)N\(_2\)O\(_2\)SNa: 377.1300, found: 377.1304.
References:

Wang, D., Wu, L., Wang, F., Wan, X., Chen, P., Lin, Z., Liu, G. Asymmetric copper-catalyzed intermolecular aminoarylation of styrenes: efficient access to optical 2,2-diarylethylamines. *J. Am. Chem. Soc.* **139**, 6811-6814 (2017).

Zhang, Z., Stateman, L. M., Nagib, D. A. δ C–H (hetero)arylation *via* Cu-catalyzed radical relay. *Chem. Sci.* **10**, 1207-1211 (2019).
Figure S2. X-Ray crystal data of 2a, related to Figure 2

Table 9 Crystal data and structure refinement for 2a, related to Figure 2.

| Identification code | 2a            |
|---------------------|---------------|
| Empirical formula   | C₁₇H₁₈N₂O₂S   |
| Formula weight      | 314.39        |
| Temperature/K       | 293(2)        |
Crystal system orthorhombic

| Parameter            | Value               |
|----------------------|---------------------|
| Space group          | P2₁2₁2₁             |
| a/Å                  | 8.93873(10)         |
| b/Å                  | 10.13670(8)         |
| c/Å                  | 18.31766(18)        |
| α/°                  | 90                  |
| β/°                  | 90                  |
| γ/°                  | 90                  |
| Volume/Å³            | 1659.75(3)          |
| Z                    | 4                   |
| ρ(calc) g/cm³        | 1.258               |
| μ/mm⁻¹               | 1.799               |
| F(000)               | 664.0               |
| Crystal size/mm³     | 0.3 × 0.3 × 0.2     |
| Radiation CuKα (λ = 1.54184) | 9.656 to 147.836 |
| 2Θ range for data collection/° | 9.656 to 147.836 |
| Index ranges         | -10 ≤ h ≤ 11, -12 ≤ k ≤ 12, -22 ≤ l ≤ 22 |
| Reflections collected| 15923               |
| Independent reflections| 3313 [R(int) = 0.0252, R(sigma) = 0.0146] |
| Data/restraints/parameters| 3313/0/199 |
| Goodness-of-fit on F² | 1.114               |
| Final R indexes [I>2σ(I)] | R₁ = 0.0344, wR₂ = 0.1209 |
| Final R indexes [all data] | R₁ = 0.0353, wR₂ = 0.1236 |
| Largest diff. peak/hole / Å⁻³ | 0.16/-0.37 |
| Flack parameter      | 0.009(6)            |

**Table 10** Fractional Atomic Coordinates (×10⁴) and Equivalent Isotropic Displacement Parameters (Å²×10⁻³) for 2a. U(eq) is defined as 1/3 of the trace of the orthogonalised U_ij tensor, related to Figure 2.

| Atom  | x      | y      | z      | U(eq)   |
|-------|--------|--------|--------|---------|
| S001  | -4627.8(6) | -1386.4(5) | -2339.6(3) | 56.6(2) |
| O002  | -5617(2)   | -262.1(18)  | -2362.4(14) | 79.9(6) |
| N1    | -5654(2)   | -2680.6(18) | -2370.3(11) | 58.0(4) |
| C1    | -3707(3)   | -1337(2)    | -1493.1(12) | 55.2(5) |
| C11   | -10477(3)  | -3162(2)    | -4098.7(12) | 57.0(5) |
| C9    | -8704(3)   | -2991(2)    | -3008.3(12) | 57.1(5) |
| O007  | -3511(2)   | -1512(3)    | -2887.8(11) | 81.3(6) |
| C8    | -8381(3)   | -2306(2)    | -2287.6(13)| 58.5(5) |
| C10   | -10138(3)  | -2483(2)    | -3377.4(13)| 56.4(5) |
| C7    | -6986(3)   | -2815(2)    | -1913.9(12)| 61.0(6) |
| C13   | -10029(5)  | -3464(4)    | -5380.9(16)| 90.5(10) |
| C17   | -10031(3)  | -1046(3)    | -3478.7(14)| 69.4(7) |
| N2    | -9918(4)   | 56(2)       | -3550.9(19)| 99.5(10) |
| C3    | -1792(5)   | -2174(4)    | -713.5(17) | 88.3(9) |
| C12   | -9728(4)   | -2818(3)    | -4727.1(15)| 75.3(7) |
| C16   | -11516(4)  | -4156(3)    | -4122.9(17)| 76.3(7) |
Table 11 Anisotropic Displacement Parameters (Å²×10³) for 2a. The Anisotropic displacement factor exponent takes the form: -2π²[h²a²U11+2hka*b*U12+…], related to Figure 2.

| Atom | U_{11} | U_{22} | U_{33} | U_{23} | U_{13} | U_{12} |
|------|--------|--------|--------|--------|--------|--------|
| S001 | 52.1(3) | 48.7(3) | 69.0(3) | 5.9(2) | 2.7(2) | -1.6(2) |
| O002 | 65.7(10) | 41.6(7) | 132.5(16) | 15.8(9) | -5.7(12) | -0.9(8) |
| N1   | 56.9(10) | 43.1(8) | 73.9(10) | -4.1(7) | -4.9(9) | 1.4(7) |
| C1   | 56.8(11) | 47.4(9) | 61.5(10) | -4.8(8) | 5.8(9) | -10.2(9) |
| C11  | 52.4(12) | 55.8(10) | 62.9(11) | 2.5(8) | -3.4(10) | 4.2(9) |
| C9   | 56.4(12) | 50.6(10) | 64.1(11) | -2.5(8) | -0.4(9) | 0.5(9) |
| O007 | 63.2(12) | 115.2(17) | 65.4(9) | 11.1(9) | 6.7(8) | -2.9(12) |
| C8   | 55.0(12) | 58.4(11) | 63.1(11) | -7.0(9) | 4.2(10) | -4.4(9) |
| C10  | 51.0(12) | 55.5(11) | 62.6(11) | -0.6(8) | 5.6(9) | -0.9(2) |
| C7   | 70.2(14) | 53.4(11) | 59.4(11) | 3.7(9) | -7.1(10) | -14.6(10) |
| C13  | 115(3) | 95(2) | 62.1(13) | -3.2(13) | 0.7(15) | 16(2) |
| C17  | 72.8(18) | 57.8(12) | 77.5(13) | -5.8(11) | -0.3(13) | 12.8(11) |
| N2   | 124(3) | 55.3(13) | 119(2) | -4.7(13) | -6(2) | 15.6(14) |
| C3   | 89(2) | 99(2) | 77.7(16) | 18.6(16) | -16.1(16) | -15.0(19) |
| C12  | 85.6(19) | 73.2(15) | 67.2(13) | 0.1(11) | 5.2(13) | -9.2(15) |
| C16  | 70.8(16) | 73.7(15) | 84.6(16) | 2.8(13) | -8.4(15) | -10.9(14) |
| C14  | 104(3) | 93(2) | 82.4(19) | -21.7(16) | -29.7(19) | 17.6(19) |
| C6   | 92(2) | 75.6(16) | 90.9(18) | -27.5(15) | 18.0(17) | -3.8(16) |
| C15  | 87(2) | 91(2) | 115(3) | -22(2) | -22(2) | -12(2) |
| C4   | 139(4) | 112(3) | 63.8(14) | 1.5(17) | -14.2(19) | -52(3) |
| C2   | 72.2(15) | 63.1(12) | 65.5(12) | 1.4(11) | -1.4(11) | 0.9(12) |
| C5   | 140(4) | 117(3) | 81(2) | -38(2) | 14(3) | -25(3) |

Table 12 Bond Lengths for 2a, related to Figure 2.

| Atom | Atom | Length/Å |
|------|------|----------|
| S001 | O002 | 1.443(19) |
| S001 | N1   | 1.6011(19) |
| S001 | C1   | 1.756(2) |
| S001 | O007 | 1.421(2) |
| N1   | C7   | 1.461(3) |
| C1   | C6   | 1.381(3) |
| C1   | C2   | 1.390(4) |
| C11  | C10  | 1.520(3) |
| C11  | C15  | 1.390(5) |
| Atom | Atom | Atom | Angle/° | Atom | Atom | Atom | Angle/° |
|------|------|------|---------|------|------|------|---------|
| O002 | S001 | N1   | 107.14(11) | C11 | C10 | C9   | 113.37(19) |
| O002 | S001 | C1   | 106.89(13) | C17 | C10 | C11  | 110.6(2)  |
| N1   | S001 | C1   | 108.82(10) | C17 | C10 | C9   | 109.4(2)  |
| O002 | S001 | O002 | 118.72(14) | N1  | C7  | C8   | 112.40(18) |
| O007 | S001 | N1   | 107.70(13) | C14 | C13 | C12  | 120.1(3)  |
| O007 | S001 | C1   | 107.29(12) | N2  | C17 | C10  | 178.5(4)  |
| C7   | N1   | S001 | 121.51(16) | C2  | C3  | C4   | 119.4(4)  |
| C6   | C1   | S001 | 120.0(2)   | C11 | C12 | C13  | 120.5(3)  |
| C6   | C1   | C2   | 121.7(3)   | C11 | C16 | C15  | 120.1(3)  |
| C2   | C1   | S001 | 118.31(18) | C13 | C14 | C15  | 119.5(3)  |
| C12  | C11  | C10  | 121.1(2)   | C1  | C6  | C5   | 118.2(4)  |
| C16  | C11  | C10  | 119.7(2)   | C14 | C15 | C16  | 120.6(4)  |
| C16  | C11  | C12  | 119.2(3)   | C5  | C4  | C3   | 121.1(3)  |
| C8   | C9   | C10  | 112.8(2)   | C3  | C2  | C1   | 118.8(3)  |
| C7   | C8   | C9   | 113.2(2)   | C4  | C5  | C6   | 120.7(4)  |

Table 13 Bond Angles for 2a, related to Figure 2.

| Atom | x     | y     | z     | U(eq) |
|------|-------|-------|-------|-------|
| H1   | -5108.69 | -3377.48 | -2339.08 | 70    |
| H9A  | -8800.19 | -3931.39 | -2922.99 | 68    |
| H9B  | -7865.15 | -2856.69 | -3335.77 | 68    |
| H8A  | -8269.39 | -1367.14 | -2375.01 | 71    |
| H8B  | -9228.68 | -2426.65 | -1964.05 | 71    |
| H10  | -10976.48 | -2656.57 | -3046.07 | 68    |
| H7A  | -6835.46 | -2331.35 | -1462.77 | 73    |
| H7B  | -7125.64 | -3737.04 | -1790.83 | 73    |
| H13  | -9510.61 | -3233.46 | -5802.07 | 109   |
| H3   | -1011.25 | -2756.37 | -620.13  | 106   |
| H12  | -9016.66 | -2149.67 | -4714.63 | 90    |
| H16  | -12024.14 | -4400.07 | -3701.04 | 92    |
| H14  | -11309.5 | -4851.88 | -5844.58 | 112   |
| H6   | -4874.57 | 191.83  | -1071.3  | 103   |
| H15  | -12506.2 | -5480.93 | -4789.51 | 117   |
| H4   | -1690.14 | -1201.77 | 246.64   | 126   |
| H2   | -2321.38 | -2870.68 | -1713.79 | 80    |
| H5   | -3544.5  | 272.51  | 19.35    | 135   |

Table 14 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for 2a, related to Figure 2.
NMR Spectra of New Compounds (\(^1\)H NMR, \(^{19}\)F NMR, \(^{13}\)C NMR)

Figure S3. \(^1\)H NMR of 1a, related to Figure 2.

Figure S4. \(^{13}\)C NMR of 1a, related to Figure 2.
Figure S5. $^{19}$F NMR of 1a, related to Figure 2.

Figure S6. $^1$H NMR of 1d, related to Figure 2.
Figure S7. $^{13}$C NMR of 1d, related to Figure 2.

Figure S8. $^{19}$F NMR of 1d, related to Figure 2.
Figure S9. $^1$H NMR of 1e, related to Figure 2.

Figure S10. $^{13}$C NMR of 1e, related to Figure 2.
Figure S11. $^{19}$F NMR of 1e, related to Figure 2.

Figure S12. $^1$H NMR of 1f, related to Figure 2.
Figure S13. $^{13}$C NMR of 1f, related to Figure 2.

Figure S14. $^{19}$F NMR of 1f, related to Figure 2.
Figure S15. $^1$H NMR of 1g, related to Figure 2.

Figure S16. $^{13}$C NMR of 1g, related to Figure 2.
Figure S17. $^{13}$C NMR of $1g$, related to Figure 2.

Figure S18. $^1$H NMR of $1h$, related to Figure 2.
Figure S19. $^{13}$C NMR of 1h, related to Figure 2.

Figure S20. $^1$H NMR of 1h, related to Figure 2.
Figure S21. $^1$H NMR of 1, related to Figure 2.

Figure S22. $^{13}$C NMR of 1, related to Figure 2.
Figure S23. \textsuperscript{19}F NMR of \textit{1i}, related to Figure 2.

Figure S24. \textsuperscript{1}H NMR of \textit{1j}, related to Figure 2.
Figure S25. $^{13}$C NMR of 1j, related to Figure 2.

Figure S26. $^{19}$F NMR of 1j, related to Figure 2.
Figure S27. $^1$H NMR of 1k, related to Figure 2.

Figure S28. $^{13}$C NMR of 1k, related to Figure 2.
Figure S29. $^{19}$F NMR of 1k, related to Figure 2.

Figure S30. $^1$H NMR of 1l, related to Figure 2.
Figure S31. $^{13}$C NMR of II, related to Figure 2.

Figure S32. $^{19}$F NMR of II, related to Figure 2.
Figure S33. $^1$H NMR of $1\text{m}$, related to Figure 2.

Figure S34. $^{13}$C NMR of $1\text{m}$, related to Figure 2.
Figure S35. $^{19}$F NMR of 1m, related to Figure 2.

Figure S36. $^1$H NMR of 1n, related to Figure 2.
Figure S37. $^1$H NMR of 1n, related to Figure 2.

Figure S38. $^1$H NMR of 1n, related to Figure 2.
Figure S39. $^1$H NMR of 1o, related to Figure 2.

Figure S40. $^{13}$C NMR of 1o, related to Figure 2.
Figure S41. $^{19}$F NMR of $1\text{o}$, related to Figure 2.

Figure S42. $^{1}$H NMR of $1\text{p}$, related to Figure 2.
Figure S43. $^{13}$C NMR of 1p, related to Figure 2.

Figure S44. $^{19}$F NMR of 1p, related to Figure 2.
Figure S45. $^1$H NMR of 1q, related to Figure 2.

Figure S46. $^{13}$C NMR of 1q, related to Figure 2.
Figure S47. $^{19}$F NMR of 1q, related to Figure 2.

Figure S48. $^1$H NMR of 1r, related to Figure 2.
Figure S49. $^{13}$C NMR of Ir, related to Figure 2.

Figure S50. $^{19}$F NMR of Ir, related to Figure 2.
Figure S51. $^1$H NMR of 1s, related to Figure 2.

Figure S52. $^{13}$C NMR of 1s, related to Figure 2.
Figure S53. $^{19}$F NMR of 1s, related to Figure 2.

Figure S54. $^1$H NMR of 1t, related to Figure 2.
Figure S55. $^{13}$C NMR of I$t$, related to Figure 2.

Figure S56. $^{19}$F NMR of I$t$, related to Figure 2.
Figure S57. $^1$H NMR of 1u, related to Figure 2.

Figure S58. $^{13}$C NMR of 1u, related to Figure 2.
Figure S59. $^{19}$F NMR of 1u, related to Figure 2.

Figure S60. $^1$H NMR of 1v, related to Figure 2.
Figure S61. $^{13}$C NMR of 1v, related to Figure 2.

Figure S62. $^{19}$F NMR of 1v, related to Figure 2.
Figure S63. $^1$H NMR of 1w, related to Figure 2.

Figure S64. $^{13}$C NMR of 1w, related to Figure 2.
Figure S65. $^{19}$F NMR of 1w, related to Figure 2.

Figure S66. $^1$H NMR of 1x, related to Figure 2.
Figure S67. $^{13}$C NMR of 1x, related to Figure 2.

Figure S68. $^{19}$F NMR of 1x, related to Figure 2.
Figure S69. $^1$H NMR of 1y, related to Figure 2.

Figure S70. $^{13}$C NMR of 1y, related to Figure 2.
Figure S71. $^{19}$F NMR of 1y, related to Figure 2.

Figure S72. $^1$H NMR of 1z, related to Figure 2.
Figure S73. $^{13}$C NMR of 1z, related to Figure 2.

Figure S74. $^{19}$F NMR of 1z, related to Figure 2.
Figure S75. $^1$H NMR of 2a, related to Figure 2.

Figure S76. $^{13}$C NMR of 2a, related to Figure 2.
Figure S77. $^1H$ NMR of 2b, related to Figure 2.

Figure S78. $^{13}C$ NMR of 2b, related to Figure 2.
Figure S79. $^1$H NMR of 2c, related to Figure 2.

Figure S80. $^{13}$C NMR of 2c, related to Figure 2.
Figure S81. $^1$H NMR of 2d, related to Figure 2.

Figure S82. $^{13}$C NMR of 2d, related to Figure 2.
Figure S83. $^1$H NMR of 2e, related to Figure 2.

Figure S84. $^{13}$C NMR of 2e, related to Figure 2.
Figure S85. $^{19}$F NMR of 2e, related to Figure 2.

Figure S86. $^1$H NMR of 2f, related to Figure 2.
Figure S87. $^{13}$C NMR of 2f, related to Figure 2.

Figure S88. $^1$H NMR of 2g, related to Figure 2.
Figure S89. $^{13}$C NMR of 2g, related to Figure 2.

Figure S90. $^1$H NMR of 2h, related to Figure 2.
Figure S91. $^{13}$C NMR of 2h, related to Figure 2.

Figure S92. $^1$H NMR of 2i, related to Figure 2.
Figure S93. $^{13}$C NMR of 2i, related to Figure 2.

Figure S94. $^1$H NMR of 2j, related to Figure 2.
Figure S95. $^{13}$C NMR of 2j, related to Figure 2.

Figure S96. $^1$H NMR of 2k, related to Figure 2.
Figure S97. $^{13}$C NMR of 2k, related to Figure 2.

Figure S98. $^{19}$F NMR of 2k, related to Figure 2.
Figure S99. $^1$H NMR of 2l, related to Figure 2.

Figure S100. $^{13}$C NMR of 2l, related to Figure 2.
Figure S101. $^1$H NMR of 2m, related to Figure 2.

Figure S102. $^{13}$C NMR of 2m, related to Figure 2.
Figure S103. $^1$H NMR of 2n, related to Figure 2.

Figure S104. $^{13}$C NMR of 2n, related to Figure 2.
Figure S105. $^{19}$F NMR of 2n, related to Figure 2.

Figure S106. $^1$H NMR of 2o, related to Figure 2.
Figure S107. $^{13}\text{C}$ NMR of 2o, related to Figure 2.

Figure S108. $^1\text{H}$ NMR of 2p, related to Figure 2.
Figure S109. $^{13}$C NMR of 2p, related to Figure 2.

Figure S110. $^1$H NMR of 2q, related to Figure 2.
Figure S11. $^{13}$C NMR of $2q$, related to Figure 2.

Figure S12. $^1$H NMR of $2r$, related to Figure 2.
Figure S113. $^{13}$C NMR of 2r, related to Figure 2.

Figure S114. $^{19}$F NMR of 2r, related to Figure 2.
Figure S115. $^1$H NMR of 2s, related to Figure 2.

Figure S116. $^{13}$C NMR of 2s, related to Figure 2.
Figure S117. $^1$H NMR of 2t, related to Figure 2.

Figure S118. $^{13}$C NMR of 2t, related to Figure 2.
Figure S119. $^{19}$F NMR of 2t, related to Figure 2.

Figure S120. $^1$H NMR of 2u, related to Figure 2.
Figure S1. $^{13}$C NMR of 2u, related to Figure 2.

Figure S12. $^{19}$F NMR of 2u, related to Figure 2.
Figure S123. $^1$H NMR of 2v, related to Figure 2.

Figure S124. $^{13}$C NMR of 2v, related to Figure 2.
Figure S12. $^1$H NMR of 2w, related to Figure 2.

Figure S12. $^{13}$C NMR of 2w, related to Figure 2.
Figure S127. $^1$H NMR of 2x, related to Figure 2.

Figure S128. $^{13}$C NMR of 2x, related to Figure 2.
Figure S129. $^1$H NMR of 2y, related to Figure 2.

Figure S130. $^{13}$C NMR of 2y, related to Figure 2.
Figure S131. $^1$H NMR of 2z, related to Figure 2.

Figure S132. $^{13}$C NMR of 2z, related to Figure 2.
Figure S13. $^1$H NMR of 4, related to Scheme 2.

Figure S134. $^{13}$C NMR of 4, related to Scheme 2.
Figure S135. $^{19}$F NMR of 4, related to Scheme 2.

Figure S136. $^1$H NMR of 5, related to Scheme 2.
Figure S137. $^{13}$C NMR of 5, related to Scheme 2.

Figure S138. $^1$H NMR of 6, related to Scheme 2.
Figure S139. $^{13}$C NMR of 6, related to Scheme 2.

Figure S140. $^{19}$F NMR of 6, related to Scheme 2.
Figure S141. $^1$H NMR of 7, related to Scheme 2.

Figure S142. $^{13}$C NMR of 7, related to Scheme 2.
Figure S143. HPLC data of rac-2a, related to Figure 2.

Figure S144. HPLC data of 2a, related to Figure 2.
Figure S145. HPLC data of rac-2b, related to Figure 2.

Figure S146. HPLC data of 2b, related to Figure 2.
Figure S147. HPLC data of rac-2c, related to Figure 2.

Figure S148. HPLC data of 2c, related to Figure 2.
Figure S149. HPLC data of rac-2d, related to Figure 2.

Figure S150. HPLC data of 2d, related to Figure 2.
Figure S151. HPLC data of rac-2e, related to Figure 2.

Figure S152. HPLC data of 2e, related to Figure 2.
Figure S153. HPLC data of rac-2f, related to Figure 2.

Figure S154. HPLC data of 2f, related to Figure 2.
Figure S155. HPLC data of rac-2g, related to Figure 2.

Figure S156. HPLC data of 2g, related to Figure 2.
Figure S157. HPLC data of rac-2h, related to Figure 2.

| 峰号 | 保留时间 | 面积 | 面积% | 高度 | 标记 |
|------|----------|------|-------|------|------|
| 1    | 19.678   | 108938346 | 48.935 | 2400876 | M    |
| 2    | 21.575   | 113679614  | 51.065 | 2278074 | M    |
| 总计 |          | 222617960 | 100.000 | 4678950 |      |

Figure S158. HPLC data of 2h, related to Figure 2.

| 峰号 | 保留时间 | 面积 | 面积% | 高度 | 标记 |
|------|----------|------|-------|------|------|
| 1    | 20.218   | 5823598  | 6.877  | 175191 | M    |
| 2    | 21.848   | 78856066 | 93.123 | 1769621 | M    |
| 总计 |          | 84679663 | 100.000 | 1944811 |      |
Figure S159. HPLC data of rac-2i, related to Figure 2.

Figure S160. HPLC data of 2i, related to Figure 2.
Figure S161. HPLC data of rac-2j, related to Figure 2.

Figure S162. HPLC data of 2j, related to Figure 2.
Figure S163. HPLC data of rac-2k, related to Figure 2.

Figure S164. HPLC data of 2k, related to Figure 2.
Figure S165. HPLC data of rac-2l, related to Figure 2.

Figure S166. HPLC data of 2l, related to Figure 2.
Figure S167. HPLC data of rac-2m, related to Figure 2.

Figure S168. HPLC data of 2m, related to Figure 2.
Figure S169. HPLC data of rac-2n, related to Figure 2.

Figure S170. HPLC data of 2n, related to Figure 2.
Figure S171. HPLC data of rac-2o, related to Figure 2.

**Figure S172. HPLC data of 2o, related to Figure 2.**
Figure S173. HPLC data of rac-2p, related to Figure 2.

| 峰号 | 保留时间 | 面积% | 面积   | 高度   | 标记 |
|------|----------|------|--------|--------|------|
| 1    | 36.386   | 49.72 | 22109730 | 337653 | M    |
| 2    | 42.959   | 50.27 | 22356073 | 291561 | M    |
| 总计 |          | 100.00 | 44465803 | 629214 |      |

Figure S174. HPLC data of 2p, related to Figure 2.

| 峰号 | 保留时间 | 面积% | 面积   | 高度 | 标记 |
|------|----------|------|--------|------|------|
| 1    | 39.338   | 3.733 | 2881025 | 41233 | M    |
| 2    | 45.535   | 96.26 | 74295852 | 843885 | M    |
| 总计 |          | 100.00 | 77178777 | 886118 |      |
Figure S175. HPLC data of rac-2q, related to Figure 2.

| 峰号 | 保留时间 | 面积% | 面积 | 高度 | 标记 |
|------|----------|------|------|------|------|
| 1    | 27.093   | 51.853 | 58740492 | 1211363 | M    |
| 2    | 32.081   | 48.147 | 54542872 | 995634  | M    |
| 总计 |          | 100.000 | 113283364 | 2206998 | M    |

Figure S176. HPLC data of 2q, related to Figure 2.

| 峰号 | 保留时间 | 面积% | 面积 | 高度 | 标记 |
|------|----------|------|------|------|------|
| 1    | 27.739   | 3.725 | 2027757 | 44497   | M    |
| 2    | 32.430   | 96.275 | 52415512 | 910129  | M    |
| 总计 |          | 100.000 | 54443269 | 954617  | M    |
Figure S177. HPLC data of rac-2r, related to Figure 2.

Figure S178. HPLC data of 2r, related to Figure 2.
Figure S179. HPLC data of rac-2s, related to Figure 2.

Figure S180. HPLC data of 2s, related to Figure 2.
Figure S181. HPLC data of rac-2t, related to Figure 2.

| 峰号 | 保留时间 | 面积% | 面积     | 高度     | 标记 |
|-----|--------|------|---------|---------|------|
| 1   | 29.460 | 49.853 | 21095675 | 587941 | M    |
| 2   | 34.157 | 50.147 | 21220385 | 505914 | M    |
| 总计 | 100.000 | 42316060 | 1093855 | 1093855 | 1093855 |

Figure S182. HPLC data of 2t, related to Figure 2.

| 峰号 | 保留时间 | 面积% | 面积     | 高度     | 标记 |
|-----|--------|------|---------|---------|------|
| 1   | 29.227 | 3.067 | 1220161 | 36392   | M    |
| 2   | 33.901 | 96.933 | 38561063 | 946462  | M    |
| 总计 | 100.000 | 39781224 | 982854 | 982854 |
Figure S183. HPLC data of rac-2u, related to Figure 2.

Figure S184. HPLC data of 2u, related to Figure 2.
Figure S185. HPLC data of rac-2\textit{v}, related to Figure 2.

| 峰号 | 保留时间 | 面积% | 面积 | 高度 | 标记 |
|------|----------|------|------|------|------|
| 1    | 30.256   | 49.631 | 15059593 | 287218 | M    |
| 2    | 32.672   | 50.369 | 15283631 | 264088 | M    |
| 总计 | 100.000  | 30343224 | 551305 |      |      |

Figure S186. HPLC data of 2\textit{v}, related to Figure 2.

| 峰号 | 保留时间 | 面积% | 面积 | 高度 | 标记 |
|------|----------|------|------|------|------|
| 1    | 30.227   | 7.501 | 4960280  | 102400 | M    |
| 2    | 32.254   | 92.499 | 61165750 | 1003022 | M    |
| 总计 | 100.000  |    | 66126029 | 1105422 |      |
Figure S187. HPLC data of rac-2w, related to Figure 2.

Figure S188. HPLC data of 2w, related to Figure 2.
Figure S189. HPLC data of rac-$2x$, related to Figure 2.

Figure S190. HPLC data of $2x$, related to Figure 2.
Figure S191. HPLC data of rac-2y, related to Figure 2.

Figure S192. HPLC data of 2y, related to Figure 2.
Figure S193. HPLC data of rac-2z, related to Figure 2.

| 峰号 | 保留时间 | 面积% | 面积 | 高度   | 标记 |
|------|-----------|------|------|--------|------|
| 1    | 12.748    | 48.951 | 53812413 | 1915599 | M    |
| 2    | 17.067    | 51.049 | 56118615 | 1575674 | M    |
| 总计 | 100.000   | 109931028 | 3491183   |        |      |

Figure S194. HPLC data of 2z, related to Figure 2.

| 峰号 | 保留时间 | 面积% | 面积 | 高度   | 标记 |
|------|-----------|------|------|--------|------|
| 1    | 13.263    | 7.554 | 3582124 | 133245 | M    |
| 2    | 17.623    | 92.446 | 43836613 | 1185247 | M    |
| 总计 | 100.000   |        | 47418737 | 1318492 |      |