Supporting Information

Enantioselective Nickel-Catalyzed Dicarbofunctionalization of 3,3,3-Trifluoropropene

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I. Supplementary Notes

1. General information and materials

**General Information**: $^1$H NMR and $^{13}$C NMR spectra were recorded on Bruker AM 400, Agilent MR 400 and Agilent MR 500 spectrometers. $^{19}$F NMR was recorded on the Agilent MR 400 spectrometer ($\text{CFCl}_3$ as an external standard and low field is positive). All $^1$H NMR, $^{13}$C NMR and $^{19}$F NMR spectra were recorded at room temperature. The chemical shifts ($\delta$) are given in parts per million (ppm) relative to CDCl$_3$ (7.26 ppm for $^1$H) or TMS (0 ppm for $^1$H) and CDCl$_3$ (77.0 ppm for $^{13}$C), and coupling constants ($J$) are reported in Hertz (Hz). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, dd = doublet of doublets, m = multiplet, br = broad. NMR yield was determined by $^{19}$F NMR using benzotrifluoride as an internal standard before working up the reaction mixture. High performance liquid chromatography was performed on Waters 2487-600E, Waters ACQUITY UPC2, and Agilent Series HPLC, using PC-3, PC-4, AY-3, IC, IG, ADH, OJH, ODH, ASH chiral columns eluted with a mixture of acetonitrile/water or hexane/isopropyl alcohol. Optical rotation was measured on Rudolph-Autopol I and Autopol VI.

**Materials**: All reagents were used as received from commercial sources unless specified otherwise, or prepared according to literatures as described below. Anhydrous 1,4-dioxane (99.5%, extra dry, with molecular sieves, water $\leq$ 50 ppm (by K.F.)), $1,2$-dimethoxyethane (DME, 99%, extra dry, with molecular sieves, water $\leq$ 50 ppm (by K.F.)) and $N,N$-dimethylacetamide (DMA, 99.8%, extra dry, with molecular sieves, water $\leq$ 50 ppm (by K.F.)) were purchased from Energy Chemical. NiBr$_2$-DME was purchased from Strem Chemicals, Inc.
II. Supplementary Methods

2. Optimizations of the nickel-catalyzed dicarbofunctionalization of 3,3,3-trifluoropropene

**Supplementary Table 1.** Ligand effect on the reaction of TFP with 2a and 3a

| Entry | Ligand | 4a, Yield (%)<sup>b</sup> | 4a, ee (%)<sup>c</sup> |
|-------|--------|--------------------------|------------------------|
| 1     | L1     | 84                       | -                      |
| 2     | L2     | 51                       | 87                     |
| 3     | L3     | 66                       | 90                     |
| 4     | L4     | 72                       | 69                     |
| 5     | L5     | 61                       | 63                     |
| 6     | L6     | 69                       | 90                     |
| 7     | L7     | 52                       | 13                     |
| 8     | L8     | n.d.                     | -                      |
| 9     | L9     | n.d.                     | -                      |

<sup>a</sup>Reaction conditions (unless otherwise specified): 1 (0.64 mmol, 0.54 mL, 1.2 M in DMA, 1.6 equiv), 2a (0.6 mmol, 1.5 equiv), 3a (0.4 mmol, 1.0 equiv), 1,4-dioxane (3.2 mL). <sup>b</sup>Determined by <sup>19</sup>F NMR using benzotrifluoride as an internal standard. <sup>c</sup>Determined by chiral HPLC. n.d., not detected.
**Supplementary Table 2.** Solvent effect on the reaction of TFP with 2a and 3a

| Entry | Solvent                  | 4a, Yield (%)<sup>b</sup> | 4a, ee (%)<sup>c</sup> |
|-------|--------------------------|---------------------------|------------------------|
| 1     | 1,4-dioxane/DMA = 6:1   | 69                        | 90                     |
| 2     | DME/DMA = 6:1           | 74 (70)                   | 91                     |
| 3     | THF/DMA = 6:1           | 65                        | 90                     |
| 4     | Diglyme/DMA = 6:1       | 76                        | 90                     |
| 5     | Acetone/DMA = 6:1       | 70                        | 86                     |
| 6     | EtOAc/DMA = 6:1         | 65                        | 90                     |
| 7     | DME/DMA = 8:1           | 66                        | 91                     |
| 8     | DME/DMA = 4:1           | 64                        | 90                     |
| 9     | DME/DMA = 2:1           | 57                        | 89.5                   |
| 10    | DME                     | 6                         | -                      |
| 11    | DMA                     | 32                        | 86                     |

<sup>a</sup>Reaction conditions (unless otherwise specified): 1 (0.64 mmol, 0.54 mL, 1.2 M in DMA, 1.6 equiv), 2a (0.6 mmol, 1.5 equiv), 3a (0.4 mmol, 1.0 equiv), solvent (3.2 mL).<sup>b</sup>Determined by <sup>19</sup>F NMR using benzotrifluoride as an internal standard, and number in parentheses is the isolated yield. <sup>c</sup>Determined by chiral HPLC.
**Supplementary Table 3.** Screening of the nickel sources for the reaction of TFP with 2a and 3a

| Entry | [Ni] | 4a, Yield (%) | 4a, ee (%) |
|-------|------|----------------|------------|
| 1     | NiBr₂·DME | 74 | 91 |
| 2     | NiCl₂·DME | 70 | 91 |
| 3     | Ni(COD)₂ | 70 | 91.5 |
| 4     | NiBr₂·Diglyme | 63 | 91 |
| 5     | NiCl₂ | n.d. | - |
| 6     | NiBr₂ | n.d. | - |
| 7     | NiI₂ | 5 | - |
| 8     | None | n.d. | - |

*aReaction conditions (unless otherwise specified): 1 (0.64 mmol, 0.54 mL, 1.2 M in DMA, 1.6 equiv), 2a (0.6 mmol, 1.5 equiv), 3a (0.4 mmol, 1.0 equiv), DME (3.2 mL). bDetermined by ¹⁹F NMR using benzotrifluoride as an internal standard. cDetermined by chiral HPLC.*
Supplementary Table 4. Ligand effect on the reaction of TFP with 2b and 3k

| Entry | Ligand | 5b, Yield (%)<sup>b</sup> | 5b, ee (%)<sup>c</sup> |
|-------|--------|--------------------------|---------------------|
| 1     | L1     | 44                       | -                   |
| 2     | L3     | 27                       | 80                  |
| 3     | L4     | 41                       | 53                  |
| 4     | L5     | 42                       | 65                  |
| 5     | L6     | 36                       | 87                  |
| 6     | L7     | 29                       | 81                  |
| 7     | L8     | 11                       | 93                  |
| 8     | None   | trace                    | -                   |

<sup>a</sup>Reaction conditions (unless otherwise specified): 1 (1.2 M in DMA; 0.27 mL, 0.32 mmol, 1.6 equiv), 2b (0.3 mmol, 1.5 equiv), 3k (0.2 mmol, 1.0 equiv), 1,4-dioxane (1.6 mL).  
<sup>b</sup>Determined by <sup>19</sup>F NMR using benzotrifluoride as an internal standard.  
<sup>c</sup>Determined by chiral HPLC.
**Supplementary Table 5. Optimization of the loading amount of 2b**

\[
\begin{array}{cccc}
\text{Entry} & x & \text{5b, Yield (%)}^b & \text{5b, ee (%)}^c \\
1 & 1.2 & 29 & - \\
2 & 1.5 & 36 & - \\
3 & 2.0 & 27 & - \\
4 & 2.5 & 31 & - \\
\end{array}
\]

\(^a\)Reaction conditions (unless otherwise specified): 1 (1.2 M in DMA; 0.27 mL, 0.32 mmol, 1.6 equiv), 3k (0.2 mmol, 1.0 equiv), 1,4-dioxane (1.6 mL). \(^b\)Determined by \(^{19}\)F NMR using benzotrifluoride as an internal standard. \(^c\)Determined by chiral HPLC.

**Supplementary Table 6. Optimization of the loading amount of nickel catalyst and ligand L6**

\[
\begin{array}{cccccc}
\text{Entry} & x & y & \text{5b, Yield (%)}^b & \text{5b, ee (%)}^c \\
1 & 10 & 10 & 36 & 87 \\
2 & 12 & 10 & 46 & 89 \\
3 & 14 & 10 & 41 & 89 \\
4 & 20 & 10 & 33 & - \\
5 & 15 & 7.5 & 35 & - \\
\end{array}
\]

\(^a\)Reaction conditions (unless otherwise specified): 1 (1.2 M in DMA; 0.27 mL, 0.32 mmol, 1.6 equiv), 2b (0.3 mmol, 1.5 equiv), 3k (0.2 mmol, 1.0 equiv), 1,4-dioxane (1.6 mL). \(^b\)Determined by \(^{19}\)F NMR using benzotrifluoride as an internal standard. \(^c\)Determined by chiral HPLC.
Supplementary Table 7. Screening of the nickel sources for the reaction of TFP with 2b and 3k

![Chemical structure](image)

| Entry | [Ni]             | \(5b\), Yield (%) \(^b\) | \(5b\), ee (%) \(^c\) |
|-------|------------------|--------------------------|------------------------|
| 1     | NiBr\(_2\)-DME   | 46                       | 89                     |
| 2     | NiCl\(_2\)-DME   | 37                       | -                      |
| 3     | NiI\(_2\)        | 39                       | -                      |
| 4     | NiBr\(_2\)-Diglyme | 33                      | -                      |
| 5     | NiBr\(_2\)(PPh\(_3\)) | 0                      | -                      |
| 6     | NiCl\(_2\)(PCy\(_3\)) | 6                      | -                      |

\(^a\)Reaction conditions (unless otherwise specified): \(1\) (1.2 M in DMA; 0.27 mL, 0.32 mmol, 1.6 equiv), \(2b\) (0.3 mmol, 1.5 equiv), \(3k\) (0.2 mmol, 1.0 equiv), 1,4-dioxane (1.6 mL). \(^b\)Determined by \(^{19}\)F NMR using benzotrifluoride as an internal standard. \(^c\)Determined by chiral HPLC.
**Supplementary Table 8.** Optimization of the solvent for the reaction of TFP with 2b and 3k<sup>a</sup>

| Entry | Solvent | 5b, Yield (%)<sup>b</sup> | 5b, ee (%)<sup>c</sup> |
|-------|---------|--------------------------|------------------------|
| 1     | 1,4-dioxane/DMA = 6:1 | 46 | 89 |
| 2     | DME/DMA = 6:1 | 52 | 87 |
| 3     | THF/DMA = 6:1 | 29 | -- |
| 4     | Acetone/DMA = 6:1 | 30 | -- |
| 5     | 1,4-dioxane/DMA = 3:1 | 42 | -- |
| 6     | 1,4-dioxane/DMA = 1:1 | 16 | -- |
| 7     | DMA | trace | -- |

<sup>a</sup>Reaction conditions (unless otherwise specified): 1 (1.2 M in DMA; 0.27 mL, 0.32 mmol, 1.6 equiv), 2b (0.3 mmol, 1.5 equiv), 3k (0.2 mmol, 1.0 equiv), solvent (1.6 mL).<sup>b</sup>Determined by <sup>19</sup>F NMR using benzotri fluoride as an internal standard. <sup>c</sup>Determined by chiral HPLC.
**Supplementary Table 9.** Additive effect on the reaction of TFP with 2b and 3k<sup>a</sup>

![Chemical structure of the reaction]

| Entry | Additive | 5b, Yield (%)<sup>b</sup> | 5b, ee (%)<sup>c</sup> |
|-------|----------|---------------------------|------------------------|
| 1     | None     | 52                        | 87                     |
| 2     | TMSCl    | 26                        | --                     |
| 3     | TBAI     | 47                        | --                     |
| 4     | NaI      | 58                        | --                     |
| 5     | FeCl₃    | 67                        | 87                     |
| 6     | LiI      | 48                        | --                     |
| 7     | ZnI₂     | 41                        | --                     |
| 8     | MgBr₂    | 42                        | --                     |
| 9     | 3 Å MS (150 mg) | 31 | -- |
| 10    | 4 Å MS (150 mg) | 39 | -- |

<sup>a</sup>Reaction conditions (unless otherwise specified): 1 (1.2 M in DMA; 0.27 mL, 0.32 mmol, 1.6 equiv), 2b (0.3 mmol, 1.5 equiv), 3k (0.2 mmol, 1.0 equiv), DME (1.6 mL).<sup>b</sup>Determined by <sup>19</sup>F NMR using benzotrifluoride as an internal standard. <sup>c</sup>Determined by chiral HPLC.
**Supplementary Table 10. Optimization of the loading amount of additive**

| Entry | Additive | 5b, Yield (%) | 5b, ee (%) |
|-------|----------|---------------|------------|
| 1     | NaI (0.25 equiv) | 54            | --         |
| 2     | NaI (0.5 equiv)   | 58            | --         |
| 3     | NaI (1.0 equiv)   | 58            | --         |
| 4     | FeCl₃ (0.25 equiv) | 70            | 87         |
| 5     | FeCl₃ (0.5 equiv) | 67            | 87         |
| 6     | FeCl₃ (1.0 equiv) | 41            | --         |

*aReaction conditions (unless otherwise specified): 1 (1.2 M in DMA; 0.27 mL, 0.32 mmol, 1.6 equiv), 2b (0.3 mmol, 1.5 equiv), 3k (0.2 mmol, 1.0 equiv), DME (1.6 mL). *bDetermined by ¹⁹F NMR using benzotrifluoride as an internal standard. *cDetermined by chiral HPLC.*
3. General procedure for the preparation of tertiary alkyl and aryl iodides.

3.1 General procedure for the preparation of tertiary alkyl iodides 2

To a mixture of NaI (2.0 equiv) and corresponding tertiary alcohol (1.0 equiv) in MeCN (0.2 M) was added methylsulfonic acid (2.0 equiv) dropwise at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 2 hours. The reaction mixture was then diluted with diethyl ether, washed with water, saturated aqueous NaHCO₃, aqueous Na₂S₂O₃, and brine. The organic layers was dried over Na₂SO₄, filtered, and concentrated. The crude product was purified by flash chromatography on silica gel or recrystallization from petroleum ether/EtOAc to afford the corresponding tertiary alkyl iodide 2.

![Chemical structures of 2b, 2c, 2d, 2e, 2f, 2g, 2h, 2i, 2j, 2k](image)

**2-(3-iodo-3-methylbutyl)isoindoline-1,3-dione (2b).** This compound was synthesized from the iodination of 2-(3-hydroxy-3-methylbutyl)isoindoline-1,3-dione in 31% yield as a white solid (recrystallization from PE/Ea). Compound 2b is known.¹³¹H NMR (400 MHz, CDCl₃) δ 7.86 (dd, J = 5.5, 3.0 Hz, 2 H), 7.72 (dd, J = 5.4, 3.0 Hz, 2 H), 3.97 – 3.87 (m, 2 H), 2.02 (m, 8 H).¹³¹C NMR (126 MHz, CDCl₃) δ 168.1, 133.9, 132.0, 123.2, 47.5, 45.2, 38.0, 37.7.
2-ido-2-methyldecane (2c). This compound was synthesized from the iodination of 2-methyldecan-2-ol in 30% yield as a yellow oil. Compound 2c is known.\(^3\) \(^{1}H\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 1.92 (s, 6 H), 1.64 – 1.58 (m, 2 H), 1.55 – 1.45 (m, 2 H), 1.37 – 1.22 (m, 10 H), 0.89 (t, \(J = 6.8\) Hz, 3 H).

1-chloro-4-ido-4-methylpentane (2d). This compound was synthesized from the iodination of 5-chloro-2-methylpentan-2-ol in 42% yield as a brown oil. Compound 2d is known.\(^4\) \(^{1}H\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 3.60 (t, \(J = 6.4\) Hz, 2 H), 2.09 – 1.99 (m, 2 H), 1.94 (s, 6 H), 1.80 – 1.69 (m, 2 H). \(^{13}C\) NMR (101 MHz, CDCl\(_3\)) \(\delta\) 50.2, 47.6, 44.5, 38.1, 31.9.

3-Iodo-3-methylbutyl 5-bromopentanoate (2e). This compound was synthesized from the iodination of 3-hydroxy-3-methylbutyl 5-bromopentanoate in 57% yield as a yellow oil. \(^{1}H\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 4.31 (t, \(J = 7.0\) Hz, 2 H), 3.41 (t, \(J = 6.7\) Hz, 2 H), 2.33 (t, \(J = 7.0\) Hz, 2 H), 2.02 (t, \(J = 7.0\) Hz, 2 H), 1.97 (s, 6 H), 1.93 – 1.83 (m, 2 H), 1.72 – 1.61 (m, 2 H), 1.53 – 1.44 (m, 2 H). \(^{13}C\) NMR (101 MHz, CDCl\(_3\)) \(\delta\) 173.2, 64.4, 47.9, 46.0, 38.4, 34.0, 33.4, 32.3, 27.5, 23.9. MS (DART): m/z (%) 408.0 (100) [M+NH\(_4\)]\(^+\). HRMS (DART) m/z: [M+H\(^+\)] Calcd. for C\(_{11}\)H\(_{21}\)BrIO\(_2\): 390.9764; Found: 390.9763. IR (neat) \(\nu_{\max}\) 2959, 1735, 1455, 1180, 1123 cm\(^{-1}\).

4-Iodo-4-methylpentyl 4-cyanobenzoate (2f). This compound was synthesized from the iodination of 4-hydroxy-4-methylpentyl 4-cyanobenzoate in 53% yield as a white solid (m.p. 60.1-61.8 °C). \(^{1}H\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.15 (d, \(J = 8.2\) Hz, 2 H), 7.76 (d, \(J = 8.2\) Hz, 2 H), 4.41 (t, \(J = 6.6\) Hz, 2 H), 2.09 – 2.01 (m, 2 H), 1.96 (s, 6 H), 1.78 – 1.71 (m, 2 H). \(^{13}C\) NMR (126 MHz, CDCl\(_3\)) \(\delta\) 164.9, 134.0, 132.2, 130.0, 117.9, 116.3, 65.2, 50.3, 46.6, 38.0, 25.6. MS (FT): m/z (%) 248 (100), 358 (24) [M+H\(^+\)]. HRMS (DART) m/z: [M+H\(^+\)] Calcd. for C\(_{14}\)H\(_{17}\)NO\(_2\)I: 358.0298; Found: 358.0296. IR (thin film) \(\nu_{\max}\) 2971, 2229, 1724, 1451, 1367, 1310, 1287, 1125, 1110, 813 cm\(^{-1}\).
**3-Iodo-3-methylbutyl 4-cyanobenzoate (2g).** This compound was synthesized from the iodination of 3-hydroxy-3-methylbutyl 4-cyanobenzoate in 59% yield as a white solid (m.p. 62.0-63.0 °C). **1H NMR** (400 MHz, CDCl₃) δ 8.14 (d, J = 8.3 Hz, 2 H), 7.75 (d, J = 8.3 Hz, 2 H), 4.61 (t, J = 6.8 Hz, 2 H), 2.18 (t, J = 6.8 Hz, 2 H), 2.03 (s, 6 H). **13C NMR** (126 MHz, CDCl₃) δ 164.7, 133.8, 132.2, 130.0, 117.9, 116.4, 65.8, 47.9, 45.3, 38.4. MS (FI): m/z (%) 216 [M-HI]+, 130, 69 (100). HRMS (FI) m/z: [M-HI]+ Calcd. for C₁₃H₁₃NO₂: 215.0941; Found: 215.0940. IR (thin film) νₘₐₓ 2978, 2228, 1721, 1470, 1404, 1324, 1273, 767 cm⁻¹.

**4-Iodo-4-methylpentyl 4-acetylbenzoate (2h).** This compound was synthesized from the iodination of 4-hydroxy-4-methylpentyl 4-acetylbenzoate in 55% yield as a yellow solid (m.p. 37.8-39.5 °C). **1H NMR** (400 MHz, CDCl₃) δ 8.14 (d, J = 8.3 Hz, 2 H), 8.02 (d, J = 8.2 Hz, 2 H), 4.41 (t, J = 6.5 Hz, 2 H), 2.65 (t, J = 6.8 Hz, 2 H), 1.97 (s, 6 H), 2.03 (s, 6 H). **13C NMR** (101 MHz, CDCl₃) δ 197.5, 165.7, 140.3, 134.0, 129.8, 128.2, 64.9, 50.4, 46.7, 38.0, 28.2, 26.9. MS (FT): m/z (%) 247 (100) [M-HI]+, 375 (18) [M+H]+. HRMS (DART) m/z: [M+H]+ Calcd. for C₁₅H₂₀O₃I: 375.0452; Found: 375.0449. IR (thin film) νₘₐₓ 3408, 2971, 1720, 1686, 1405, 1281, 1114, 769 cm⁻¹.

**4-Iodo-4-methylpentyl 1-naphthoate (2i).** This compound was synthesized from the iodination of 4-hydroxy-4-methylpentyl 1-naphthoate in 32% yield according to the literature method as a yellow solid (m.p. 46.6-48.5 °C). **1H NMR** (400 MHz, CDCl₃) δ 8.92 (d, J = 8.6 Hz, 1 H), 8.20 (d, J = 7.3 Hz, 1 H), 8.04 (d, J = 8.1 Hz, 1 H), 7.90 (d, J = 8.3 Hz, 1 H), 7.66 – 7.59 (m, 1 H), 7.58 – 7.48 (m, 2 H), 4.47 (t, J = 6.4 Hz, 2 H), 2.15 – 2.04 (m, 2 H), 1.98 (s, 6 H), 1.86 – 1.77 (m, 2 H). **13C NMR** (101 MHz, CDCl₃) δ 167.5, 133.8, 133.6, 131.3, 130.1, 128.5, 127.7, 127.1, 126.2, 125.8, 124.5, 64.5, 50.6, 46.9, 38.0, 28.3. MS (FT): m/z (%) 400 (100) [M+NH₄]+. HRMS (DART) m/z: [M+NH₄]+ Calcd. for C₁₇H₁₅NO₂I: 400.0768; Found: 400.0763. IR (thin film) νₘₐₓ 2982, 2893, 1713, 1507, 1461, 1386, 1287, 1164, 782 cm⁻¹.
3-Iodo-3-methylbutyl 1-methyl-1H-indole-2-carboxylate (2j). This compound was synthesized from the iodination of 3-hydroxy-3-methylbutyl 1-methyl-1H-indole-2-carboxylate in 28% yield as a white solid (m.p. 59.8-60.9 °C). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.68 (d, $J = 7.9$ Hz, 1 H), 7.43 – 7.32 (q, $J = 8.4$ Hz, 2 H), 7.28 (s, 1 H), 7.16 (t, $J = 7.2$ Hz, 1 H), 4.56 (t, $J = 6.7$ Hz, 2 H), 4.09 (s, 3 H), 2.19 (t, $J = 6.8$ Hz, 2 H). 2.05 (s, 6 H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 161.9, 139.6, 127.5, 125.7, 125.0, 122.5, 120.6, 110.2, 110.2, 64.6, 48.1, 46.3, 38.5, 31.5. MS (FT): m/z (%) 372 (100) [M+H]$^+$, 300 (4) [M]+. HRMS (DART) m/z: [M+H]$^+$ Calcd. for C$_{15}$H$_{19}$NO$_2$I: 372.0455; Found: 372.0448. IR (thin film) $v_{\text{max}}$ 2979, 1700, 1526, 1466, 1359, 1259, 1123, 751 cm$^{-1}$.

4-Iodo-4-methylcyclohexylbenzene (2k). This compound was synthesized from the iodination of 1-methyl-4-phenylcyclohexan-1-ol in 86% yield as a yellow solid (m.p. 88.9-90.2 °C). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.36 – 7.25 (m, 4 H), 7.24 – 7.18 (m, 1 H), 2.51 (tt, $J = 12.4$, 3.9 Hz, 1 H), 2.29 – 2.21 (m, 2 H), 2.18 (s, 3 H), 2.08 – 1.96 (m, 2 H), 1.92 – 1.82 (m, 2 H), 1.13 – 1.01 (m, 2 H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 146.5, 128.4, 126.9, 126.2, 58.5, 45.8, 43.5, 39.4, 32.7. MS (EI): m/z (%) 173 (100) [M-I]$^+$, 300 (4) [M]+. HRMS (EI) m/z: [M]+ Calcd. for C$_{13}$H$_{17}$I: 300.0369; Found: 300.0376. IR (thin film) $v_{\text{max}}$ 3056, 2968, 2910, 1491, 1442, 1298, 1224, 1107, 757 cm$^{-1}$.

3.2 General procedure for the preparation of aryl iodides 3.

**tert-Butyl (R)-3-hydroxy-1-((4-iodobenzyl)amino)-1-oxopropan-2-yl)carbamate (3n).** Under Ar atmosphere, (tert-butoxycarbonyl)-L-serine (2.05 g, 10 mmol, 1.0 equiv) and anhydrous THF (80 mL) were added to a 250 mL of Schlenk flask. After cooling down to -78 °C, 4-methylmorpholine (1.22 g, 12 mmol, 1.2 equiv) was added and the mixture was stirred at same temperature for 2 minutes. Isobutyl carbonochloridate was added, and the mixture was stirred at -78 °C for another 5 minutes. (4-Iodophenyl)methanamine was then added dropwise, and the resulting solution was slowly warmed to room temperature and stirred for additional 3 h. Upon completion, the reaction mixture was filtered...
through a pad of Celite and washed with EtOAc. After removal of solvents, the crude product was recrystallized from EtOAc to give \(3n\) (2.54 g, 60%) as a white crystal (m.p. 125.8-127.4 °C). The spectral data was in accordance with the literature.\(^5\)

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\text{4-Iodobenzyl (2S, 5R)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate 4,4-dioxide (3o). To a 50 mL of Schlenk flask were added (4-iodophenyl)methanol 3c (0.936 g, 4 mmol, 2.0 equiv), 4-(dimethylamino)pyridine (48.9 mg, 0.4 mmol, 0.2 equiv), N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (EDCI-HCl) (0.767 g, 2.4 mmol, 1.2 equiv), (2S,5R)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid 4,4-dioxide (0.467 g, 2 mmol, 1.0 equiv), and anhydrous CH\(_2\)Cl\(_2\) (20 mL) under Ar atmosphere. After the mixture was stirred at room temperature for 12 h, the reaction mixture was diluted with CH\(_2\)Cl\(_2\) and washed with water and brine. The organic layer was dried over anhydrous Na\(_2\)SO\(_4\), filtered, and concentrated. The product 3o (0.50 g, 56% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 10:1 to 4:1) as a white solid (m.p. 49.0-50.9 °C).}

**1H NMR** (400 MHz, CDCl\(_3\)) \(\delta\) 7.73 (d, \(J = 8.1\) Hz, 2 H), 7.12 (d, \(J = 8.1\) Hz, 2 H), 5.21 (d, \(J = 12.1\) Hz, 1 H), 5.11 (d, \(J = 12.1\) Hz, 1 H), 4.60 (dd, \(J = 4.2, 2.2\) Hz, 1 H), 4.41 (s, 1 H), 3.63 – 3.36 (m, 2 H), 1.56 (s, 3 H), 1.30 (s, 3 H). **13C NMR** (101 MHz, CDCl\(_3\)) \(\delta\) 170.7, 166.7, 138.0, 133.9, 130.6, 94.9, 67.4, 63.1, 62.7, 61.0, 38.3, 20.2, 18.6. MS (ESI): m/z (%) 472 [M+Na]\(^+\). HRMS (DART) m/z: [M+H]\(^+\) Calcd. for C\(_{15}\)H\(_{16}\)NO\(_5\)NaSI: 471.9686; Found: 471.9678. IR (thin film) \(\nu\)\(_{max}\) 2977, 2933, 1791, 1759, 1486, 1356, 1166 cm\(^{-1}\).

### 4. General procedure for the nickel-catalyzed enantioselective dicarbofunctionalization of TFP

**General Procedure A:**

To a 25 mL of Schlenk tube were added Zn dust (1.5 equiv), tertiary alkyl iodide 2 (1.5 equiv), aryl iodide 3 (0.4 mmol, 1.0 equiv), L6 (10 mol%) and NiBr\(_2\)-DME (10 mol%) in a glovebox. The tube
was then taken out of the glovebox and evacuated and backfilled with Ar (3 times). Anhydrous DME (3.2 mL) and TFP solution (1.2 M in DMA, 0.54 mL, 1.6 equiv) were added under Ar. The Schlenk tube was screw capped and stirred (800 rpm) for 12 h at room temperature. The reaction mixture was then diluted with EtOAc and filtered through a pad of Celite. The filtrate was washed with Na$_2$S$_2$O$_3$, water and brine, the combined organic layers were dried over Na$_2$SO$_4$, filtered and concentrated. The residue was purified with silica gel chromatography to give the corresponding product 4.

**General Procedure B:**

To a 25 mL of Schlenk tube were added Zn dust (1.5 equiv), tertiary alkyl iodide 2 (1.5 equiv), aryl iodide 3 (0.2 mmol, 1.0 equiv), L6 (10 mol%), NiBr$_2$-DME (10 or 12mol%) and additive (FeCl$_3$ (0.25 equiv), FeBr$_2$ (0.25 equiv) or NaI (0.5 equiv)) in a glovebox. The tube was then taken out of the glovebox, evacuated and backfilled with Ar (3 times). Anhydrous DME (1.6 mL) and TFP solution (1.2 M in DMA, 0.27 mL, 1.6 equiv) were added under Ar. The Schlenk tube was screw capped and stirred (800 rpm) for 12 h at room temperature. The reaction mixture was then diluted with EtOAc and filtered through a pad of Celite. The filtrate was washed with Na$_2$S$_2$O$_3$, water and brine, the combined organic layers were dried over Na$_2$SO$_4$, filtered and concentrated. The residue was purified with silica gel chromatography to give the corresponding product 5.

5. **Characterization data for compounds 4 and 5**

![Ethyl (R)-4-(1,1,1-trifluoro-4,4-dimethylpentan-2-yl)benzoate (4a)](image)

**General Procedure A.** The product (84.5 mg, 70% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 30:1) as a white solid (m.p. 44.5-45.0 °C). $[\alpha]_{D}^{20} = -22.60$ (c = 0.97, CHCl$_3$) for a sample with 91% ee. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.03 (d, $J = 8.4$ Hz, 2 H), 7.42 (d, $J = 8.1$ Hz, 2 H), 4.38 (q, $J = 7.1$ Hz, 2 H), 3.40 (qt, $J = 9.6$, 5.8 Hz, 1 H), 1.94 (d, $J = 6.0$ Hz, 1 H), 1.39 (t, $J = 7.1$ Hz, 3 H), 0.79 (s, 9 H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 166.2, 141.8 (q, C-F, $^3$J$_{C-F} = 2.1$ Hz), 130.3, 129.8, 129.4, 126.9 (q, C-F, $^1$J$_{C-F} = 279.6$ Hz), 61.0, 47.1 (q, C-F, $^2$J$_{C-F} = 26.4$ Hz), 42.1, 30.8, 29.6, 14.3. $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -70.11 (d, $J = 9.9$ Hz, 3 F). MS (EI): m/z (%) 57 (100), 246, 257, 302 [M]$^+$. HRMS (EI) m/z: [M]$^+$ Calcd. for C$_{16}$H$_{21}$O$_2$F$_3$: S18
302.1488; Found: 302.1483. IR (thin film): $\nu_{\text{max}}$ 2991, 2959, 1717, 1510, 1451, 1369, 1282, 1106, 716 cm$^{-1}$. Enantiomeric purity (91% ee) was measured by chiral HPLC on IG column (Hexane/PrOH = 98:2, 0.7 mL/min, UV detection at 214 nm); retention time = 7.51 min (major), retention time = 7.22 min (minor).

Using ethyl 4-bromobenzoate instead of ethyl 4-iodobenzoate gives corresponding product 4a with 40% yield and 90% ee. Enantiomeric purity (90% ee) was measured by chiral HPLC on IG column (Hexane/PrOH = 98:2, 0.7 mL/min, UV detection at 214 nm); retention time = 7.52 min (major), retention time = 7.19 min (minor).

**Ethyl (R)-3-(1,1,1-trifluoro-4,4-dimethylpentan-2-yl)benzoate (4b).** General Procedure A. The product (84.0 mg, 70% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 30:1) as a colorless liquid. $[\alpha]_{D}^{20} = -18.34$ ($c = 0.41$, CHCl$_3$) for a sample with 92% ee. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.04 – 7.97 (m, 1 H), 7.53 (d, $J = 7.7$ Hz, 2 H), 7.47 – 7.39 (m, 2 H), 4.39 (q, $J = 7.1$ Hz, 2 H), 3.40 (dt, $J = 16.7$, 9.8, 5.2 Hz, 1 H), 2.01 – 1.90 (m, 2 H), 1.41 (t, $J = 7.2$ Hz, 3 H), 0.80 (s, 9 H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 166.2, 137.3 (q, C-F, $^3J_{C-F} = 2.0$ Hz), 133.6, 130.9, 130.6, 129.2, 128.6, 127.0 (q, C-F, $^1J_{C-F} = 279.8$ Hz), 61.1, 46.9 (q, C-F, $^2J_{C-F} = 26.3$ Hz), 42.0 (q, C-F, $^3J_{C-F} = 1.4$ Hz), 30.8, 29.7, 14.3. $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ 70.32 (d, $J = 9.7$ Hz, 3 F). MS (EI): m/z (%) 57 (100), 246, 257, 302 [M]$^{+}$. HRMS (EI) m/z: [M]$^{+}$ Calcd. for C$_{16}$H$_{21}$O$_2$F$_3$: 302.1488; Found: 302.1483. IR (thin film) $\nu_{\text{max}}$ 2960, 2870, 1720, 1477, 1398, 1284, 1260, 1108, 712 cm$^{-1}$. Enantiomeric purity (92% ee) was measured by chiral HPLC on ODH column (Hexane/PrOH = 98:2, 0.7 mL/min, UV detection at 214 nm); retention time = 5.55 min (major), retention time = 6.11 min (minor).

**Gram-scale synthesis of 4b**

To a 100 mL of Schlenk tube were added Zn dust (784.6 mg, 12 mmol, 1.5 equiv), L6 (201.9 mg, 0.8 mmol, 10 mol%). The tube was then transferred to a glovebox, NiBr$_2$-DME (246.9 mg, 0.8 mmol, 10 mol%) was added. The tube was taken out of the glovebox and evacuated and backfilled with Ar (3 times). 2a (2.21 g, 12 mmol, 1.5 equiv), 3b (2.14 g, 8 mmol, 1.0 equiv), anhydrous DME (64 mL) and TFP solution (10.7 mL, 1.2 M in DMA, 1.6 equiv) were added under Ar at 0 °C. The Schlenk tube was screw capped and stirred (800 rpm) for 8 h at room temperature. The reaction mixture was then diluted
with EtOAc and filtered through a pad of Celite. The filtrate was washed with Na₂S₂O₃, water and brine, the combined organic layers were dried over Na₂SO₄, filtered and concentrated. The residue was purified with silica gel chromatography to give 4b as a colorless oil (1.83 g, 76%, 90% ee).

**Ethyl 2-(1,1,1-trifluoro-4,4-dimethylpentan-2-yl)benzoate (4c).** General Procedure A. The product (25.2 mg, 21% yield) was purified with silica gel chromatography (Petroleum ether/DCM = 5:1) as a colorless liquid. [α]D²⁰ = -0.65 (c = 0.99, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.90 (dd, J = 7.8, 1.6 Hz, 1 H), 7.61 – 7.56 (m, 1 H), 7.52 (td, J = 7.7, 1.6 Hz, 1 H), 7.39 – 7.33 (m, 1 H), 5.10 – 4.96 (m, 1 H), 4.39 (qd, J = 7.1, 1.4 Hz, 2 H), 2.03 – 1.92 (m, 2 H), 1.40 (t, J = 7.1 Hz, 3 H), 0.81 (s, 9 H). ¹³C NMR (101 MHz, CDCl₃) δ 167.7, 131.7, 131.7, 130.7, 129.2, 127.5, 127.3 (q, C-F, ¹Jₐ-C = 279.8 Hz), 61.3, 42.7, 39.7 (q, C-F, ²Jₐ-C = 26.2 Hz), 31.0, 29.6, 14.2. ¹⁹F NMR (376 MHz, CDCl₃) δ -69.80 (d, J = 10.9 Hz). MS (FI): m/z (%) 206, 282 (100), 302 [M]+. HRMS (FI) m/z: [M]+ Calcd. for C₁₆H₂₁O₂F₃: 302.1488; Found: 302.1486. IR (thin film) ν max 2956, 2869, 1718, 1466, 1398, 1298, 1247, 1176, 1108, 719 cm⁻¹.

(R)-1-(4-(1,1,1-Trifluoro-4,4-dimethylpentan-2-yl)phenyl)ethan-1-one (4d). General Procedure A. The product (79.1 mg, 73% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 20:1) as a white solid (m.p. 48.0-48.9 °C). [α]D²⁰ = -30.51 (c = 0.47, CHCl₃) for a sample with 92% ee. ¹H NMR (400 MHz, CDCl₃) δ 7.94 (d, J = 8.4 Hz, 2 H), 7.44 (d, J = 8.0 Hz, 2 H), 3.40 (tdd, J = 11.5, 9.6, 5.5 Hz, 1 H), 2.61 (s, 3 H), 2.02 – 1.88 (m, 2 H), 0.80 (s, 9 H). ¹³C NMR (101 MHz, CDCl₃) δ 197.5, 142.1 (q, C-F, ³Jₐ-C = 2.2 Hz), 136.8, 129.7, 128.5, 126.9 (q, C-F, ¹Jₐ-C = 279.9 Hz), 47.1 (q, C-F, ²Jₐ-C = 26.4 Hz), 42.1 (q, C-F, ³Jₐ-C = 1.7 Hz), 30.8, 29.7, 26.6. ¹⁹F NMR (376 MHz, CDCl₃) δ -70.05 (d, J = 9.7 Hz, 3 F). MS (EI): m/z (%) 257 (100), 272 [M]+. HRMS (EI) m/z: [M]+ Calcd. for C₁₅H₁₉OF₃: 272.1383; Found: 272.1379. IR (thin film) ν max 2963, 2870, 1610, 1479, 1468, 1371, 1258, 1174, 1099, 827, 705 cm⁻¹. Enantiomeric purity (92% ee) was measured by chiral HPLC on ASH column (Hexane/iPrOH = 98:2, 0.7 mL/min, UV detection at 214 nm); retention time = 7.14 min (major), retention time = 6.71 min (minor).
(R)-1-(3-(1,1,1-Trifluoro-4,4-dimethylpentan-2-yl)phenyl)ethan-1-one (4e). General Procedure A. The product (85.0 mg, 78% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 20:1) as a colorless liquid. \([\alpha]_D^{20} = -23.82 \) (c = 0.34, CHCl₃) for a sample with 90% ee. \(^1\)H NMR (400 MHz, CDCl₃) \(\delta 7.98 – 7.86 (m, 2 H), 7.56 \) (d, \(J = 7.7 \) Hz, 1 H), 7.47 (t, \(J = 7.7 \) Hz, 1 H), 3.41 (m, 1 H), 2.63 (s, 3 H), 1.95 (d, \(J = 6.0 \) Hz, 2 H), 0.80 (s, 9 H). \(^13\)C NMR (101 MHz, CDCl₃) \(\delta 197.7, 137.6 \) (q, C-F, \(^3J_{C-F} = 2.1 \) Hz), 137.4, 133.9, 129.1, 128.9, 128.2, 127.0 (q, C-F, \(^1J_{C-F} = 279.8 \) Hz), 47.0 (q, C-F, \(^2J_{C-F} = 26.3 \) Hz), 42.0 (q, C-F, \(^3J_{C-F} = 1.8 \) Hz), 30.8, 29.7, 26.6. \(^19\)F NMR (376 MHz, CDCl₃) \(\delta -70.31 \) (d, \(J = 9.9 \) Hz, 3 F). MS (EI): m/z (%) 257 (100), 272 [M]+. HRMS (EI) m/z: [M]+ Calcd. for C₁₅H₁₁OF₃: 272.1383; Found: 272.1389. IR (thin film) \(v_{max} 2960, 2870, 1690, 1477, 1399, 1369, 1295, 1108, 701 \) cm⁻¹. Enantiomeric purity (90% ee) was measured by chiral HPLC on AY3 column (Hexane/iPrOH = 98:2, 0.7 mL/min, UV detection at 214 nm); retention time = 4.72 min (major), retention time = 4.45 min (minor).

(R)-4-(1,1,1-Trifluoro-4,4-dimethylpentan-2-yl)benzaldehyde (4f). General Procedure A. The product (78.5 mg, 76% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 50:1) as a white solid (m.p. 34.9-35.6 °C). \([\alpha]_D^{20} = -28.41 \) (c = 0.88, CHCl₃) for a sample with 90% ee. \(^1\)H NMR (400 MHz, CDCl₃) \(\delta 10.02 \) (s, 1 H), 7.88 (d, \(J = 8.2 \) Hz, 2 H), 7.53 (d, \(J = 7.9 \) Hz, 2 H), 3.45 (qdd, \(J = 9.7, 6.9, 5.1 \) Hz, 1 H), 2.00 – 1.90 (m, 2 H), 0.80 (s, 9 H). \(^13\)C NMR (101 MHz, CDCl₃) \(\delta 191.6, 143.6 \) (q, C-F, \(^3J_{C-F} = 2.1 \) Hz), 136.1, 130.1, 129.8, 126.8 (q, C-F, \(^1J_{C-F} = 279.7 \) Hz), 47.2 (q, C-F, \(^2J_{C-F} = 26.4 \) Hz), 42.1 (q, C-F, \(^3J_{C-F} = 1.9 \) Hz), 30.8, 29.6. \(^19\)F NMR (376 MHz, CDCl₃) \(\delta -69.95 \) (d, \(J = 9.6 \) Hz, 3 F). MS (EI): m/z (%) 159, 202 (100), 215, 258 [M]+. HRMS (EI) m/z: [M]+ Calcd. for C₁₄H₁₉OF₃: 258.1226; Found: 258.1225. IR (thin film) \(v_{max} 2960, 2869, 1698, 1610, 1477, 1370, 1296, 1259, 1153, 1107 \) cm⁻¹. Enantiomeric purity (90% ee) was measured by chiral HPLC on ASH column (Hexane/iPrOH = 98:2, 0.7 mL/min, UV detection at 214 nm); retention time = 6.72 min (major), retention time = 6.35 min (minor).

(R)-3-(1,1,1-Trifluoro-4,4-dimethylpentan-2-yl)benzaldehyde (4g). General Procedure A. The product (84.7 mg, 82% yield) was purified with silica gel
chromatography (Petroleum ether/EtOAc = 50:1) as a colorless liquid. [α]$_D^{20}$ = -18.46 ($c = 0.57$, CHCl$_3$) for a sample with 89% ee. $^1$H NMR (400 MHz, CDCl$_3$) δ 10.04 (s, 1 H), 7.89 – 7.81 (m, 2 H), 7.62 (d, $J = 7.6$ Hz, 1 H), 7.54 (t, $J = 7.6$ Hz, 1 H), 3.44 (qdd, $J = 9.8, 7.0, 4.9$ Hz, 1 H), 2.06 – 1.88 (m, 2 H), 0.80 (s, 9 H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 191.9, 138.1 ($q$, C-F, $^3J_{C-F} = 2.1$ Hz), 136.7, 135.4, 130.2, 129.7, 129.3, 126.9 ($q$, C-F, $^1J_{C-F} = 279.8$ Hz), 46.8 (q, C-F, $^2J_{C-F} = 26.5$ Hz), 42.0 (q, C-F, $^3J_{C-F} = 1.8$ Hz), 30.8, 29.7. $^{19}$F NMR (376 MHz, CDCl$_3$) δ -70.32 (d, $J = 9.8$ Hz, 3 F). MS (EI): m/z (%) 202 (100), 258 [M$^+$]. HRMS (EI) m/z: [M$^+$] Calcd. for C$_{14}$H$_{17}$OF$_3$: 258.1226; Found: 258.1224. IR (thin film) $v_{max}$ 2960, 2870, 2685, 2559, 1698, 1590, 1476, 1284, 1260, 1108, 712 cm$^{-1}$. The enantiomeric purity of 4g (89% ee) was determined by 4g', which was derived from 4g through reduction as showing below.

(R)-(3-(1,1,1-Trifluoro-4,4-dimethylpentan-2-yl)phenyl)methanol (4g'). To a solution of (R)-(4-(1,1,1-trifluoro-4,4-dimethylpentan-2-yl)phenyl)methanol 4g (126.1 mg, 0.5 mmol) in MeOH (2 mL) was added NaBH$_4$ (22.7 mg, 0.6 mmol). The mixture was stirred at rt for 2 h and then quenched with H$_2$O. The solvent was evaporated, the crude product was redissolved in EtOAc and washed with H$_2$O. The organic layer was dried (Na$_2$SO$_4$), filtered, and concentrated. The residue was purified with silica gel chromatography (Petroleum ether/EtOAc = 6:1) to give 4g' as a colorless oil. (109.4 mg, 84%), [α]$_D^{20}$ = -24.67 ($c = 0.95$, CHCl$_3$) for a sample with 89% ee. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.37 – 7.15 (m, 4 H), 4.64 (s, 2 H), 3.32 (m, 1 H), 2.27 (br, 1 H), 2.01 – 1.83 (m, 2 H), 0.79 (s, 9 H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 141.2, 137.1 (q, C-F, $^3J_{C-F} = 1.8$ Hz), 128.7, 128.6, 127.8, 127.2 (q, $^1J_{C-F} = 279.6$ Hz), 126.4, 64.9 (d, $J = 4.5$ Hz), 47.0 (q, $^2J_{C-F} = 26.1$ Hz), 42.0 (q, C-F, $^3J_{C-F} = 2.0$ Hz), 30.8, 29.6. $^{19}$F NMR (376 MHz, CDCl$_3$) δ -70.23 (d, $J = 9.8$ Hz, 3 F). MS (FT): m/z (%) 278 (100) [M+NH$_4^+$]. HRMS (DART) m/z: [M+NH$_4^+$] Calcd. for C$_{14}$H$_{23}$NOF$_3$: 278.1726; Found: 278.1724. IR (thin film) $v_{max}$ 3320, 2959, 2869, 1476, 1370, 1261, 1177, 1107, 707 cm$^{-1}$. Enantiomeric purity (89% ee) was measured by chiral HPLC on OJH column (Hexane/iPrOH = 98:2, 0.7 mL/min, UV detection at 214 nm); retention time = 13.83 min (major), retention time = 16.91 min (minor).
(R)-4-(1,1,1-Trifluoro-4,4-dimethylpentan-2-yl)benzonitrile (4h). General Procedure A. The product (74.5 mg, 73% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 30:1) as a white solid (m.p. 40.4–40.8 °C). \([\alpha]_D^{20} = -31.48\) (c = 0.50, CHCl₃) for a sample with 91% ee. \(^1\)H NMR (400 MHz, CDCl₃) \(\delta\) 7.66 (d, \(J = 8.4\) Hz, 2 H), 7.47 (d, \(J = 8.1\) Hz, 2 H), 3.40 (pd, \(J = 9.5, 2.6\) Hz, 1 H), 2.01 – 1.85 (m, 2 H), 0.79 (s, 9 H). \(^{13}\)C NMR (101 MHz, CDCl₃) \(\delta\) 142.2 (q, C-F, \(^3\)J_C-F = 1.9 Hz), 132.3, 130.2, 126.6 (q, C-F, \(^1\)J_C-F = 279.9 Hz), 118.3, 112.1, 47.1 (q, C-F, \(^2\)J_C-F = 26.7 Hz), 42.0 (q, C-F, \(^3\)J_C-F = 1.8 Hz), 30.8, 29.6. \(^1^9\)F NMR (376 MHz, CDCl₃) \(\delta\) -70.04 (d, \(J = 9.6\) Hz, 3 F). MS (EI): m/z (%) 57 (100), 184, 240, 255 [M]+. HRMS (EI) m/z: [M]+ Calcd for C\(_{14}\)H\(_{16}\)NF\(_3\): 255.1229; Found: 255.1229. IR (thin film) \(v_{\max}\) 2964, 2871, 2230, 1508, 1476, 1399, 1287, 1175, 1105, 831 cm\(^{-1}\).

The enantiomeric purity of 4h (91% ee) was determined by \(^1\)H NMR (400 MHz, CDCl₃) \(\delta\) 7.66 (d, \(J = 8.4\) Hz, 2 H), 7.47 (d, \(J = 8.1\) Hz, 2 H), 3.40 (pd, \(J = 9.5, 2.6\) Hz, 1 H), 2.01 – 1.85 (m, 2 H), 0.79 (s, 9 H). \(^{13}\)C NMR (101 MHz, CDCl₃) \(\delta\) 142.2 (q, C-F, \(^3\)J_C-F = 1.9 Hz), 132.3, 130.2, 126.6 (q, C-F, \(^1\)J_C-F = 279.9 Hz), 118.3, 112.1, 47.1 (q, C-F, \(^2\)J_C-F = 26.7 Hz), 42.0 (q, C-F, \(^3\)J_C-F = 1.8 Hz), 30.8, 29.6. \(^1^9\)F NMR (376 MHz, CDCl₃) \(\delta\) -70.04 (d, \(J = 9.6\) Hz, 3 F). MS (EI): m/z (%) 274 (26) [M]+. HRMS (ESI) m/z: [M+H]+ Calcd. for C\(_{14}\)H\(_{19}\)NOF\(_3\): 274.1413; Found: 274.1406. IR (thin film) \(v_{\max}\) 3382, 3199, 2961, 2870, 1656, 1615, 1508, 1476, 1399, 1287, 1175, 1105, 831 cm\(^{-1}\). The enantiomeric purity of 4h (91% ee) was determined by 4h', which was derived from 4h through oxidation as showing below.

(R)-4-(1,1,1-Trifluoro-4,4-dimethylpentan-2-yl)benzamide (4h'). To a solution of (R)-4-(1,1,1-trifluoro-4,4-dimethylpentan-2-yl)benzonitrile 4h (102.1 mg, 0.4 mmol) in a mixture of EtOH (0.3 mL) and aqueous NaOH (25 wt%, 0.05 mL) was added aqueous H\(_2\)O\(_2\) (30 wt%, 0.2 mL). After stirring at rt for 6 h, the reaction was quenched with 2 drops of 50% H\(_2\)SO\(_4\). EtOH was evaporated, and the resulting residue was redissolved in EtOAc and washed with H\(_2\)O. The combined organic layers were dried (Na\(_2\)SO\(_4\)), filtered, and concentrated to give a thick oil. The resulting thick white suspension was diluted with hexane (10 mL) and DCM (1 mL), and filtered. The solid was washed with hexane (5 mL) and dried in vacuo affording the product as a white solid (76.5 mg, 75%, m.p. 120.7-121.2 °C), \([\alpha]_D^{20} = -26.99\) (c = 0.69, CHCl₃) for a sample with 91% ee. \(^1\)H NMR (400 MHz, CDCl₃) \(\delta\) 7.81 (d, \(J = 8.0\) Hz, 2 H), 7.41 (d, \(J = 7.8\) Hz, 2 H), 6.39 (br, 2 H), 3.38 (qd, \(J = 10.1, 4.3\) Hz, 1 H), 2.04 – 1.81 (m, 2 H), 0.79 (s, 9 H). \(^{13}\)C NMR (101 MHz, CDCl₃) \(\delta\) 169.3, 140.9, 133.1, 129.7, 127.6, 126.9 (q, C-F, \(^1\)J_C-F = 279.7 Hz), 46.9 (q, C-F, \(^2\)J_C-F = 26.3 Hz), 42.0, 30.8, 29.6. \(^1^9\)F NMR (376 MHz, CDCl₃) \(\delta\) -70.04 (d, \(J = 9.5\) Hz, 3 F). MS (EI): m/z (%) 274 (26) [M]+. HRMS (ESI) m/z: [M+H]+ Calcd. for C\(_{14}\)H\(_{19}\)NOF\(_3\): 274.1413; Found: 274.1406. IR (thin film) \(v_{\max}\) 3382, 3199, 2961, 2870, 1656, 1615, 1508, 1476, 1399, 1287, 1175, 1105, 831 cm\(^{-1}\).
Enantiomeric purity (91% ee) was measured by chiral HPLC on ASH column (Hexane/iPrOH/DEA = 96:4:0.1, 0.7 mL/min, UV detection at 230 nm); retention time = 55.67 min (major), retention time = 64.53 min (minor).

(R)-4,4,5,5-Tetramethyl-2-(4-(1,1,1-trifluoro-4,4-dimethylpentan-2-yl)phenyl)-1,3,2-dioxaborolane (4i). General Procedure A. The product (78.7 mg, 55% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 50:1) as a white solid (m.p. 137.5-138.5 °C). \([\alpha]_D^{20} = -17.00 \) (c = 0.50, CHCl₃) for a sample with 89% ee. ¹H NMR (400 MHz, CDCl₃) δ 7.79 (d, \( J = 7.3 \) Hz, 2 H), 7.34 (d, \( J = 7.7 \) Hz, 2 H), 3.33 (pd, \( J = 9.7, 3.0 \) Hz, 1 H), 2.01 – 1.84 (m, 2 H), 1.34 (s, 12 H), 0.78 (s, 9 H). ¹³C NMR (101 MHz, CDCl₃) δ 139.9 (q, C-F, \( J_{C-F} = 2.2 \) Hz), 134.9, 128.8, 127.6 (q, C-F, \( J_{C-F} = 279.9 \) Hz), 83.8, 47.2 (q, C-F, \( J_{C-F} = 26.3 \) Hz), 42.0, 30.8, 29.7, 24.9. ¹⁹F NMR (376 MHz, CDCl₃) δ -70.16 (d, \( J = 9.8 \) Hz, 3 F). MS (ESI): m/z (%) 219, 357 (100) [M+H]⁺. HRMS (EI) m/z: [M⁺] Calcd. for C₁₉H₂₈F₁₀BO₂: 355.2165; Found: 355.2160. IR (thin film) \( \nu_{max} \) 2961, 2869, 1614, 1400, 1362, 1258, 1145, 1093, 690 cm⁻¹. Enantiomeric purity (89% ee) was measured by chiral HPLC on IG column (Hexane/iPrOH = 99:1, 0.7 mL/min, UV detection at 214 nm); retention time = 4.97 min (major), retention time = 5.36 min (minor).

Supplementary Figure 1. X-ray crystal structure of compound 4i

(R)-4-(1,1,1-Trifluoro-4,4-dimethylpentan-2-yl)benzenesulfonamide (4j). General Procedure A. The product (85.9 mg, 70% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 2:1) as a white solid (m.p. 142.1-143.2 °C). \([\alpha]_D^{20} = -19.36 \) (c = 0.56, CHCl₃) for a sample with 91% ee. ¹H NMR (400 MHz, CDCl₃) δ 7.92 (d, \( J = 8.0 \) Hz, 2 H), 7.50 (d, \( J = 8.0 \) Hz, 2 H), 5.14 (s, 2 H), 3.41 (pd, \( J = 9.5, 2.7 \) Hz, 1H), 2.03 – 1.85 (m, 2 H), 0.80 (s, 9 H). ¹³C NMR (101 MHz, CDCl₃) δ 142.1 (q, C-F, \( J_{C-F} = 1.9 \) Hz), 141.6, 130.2, 126.7, 126.7 (q, C-F, \( J_{C-F} = 280.1 \) Hz), 46.9 (q, C-F, \( J_{C-F} = 26.6 \) Hz), 42.1 (q, C-F, \( J_{C-F} = 1.8 \) Hz).
Hz), 30.8, 29.7. \(^{19}\text{F NMR}\) (376 MHz, CDCl\(_3\)) \(\delta\) -70.02 (d, \(J = 9.6\) Hz, 3 F). MS (ESI): m/z (%): 332 (100) \([\text{M}+\text{Na}]^+\). HRMS (ESI) m/z: \([\text{M}+\text{Na}]^+\) Calcd. for C\(_{13}\)H\(_{18}\)NO\(_2\)F\(_3\)NaS: 332.0903; Found: 332.0901. 
IR (thin film) \(v_{\text{max}}\) 3375, 3275, 2963, 2870, 1550, 1478, 1400, 1331, 1163, 672 cm\(^{-1}\). Enantiomeric purity (91\% ee) was measured by chiral HPLC on ADH column (Hexane/iPrOH = 9:1, 0.7 mL/min, UV detection at 214 nm); retention time = 11.88 min (major), retention time = 10.76 min (minor).

\((R)-(4-(1,1,1-\text{Trifluoro}-4,4-\text{dimethylpentan}-2-yl)\text{-phenyl})\text{-methanol}\) (4k). General Procedure A. 0.5 equiv of NaI was used. The product (64.4 mg, 62\% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 6:1) as a colorless liquid. 

\([\alpha]_{D}^{20} = -18.48\) (c = 0.67, CHCl\(_3\)) for a sample with 93\% ee. \(^{1}\text{H NMR}\) (400 MHz, CDCl\(_3\)) \(\delta\) 7.33 (m, 4 H), 4.68 (s, 2 H), 3.33 (dtt, \(J = 14.0, 5.8, 2.9\) Hz, 1 H), 2.00 – 1.86 (m, 2 H), 1.79 (br, 1 H), 0.79 (s, 9 H). \(^{13}\text{C NMR}\) (101 MHz, CDCl\(_3\)) \(\delta\) 140.6, 136.2 (q, \(J_{\text{CF}} = 2.3\) Hz), 129.6, 127.2 (q, \(J_{\text{CF}} = 279.6\) Hz), 127.1, 64.9, 46.8 (q, \(J_{\text{CF}} = 26.3\) Hz), 42.0 (q, \(J_{\text{CF}} = 2.3\) Hz), 30.8, 29.7. \(^{19}\text{F NMR}\) (376 MHz, CDCl\(_3\)) \(\delta\) -70.37 (d, \(J = 10.2\) Hz). MS (ESI): m/z (%) 243 (100) \([\text{M} - \text{OH}]^+\). HRMS (EI) m/z: \([\text{M}]^+\) Calcd. for C\(_{14}\)H\(_{19}\)OF\(_3\): 260.1383; Found: 260.1381. 
IR (thin film) \(v_{\text{max}}\) 3346, 2959, 2869, 1476, 1370, 1246, 1174, 1105 cm\(^{-1}\). Enantiomeric purity (93\% ee) was measured by chiral HPLC on PC4 column (Hexane/iPrOH = 9:1, 0.7 mL/min, UV detection at 224 nm); retention time = 22.70 min (major), retention time = 26.64 min (minor).

\((R)-(4-(1,1,1-\text{Trifluoro}-4,4-\text{dimethylpentan}-2-yl)-1,1'-\text{biphenyl}\) (4l). General Procedure A. The product (97.5 mg, 79\% yield) was purified with silica gel chromatography (Petroleum ether) as a white solid (m.p. 101.2-101.9 \(^{\circ}\)C). \([\alpha]_{D}^{20} = -21.64\) (c = 0.55, CHCl\(_3\)) for a sample with 88\% ee. \(^{1}\text{H NMR}\) (400 MHz, CDCl\(_3\)) \(\delta\) 7.65 – 7.51 (m, 4 H), 7.49 – 7.29 (m, 5 H), 3.36 (dtd, \(J = 17.6, 10.0, 4.2\) Hz, 1 H), 2.03 – 1.86 (m, 2 H), 0.82 (s, 9 H). \(^{13}\text{C NMR}\) (101 MHz, CDCl\(_3\)) \(\delta\) 140.8, 140.5, 135.8 (q, \(J_{\text{CF}} = 2.1\) Hz), 129.8, 128.8, 127.4, 127.2, 127.0, 127.3 (q, \(J_{\text{CF}} = 279.6\) Hz), 46.7 (q, \(J_{\text{CF}} = 26.2\) Hz), 42.1 (q, \(J_{\text{CF}} = 1.9\) Hz), 30.8, 29.7. \(^{19}\text{F NMR}\) (376 MHz, CDCl\(_3\)) \(\delta\) -70.01 (d, \(J = 9.6\) Hz, 3 F). MS (EI): m/z (%) 306 (100) \([\text{M}]^+\). HRMS (EI) m/z: \([\text{M}]^+\) Calcd. for C\(_{19}\)H\(_{21}\)F\(_3\): 306.1590; Found: 306.1595. IR (thin film) \(v_{\text{max}}\) 2962, 2870, 1489, 1452, 1370, 1208, 1100, 763 cm\(^{-1}\). Enantiomeric purity (88\% ee) was measured by chiral HPLC. 

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on PC-3 column (MeCN/H$_2$O = 70:30, 0.7 mL/min, UV detection at 214 nm); retention time = 12.75 min (major), retention time = 11.07 min (minor).

(R)-1-Methoxy-4-(1,1,1-trifluoro-4,4-dimethylpentan-2-yl)benzene (4m). General Procedure A. 10 mol% DMAP, 2a (0.4 mmol, 1.0 equiv), 3m (0.6 mmol, 1.5 equiv), and 0.5 equiv of NaI were used. The product (40.4 mg, 40% yield) was purified with silica gel chromatography (Petroleum ether/DCM = 50:1) as a colorless oil. [α]$_D^{20}$ = -12.37 (c = 1.18, CHCl$_3$) for a sample with 88% ee.

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.23 (d, $J$ = 8.5 Hz, 2 H), 6.86 (d, $J$ = 8.6 Hz, 2 H), 3.79 (s, 3 H), 3.26 (tq, $J$ = 9.8, 5.4, 4.8 Hz, 1 H), 1.94 – 1.81 (m, 2 H), 0.79 (s, 9 H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 159.2, 130.4, 128.7 (q, C-F, $^3$J$_{C-F}$ = 2.0 Hz), 127.4 (q, C-F, $^1$J$_{C-F}$ = 279.7 Hz), 113.9, 55.1, 46.2 (q, C-F, $^2$J$_{C-F}$ = 26.1 Hz), 42.0 (q, C-F, $^3$J$_{C-F}$ = 2.0 Hz), 30.7, 29.7.

$^{19}$F NMR (376 MHz, CDCl$_3$) δ -70.70 (d, $J$ = 9.5 Hz). MS (FI): m/z (%) 260 (100) [M]$^+$.

HRMS (FI) m/z: [M]$^+$ Calcd. for C$_{14}$H$_{19}$OF$_3$: 260.1388; Found: 260.1386.

IR (thin film) $v_{max}$ 2958, 1615, 1518, 1467, 1248, 1104, 825 cm$^{-1}$.

Enantiomeric purity (88% ee) was measured by chiral HPLC on OJH column (Hexane/PrOH = 6:4, 0.7 mL/min, UV detection at 214 nm); retention time = 5.63 min (major), retention time = 6.14 min (minor).

(R)-1-Methoxy-3-(1,1,1-trifluoro-4,4-dimethylpentan-2-yl)benzene (4n). General Procedure A. The product (59.3 mg, 57% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 50:1) as a colorless liquid. [α]$_D^{20}$ = -19.53 (c = 0.38, CHCl$_3$) for a sample with 89% ee.

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.32 – 7.16 (m, 1 H), 6.95 – 6.79 (m, 3 H), 3.81 (s, 3 H), 3.29 (dtd, $J$ = 19.7, 9.9, 4.0 Hz, 1 H), 1.98 – 1.82 (m, 2 H), 0.81 (s, 9 H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 159.6, 138.3 (q, C-F, $^3$J$_{C-F}$ = 2.3 Hz), 129.4, 127.2 (q, C-F, $^1$J$_{C-F}$ = 279.7 Hz), 121.9, 115.5, 112.9, 55.2, 47.0 (q, C-F, $^2$J$_{C-F}$ = 26.0 Hz, 3 F), 42.1 (q, C-F, $^3$J$_{C-F}$ = 1.9 Hz), 30.8, 29.7.

$^{19}$F NMR (376 MHz, CDCl$_3$) δ -70.70 (d, $J$ = 9.5 Hz). MS (EI): m/z (%) 122 (100) [M]$^+$. HRMS (EI) m/z: [M]$^+$ Calcd. for C$_{14}$H$_{19}$OF$_3$: 260.1383; Found: 260.1385.

IR (thin film) $v_{max}$ 2958, 2869, 1604, 1588, 1495, 1457, 1370, 1260, 1108, 707 cm$^{-1}$. Enantiomeric purity (89% ee) was measured by chiral HPLC on OJH column (Hexane/PrOH = 98:2, 0.7 mL/min, UV detection at 214 nm); retention time = 5.18 min (major), retention time = 5.46 min (minor).
**(R)-2-Methoxy-4-(1,1,1-trifluoro-4,4-dimethylpentan-2-yl)pyridine (4o).** General Procedure A. The product (55.1 mg, 53% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 50:1) as a colorless liquid. $[\alpha]_D^{20} = -9.23$ (c = 0.39, CHCl$_3$) for a sample with 91% ee. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.14 (d, $J = 5.3$ Hz, 1 H), 6.86 (d, $J = 5.3$ Hz, 1 H), 6.73 (s, 1 H), 3.95 (s, 3 H), 3.33 – 3.19 (m, 1 H), 1.97 – 1.77 (m, 2 H), 0.82 (s, 9 H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 164.5, 148.6 (q, C-F, $^3$J$_{C-F} = 2.1$ Hz), 147.1, 126.6 (q, C-F, $^1$J$_{C-F} = 279.9$ Hz), 117.6, 111.9, 53.5, 46.5 (q, C-F, $^2$J$_{C-F} = 26.6$ Hz), 41.7 (q, C-F, $^3$J$_{C-F} = 1.8$ Hz), 30.8, 29.6. $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -70.01 (d, $J = 9.6$ Hz, 3 F). MS (ESI): m/z (%) 262 (100) [M+H$^+$]. HRMS (ESI) m/z: [M+H]$^+$ Calcd. for C$_{13}$H$_{19}$NOF$_3$: 262.1413; Found: 262.1411. Enantiomeric purity (91% ee) was measured by chiral HPLC on ASH column (Hexane/iPrOH = 98:2, 0.7 mL/min, UV detection at 214 nm); retention time = 4.86 min (major), retention time = 5.24 min (minor).

**IR** ($\nu_{\text{max}}$) 2958, 2870, 1614, 1562, 1484, 1403, 1316, 1261, 1109, 708 cm$^{-1}$.

**(R)-2-(4-Fluorophenyl)-5-(2-methyl-5-(1,1,1-trifluoro-4,4-dimethylpentan-2-yl)benzyl)thiophene (4p).** General Procedure A. 0.5 equiv of NaI was used. The product (142.9 mg, 82% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 100:1) as a colorless oil. $[\alpha]_D^{20} = -7.44$ (c = 0.78, CHCl$_3$) for a sample with 88% ee. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.53 – 7.39 (m, 2 H), 7.18 (s, 1 H), 7.15 (s, 2 H), 7.09 – 6.92 (m, 3 H), 6.60 (m, 1 H), 4.12 (s, 2 H), 3.38 – 3.20 (m, 1 H), 2.28 (s, 3 H), 1.97 – 1.83 (m, 2 H), 0.81 (s, 9 H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 162.1 (d, C-F, $^1$J$_{C-F} = 246.8$ Hz), 143.4, 141.5, 138.2, 136.2, 134.6 (q, C-F, $^3$J$_{C-F} = 1.8$ Hz), 130.9 (d, C-F, $^4$J$_{C-F} = 3.3$ Hz), 130.8, 130.7, 127.9, 127.3 (q, C-F, $^1$J$_{C-F} = 275.5$ Hz), 127.1 (d, C-F, $^3$J$_{C-F} = 8.1$ Hz), 125.8, 122.6, 115.7 (d, C-F, $^2$J$_{C-F} = 21.8$ Hz), 46.7 (q, C-F, $^2$J$_{C-F} = 26.0$ Hz), 42.0, 34.2, 30.8, 29.8, 19.1. $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -70.35 (d, $J = 10.1$ Hz, 3 F), -115.20 (m, 1 F). MS (ESI): m/z (%) 435 (100) [M$^+$], 452 [M+NH$_4$]$^+$ HRMS (DART) m/z: [M+H]$^+$ Calcd. for C$_{25}$H$_{27}$F$_4$S: 435.1764; Found: 435.1762. IR (thin film) $\nu_{\text{max}}$ 2957, 2867, 1509, 1469, 1398, 1234, 1174, 1106, 833 cm$^{-1}$. Enantiomeric purity (88% ee) was measured by chiral HPLC on OJH column (Hexane/iPrOH = 85:15, 0.7 mL/min, UV detection at 214 nm); retention time = 7.76 min (major), retention time = 6.97 min (minor).
**tert-Butyl** ((R)-3-hydroxy-1-oxo-1-((4-((R)-1,1,1-trifluoro-4,4-dimethylpentan-2-yl)benzyl)amino)propan-2-yl)carbamate (4q). General Procedure A. 0.5 equiv of NaI, 13 mol% NiBr$_2$·DME and 13 mol% L6 were used. The product (40.9 mg, 46% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 2:1) as a colorless liquid. [α]$_D^{20}$ = -39.26 (c = 1.03, CHCl$_3$) for a sample with 88% ee.

1H NMR (400 MHz, CDCl$_3$) $\delta$ 7.27 (d, J = 8.0 Hz, 2 H), 7.22 (d, J = 8.0 Hz, 2 H), 7.18 (br, 1 H), 5.69 (d, J = 7.1 Hz, 1 H), 4.56 – 4.33 (m, 2 H), 4.21 (s, 1 H), 4.15 – 4.02 (m, 1 H), 3.69 (s, 1 H), 3.47 (s, 1 H), 3.36 – 3.22 (m, 1 H), 1.93 – 1.85 (m, 2 H), 1.40 (s, 9 H), 0.79 (s, 9 H).

13C NMR (101 MHz, CDCl$_3$) $\delta$ 171.4, 156.3, 137.5, 136.1, 129.7, 127.6, 127.1 (q, C-F, $^2$J$_{C-F}$ = 279.7 Hz), 80.6, 62.7, 55.0, 46.6 (q, C-F, $^2$J$_{C-F}$ = 26.3 Hz), 42.9, 42.0, 30.8, 29.7, 28.2. 19F NMR (376 MHz, CDCl$_3$) $\delta$ -70.36 (d, J = 9.5 Hz, 3 F). MS (ESI): m/z (%) 469 (100) [M+Na]$^+$, 447 (57) [M+H]$^+$. HRMS (FT) m/z: [M+H]$^+$ Calcd for C$_{22}$H$_{34}$N$_2$O$_4$F$_3$: 447.2465; Found: 447.2473.

IR (thin film) $\nu_{max}$ 3301, 2961, 2870, 1701, 1648, 1541, 1475, 1368, 1261, 1105 cm$^{-1}$. The enantiomeric purity of 4q (88% ee) was determined by 4q', which was derived from 4q as showing below.

**tert-Butyl** (R)-(3-oxo-3-((4-((1,1,1-trifluoro-4,4-dimethylpentan-2-yl)benzyl)amino)prop-1-en-2-yl)carbamate (4q'). To a 25 mL Schlenk tube was added tert-butyl ((R)-3-hydroxy-1-oxo-1-((4-((R)-1,1,1-trifluoro-4,4-dimethylpentan-2-yl)benzyl)amino)propan-2-yl)carbamate (4q) (178.6 mg, 0.4 mmol), EDCI·HCl (84.3 mg, 0.44 mmol) and CuCl (11.9 mg, 0.12 mmol). The tube was then purged with Ar for three times. Anhydrous DCM (4 mL) were added under Ar. The tube was sealed with Teflon cap. After stirring at 800 rpm for 18 h at room temperature, the reaction mixture was diluted with DCM, washed with water and brine. The organic layer was dried over Na$_2$SO$_4$, filtered and concentrated. The resulting mixture was purified with silica gel chromatography (Petroleum ether/EtOAc = 8:1) to give product 4q' as a colorless oil (80.7 mg, 47%) with 88% ee. [α]$_D^{20}$ = -7.71 (c = 1.11, CHCl$_3$) for a sample with 88% ee. 1H NMR (400 MHz, CDCl$_3$) $\delta$ 7.35 (br, 1 H), 7.30 (d, J
= 8.2 Hz, 2 H), 7.24 (d, J = 8.1 Hz, 2 H), 6.57 (t, J = 6.0 Hz, 1 H), 6.04 – 5.96 (m, 1 H), 5.07 (t, J = 1.8 Hz, 1 H), 4.50 (d, J = 5.9 Hz, 2 H), 3.39 – 3.23 (m, 1 H), 1.94 – 1.85 (m, 2 H), 1.47 (s, 9 H), 0.79 (s, 9 H). \[ ^{13} \text{C NMR} \] (126 MHz, CDCl\(_3\)) \( \delta \) 164.0, 152.7, 137.3, 136.3 (q, C-F, \( ^{3} J_{C-F} = 1.3 \) Hz), 134.8, 129.8, 127.8, 127.1 (q, C-F, \( ^{1} J_{C-F} = 279.6 \) Hz), 97.6, 80.6, 46.6 (q, C-F, \( ^{2} J_{C-F} = 26.1 \) Hz), 43.5, 42.0, 30.8, 29.6, 28.2. \[ ^{19} \text{F NMR} \] (376 MHz, CDCl\(_3\)) \( \delta \) -70.32 (d, \( ^{1} J_{C-F} = 9.5 \) Hz). MS (ESI): m/z (%) 373 (100) \([M-C_4H_7]^+\), 429 (5) \([M+H]^+\). Enantiomeric purity (88% ee) was measured by chiral HPLC on ODH column (Hexane/PrOH = 95:5, 0.7 mL/min, UV detection at 214 nm); retention time = 20.00 min (major), retention time = 15.68 min (minor).

4-((R)-1,1,1-Trifluoro-4,4-dimethylpentan-2-yl)benzyl (2S,5R)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate 4,4-dioxide (4r). General Procedure A. The product (122.9 mg, 65% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 6:1) as a white solid (m.p. 49.0 – 50.9 \(^\circ\)C). \([\alpha]_d^{20} = 126.85 \) (c = 0.82, CHCl\(_3\)) for a sample with 90% de. \[^{1} \text{H NMR} \] (400 MHz, CDCl\(_3\)) \( \delta \) 7.36 (m, 4 H), 5.30 (d, \( J = 12.1 \) Hz, 1 H), 5.15 (d, \( J = 12.0 \) Hz, 1 H), 4.64 – 4.55 (m, 1 H), 4.41 (s, 1 H), 3.55 – 3.25 (m, 3 H), 2.00 – 1.84 (m, 2 H), 1.53 (s, 3 H), 1.19 (s, 3 H), 0.78 (s, 9 H). \[^{13} \text{C NMR} \] (101 MHz, CDCl\(_3\)) \( \delta \) 170.7, 166.7, 137.7 (q, C-F, \( ^{3} J_{C-F} = 2.1 \) Hz), 134.1, 129.8, 129.0, 127.0 (q, C-F, \( ^{1} J_{C-F} = 279.8 \) Hz), 67.5, 63.0, 62.6, 61.0, 46.7 (q, C-F, \( ^{2} J_{C-F} = 26.3 \) Hz), 41.9, 38.2, 30.7, 29.6, 19.8, 18.4. \[^{19} \text{F NMR} \] (376 MHz, CDCl\(_3\)) \( \delta \) -70.26 (d, \( J = 9.5 \) Hz). MS (ESI): m/z (%) 498 (100) \([M+Na]^+\). HRMS (ESI) m/z: \([M+Na]^+\) Calcd. for C\(_{22}\)H\(_{28}\)NO\(_5\)F\(_3\)NaS: 498.1533; Found: 498.1530. IR (thin film) \( \nu_{\max} \) 2960, 2870, 1800, 1757, 1467, 1399, 1262, 1186, 1105 cm\(^{-1}\). Enantiomeric purity (90% de) was measured by chiral HPLC on ADH column (Hexane/PrOH = 9:1, 0.7 mL/min, UV detection at 214 nm); retention time = 19.59 min (major), retention time = 18.64 min (minor).

(R,E)-1-(5,5-Dimethyl-3-(trifluoromethyl)hex-1-en-1-yl)-4-methoxybenzene (4s). General Procedure A. The product (45.5 mg, 40% yield) was purified with silica gel chromatography (Petroleum ether/DCM = 10:1) as a colorless oil. \([\alpha]_d^{20} = -69.14 \) (c = 0.88, CHCl\(_3\)) for a sample with 73% ee. \[^{1} \text{H NMR} \] (400 MHz, CDCl\(_3\)) \( \delta \) 7.31 (d, \( J = 8.7 \) Hz, 2 H), 6.86 (d, \( J = 8.7 \) Hz, 2 H), 6.51 (d, \( J = 15.8 \) Hz, 1 H), 5.82 (dd, \( J = 15.9, 9.2 \) Hz, 1 H), 3.81
(s, 3 H), 2.92 (qd, J = 9.5, 2.2 Hz, 1 H), 1.72 (dd, J = 14.1, 2.2 Hz, 1 H), 1.52 (dd, J = 14.1, 9.4 Hz, 1 H), 0.94 (s, 9 H). $^1$H NMR (101 MHz, CDCl$_3$) $\delta$ 159.5, 134.5, 129.3, 127.6, 127.2 (q, C-F, $^1$J$_{C,F}$ = 279.7 Hz), 123.2 (q, C-F, $^3$J$_{C,F}$ = 2.3 Hz), 114.0, 55.3, 44.8 (q, C-F, $^2$J$_{C,F}$ = 26.1 Hz), 41.3, 30.7, 29.8. $^{13}$C NMR (101 MHz, CDCl$_3$) m/z: 159.5, 134.5, 129.3, 127.6, 127.2 (q, C-F, $^1$J$_{C,F}$ = 279.7 Hz), 123.2 (q, C-F, $^3$J$_{C,F}$ = 2.3 Hz), 114.0, 55.3, 44.8 (q, C-F, $^2$J$_{C,F}$ = 26.1 Hz), 41.3, 30.7, 29.8. $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -71.27 (d, J = 8.9 Hz). MS (FI): m/z (%) 286 (100) [M$^+$]. HRMS (FI) m/z: [M$^+$] Calcd. for C$_{16}$H$_{21}$OF$_3$: 286.1543; Found: 286.1539.

IR (thin film) $v_{max}$ 2957, 2867, 1608, 1513, 1466, 1254, 1173, 1107 cm$^{-1}$. Enantiomeric purity (73% ee) was measured by chiral HPLC on PC-3 column (MeCN/H$_2$O = 55:45, 0.7 mL/min, UV detection at 214 nm); retention time = 21.39 min (major), retention time = 19.80 min (minor).

(R)-2-(6,6,6-Trifluoro-3,3-dimethyl-5-phenylhexyl)isoindoline-1,3-dione (5a). General Procedure B. FeBr$_2$ (0.25 equiv) instead of FeCl$_3$ (0.25 equiv) was used. The product (50.0 mg, 64% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 15:1) as a colorless oil. [α]$_D^{20}$ = -35.50 (c = 1.11, CHCl$_3$) for a sample with 86% ee. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.88 – 7.80 (m, 2 H), 7.75 – 7.66 (m, 2 H), 7.39 – 7.27 (m, 5 H), 3.69 – 3.59 (m, 2 H), 3.46 (qdd, J = 9.9, 7.1, 4.8 Hz, 1 H), 2.08 – 1.96 (m, 2 H), 1.65 – 1.56 (m, 1 H), 1.55 – 1.45 (m, 1 H), 0.85 (s, 3 H), 0.82 (s, 3 H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 168.2, 136.4 (q, C-F, $^3$J$_{C,F}$ = 1.9 Hz), 133.9, 132.2, 129.4, 128.6, 128.0, 127.1 (q, C-F, $^1$J$_{C,F}$ = 279.9 Hz), 123.1, 46.4 (q, C-F, $^2$J$_{C,F}$ = 26.3 Hz), 40.0 (q, C-F, $^3$J$_{C,F}$ = 1.8 Hz), 33.9, 32.8, 27.3, 27.0. $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -70.26 (d, J = 10.2 Hz, 3 F). MS (ESI): m/z (%) 390 (100) [M+H$^+$]. HRMS (DART) m/z: [M+H$^+$] Calcd. for C$_{22}$H$_{23}$NO$_2$F$_3$: 390.1675; Found: 390.1675. IR (thin film) $v_{max}$ 2960, 2873, 1712, 1468, 1401, 1256, 1161, 1106, 720 cm$^{-1}$. Enantiomeric purity (86% ee) was measured by chiral HPLC on IG column (Hexane/iPrOH = 96:4, 0.7 mL/min, UV detection at 214 nm); retention time = 13.63 min (major), retention time = 14.96 min (minor).

(R)-2-(5-(1,1'-Biphenyl)-4-yl)-6,6,6-trifluoro-3,3-dimethylhexylisoindoline-1,3-dione (5b). General Procedure B. The product (66.1 mg, 71% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 15:1) as a colorless oil. [α]$_D^{20}$ = -22.93 (c = 0.41, CHCl$_3$) for a sample with 87% ee. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.82 (dt, J = 7.8, 3.7 Hz, 2
\[ \delta_{\text{H}} \text{ NMR (400 MHz, CDCl}_3 \] 
\[ \delta \text{ 7.88 – 7.80 (m, 2 H), 7.75 – 7.66 (m, 2 H), 7.30 – 7.21 (m, 1 H), 6.94 (d, \ J = 7.4 Hz, 1 H), 6.89 (s, 1 H), 6.84 (d, \ J = 8.2 Hz, 1 H), 3.81 (s, 3 H), 3.72 – 3.57 (m, 2 H), 3.50 – 3.35 (m, 1 H), 2.06 – 1.92 (m, 2 H), 1.66 – 1.54 (m, 2 H), 0.87 (s, 3 H), 0.83 (s, 3 H).} \] 

\[ \delta_{\text{C}} \text{ NMR (101 MHz, CDCl}_3 \] 
\[ \delta 168.2, 159.7, 137.9 (q, C-F, 3\ J_{C-F} = 2.3 Hz), 133.9, 132.2, 129.6, 127.1 (q, C-F, 1\ J_{C-F} = 279.7 Hz), 123.1, 121.8, 115.4, 113.2, 55.2, 46.5 (q, \ C-F, 2\ J_{C-F} = 26.1 Hz), 40.1, 40.0, 34.0, 32.8, 27.3, 27.0.} \] 

\[ \delta_{\text{F}} \text{ NMR (376 MHz, CDCl}_3 \] 
\[ \delta -70.17 (d, \ J = 9.5 Hz, 3 F).} \] 

MS (ESI): m/z (%) 442 (100) [M+Na]+. HRMS (ESI) m/z: [M+Na]+ Calcd. for C_{23}H_{24}NO_3F_3Na: 442.1601; Found:

**Supplementary Figure 2.** X-ray crystal structure of compound 5b

(R)-2-(6,6,6-Trifluoro-5-(3-methoxyphenyl)-3,3-dimethylhexyl)isoindoline-1,3-dione (5c). General Procedure B. The product (52.1 mg, 62% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 10:1) as a colorless oil. \([\alpha]_{D}^{20} = -37.21 \ (c = 1.27, \text{CHCl}_3)\) for a sample with 88% ee. \(1^H \text{ NMR (400 MHz, CDCl}_3 \] 
\[ \delta 7.88 – 7.80 (m, 2 H), 7.75 – 7.66 (m, 2 H), 7.30 – 7.21 (m, 1 H), 6.94 (d, \ J = 7.4 Hz, 1 H), 6.89 (s, 1 H), 6.84 (d, \ J = 8.2 Hz, 1 H), 3.81 (s, 3 H), 3.72 – 3.57 (m, 2 H), 3.50 – 3.35 (m, 1 H), 2.06 – 1.92 (m, 2 H), 1.66 – 1.54 (m, 2 H), 0.87 (s, 3 H), 0.83 (s, 3 H).} \] 

\[ \delta_{\text{C}} \text{ NMR (101 MHz, CDCl}_3 \] 
\[ \delta 168.2, 159.7, 137.9 (q, C-F, 3\ J_{C-F} = 2.3 Hz), 133.9, 132.2, 129.6, 127.1 (q, C-F, 1\ J_{C-F} = 279.7 Hz), 123.1, 121.8, 115.4, 113.2, 55.2, 46.5 (q, \ C-F, 2\ J_{C-F} = 26.1 Hz), 40.1, 40.0, 34.0, 32.8, 27.3, 27.0.} \] 

\[ \delta_{\text{F}} \text{ NMR (376 MHz, CDCl}_3 \] 
\[ \delta -70.17 (d, \ J = 9.5 Hz, 3 F).} \] 

MS (ESI): m/z (%) 442 (100) [M+Na]+. HRMS (ESI) m/z: [M+Na]+ Calcd. for C_{23}H_{24}NO_3F_3Na: 442.1601; Found:
Enantiomeric purity (88% ee) was measured by chiral HPLC on OJH column (Hexane/iPrOH = 98:2, 0.7 mL/min, UV detection at 214 nm); retention time = 15.66 min (major), retention time = 14.89 min (minor).

(R)-2-(5-(4-Acetylphenyl)-6,6,6-trifluoro-3,3-dimethylhexyl)isoindoline-1,3-dione (5d). General Procedure B. FeBr2 (0.25 equiv) instead of FeCl3 (0.25 equiv) was used. The product (53.4 mg, 62% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 8:1) as a colorless oil. [α]D20 = -53.56 (c = 0.37, CHCl3) for a sample with 88% ee. 1H NMR (400 MHz, CDCl3) δ 7.94 (d, J = 8.0 Hz, 2 H), 7.88 – 7.78 (m, 2 H), 7.76 – 7.66 (m, 2 H), 7.48 (d, J = 8.0 Hz, 2 H), 3.72 – 3.61 (m, 2 H), 3.61 – 3.48 (m, 1 H), 2.60 (s, 3 H), 2.11 – 1.97 (m, 2 H), 1.61 – 1.54 (m, 1 H), 1.54 – 1.45 (m, 1 H), 0.86 (s, 3 H), 0.81 (s, 3 H). 13C NMR (101 MHz, CDCl3) δ 197.6, 168.2, 141.7, 136.9, 133.9, 132.1, 129.7, 128.7, 126.8 (q, C-F, 1JCF = 280.1 Hz), 123.2, 46.5 (q, C-F, 2JCF = 26.4 Hz), 40.0, 39.8, 33.9, 32.9, 27.4 27.2, 26.6. 19F NMR (376 MHz, CDCl3) δ -69.90 (d, J = 9.7 Hz, 3 F). MS (ESI): m/z (%) 454 (100) [M+Na]+. HRMS (ESI) m/z: [M+Na]+ Calcd. for C24H24NO3F3Na: 454.1601; Found: 454.1592.

IR (thin film) νmax 2960, 2873, 1714, 1402, 1373, 1256, 1161, 1107, 720 cm⁻¹. Enantiomeric purity (88% ee) was measured by chiral HPLC on OJH column (Hexane/iPrOH = 95:5, 0.7 mL/min, UV detection at 214 nm); retention time = 41.13 min (major), retention time = 46.65 min (minor).

(R)-4-(6-(1,3-Dioxoisoindolin-2-yl)-1,1,1-trifluoro-4,4-dimethylhexan-2-yl)benzenesulfonamide (5e). General Procedure B. FeBr2 (0.25 equiv) instead of FeCl3 (0.25 equiv) was used. The product (54.3 mg, 58% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 3:1) as a white solid. [α]D20 = -48.88 (c = 0.61, CHCl3) for a sample with 87% ee. 1H NMR (400 MHz, CDCl3) δ 7.94 (d, J = 8.3 Hz, 2 H), 7.87 – 7.77 (m, 2 H), 7.76 – 7.66 (m, 2 H), 7.54 (d, J = 8.3 Hz, 2 H), 5.12 (s, 2 H), 3.65 – 3.48 (m, 3 H), 2.11 – 1.94 (m, 2 H), 1.60 – 1.36 (m, 2 H), 0.90 (s, 3 H), 0.85 (s, 3 H). 13C NMR (101 MHz, CDCl3) δ 168.2, 141.8, 141.5, 134.0, 132.0, 130.2, 126.9, 126.6 (q, C-F, 1JCF = 280.3 Hz), 123.2, 46.4 (q, C-F, 2JCF = 26.8 Hz), 39.9, 39.5, 33.8, 32.8, 27.6, 27.4. 19F NMR (376 MHz, CDCl3) δ -69.90
(d, J = 9.5 Hz, 3 F). MS (ESI): m/z (%): 491 (100) [M+Na]⁺. HRMS (ESI) m/z: [M+Na]⁺ Calcd. for C_{22}H_{23}N_{2}O_{4}F_{3}S: 491.1223; Found: 491.1221. IR (thin film) ν_{max} 3351, 3267, 2960, 2873, 1709, 1404, 1339, 1255, 1165, 1107, 721 cm⁻¹. Enantiomeric purity (87% ee) was measured by chiral HPLC on IG column (Hexane/iPrOH = 6:4, 0.7 mL/min, UV detection at 214 nm); retention time = 12.59 min (major), retention time = 11.80 min (minor).

(R)-2-(5-(3-Bromophenyl)-6,6,6-trifluoro-3,3-dimethylhexyl)isoindoline-1,3-dione (5f). General Procedure B. The product (49.6 mg, 53% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 15:1). An analytical pure sample was purified with reversed-phase HPLC, the pure product was obtained as a white solid (m.p. 117.8-118.8 °C). [α]_{D}^{20} = -35.50 (c = 1.11, CHCl₃) for a sample with 88% ee. ¹H NMR (400 MHz, CDCl₃) δ 7.87–7.81 (m, 2 H), 7.75–7.68 (m, 2 H), 7.51 (t, J = 2.1 Hz, 1 H), 7.45 (ddd, J = 7.8, 2.0, 1.0 Hz, 1 H), 7.30 (d, J = 8.5 Hz, 1 H), 7.23 (t, J = 7.8 Hz, 1 H), 3.73–3.57 (m, 2 H), 3.44 (pd, J = 9.8, 2.1 Hz, 1 H), 2.09–1.89 (m, 2 H), 1.65–1.56 (m, 1 H), 1.56–1.46 (m, 1 H), 0.87 (s, 3 H), 0.82 (s, 3 H). ¹³C NMR (101 MHz, CDCl₃) δ 168.2, 138.7 (q, C-F, 3J_{C-F} = 2.3 Hz), 133.9, 132.3, 132.2, 131.3, 130.2, 128.1, 126.8 (q, C-F, 1J_{C-F} = 279.8 Hz), 123.2, 122.7, 46.1 (q, C-F, 2J_{C-F} = 26.8 Hz), 40.0, 39.9, 33.9, 32.9, 27.4, 27.1. ¹⁹F NMR (376 MHz, CDCl₃) δ -70.18 (d, J = 9.5 Hz, 3 F). MS (FT): m/z (%) 468, 470 (100) [M+H]⁺. HRMS (DART) m/z: [M+H]⁺ Calcd. for C_{22}H_{22}NO_{2}F_{3}Br: 468.0781; Found: 468.0775. IR (thin film) ν_{max} 2959, 2872, 1713, 1468, 1401, 1254, 1160, 1108, 714 cm⁻¹. Enantiomeric purity (88% ee) was measured by chiral HPLC on ADH column (Hexane/iPrOH = 97:3, 0.7 mL/min, UV detection at 214 nm); retention time = 14.60 min (major), retention time = 13.21 min (minor).

(R)-4-(1,1,1-Trifluoro-4,4-dimethyldodecan-2-yl)-1,1'-biphenyl (5g). General Procedure B. NaI (0.5 equiv) instead of FeCl₃ (0.25 equiv) was used. The product (44.6 mg, 55% yield) was purified with silica gel chromatography (Petroleum ether) as a white solid (m.p. 43.1-44.3 °C). [α]_{D}^{20} = -20.06 (c = 1.22, CHCl₃) for a sample with 91% ee. ¹H NMR (400 MHz, CDCl₃) δ 7.64–7.50 (m, 4 H), 7.49–7.31 (m, 5 H), 3.34 (qt, J = 9.8, 4.8 Hz, 1 H), 2.04–1.83 (m, 2 H), 1.29–0.99 (m, 14 H), 0.85 (t, J = 6.9
Hz, 3 H), 0.78 (s, 3 H), 0.77 (s, 3 H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 140.8, 140.5, 135.9 (q, C-F, $^3$J$_{C-F} = 2.3$ Hz), 129.8, 128.7, 127.5 (q, C-F, $^1$J$_{C-F} = 279.8$ Hz), 127.4, 127.2, 127.0, 46.3 (q, C-F, $^2$J$_{C-F} = 26.3$ Hz), 42.1, 39.9, 33.3, 31.9, 30.4, 29.6, 29.3, 27.7, 27.5, 23.8, 22.6, 14.1. $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -70.15 (d, $J = 9.5$ Hz, 3 F). MS (FT): m/z (%) 404 (67) [M]$^+$, HRMS (DART) m/z: [M]$^+$ Calcd. for C$_{26}$H$_{35}$F$_3$: 404.2685; Found: 404.2684.

IR (thin film) $v_{\text{max}}$ 3346, 2950, 2931, 2870, 2847, 1489, 1466, 1314, 1275, 1172, 1122, 736 cm$^{-1}$. Enantiomeric purity (91% ee) was measured by chiral HPLC on PC-3 column (MeCN/H$_2$O = 65:35, 0.7 mL/min, UV detection at 214 nm); retention time = 40.51 min (major), retention time = 37.57 min (minor).

(R)-4-(7-Chloro-1,1,1-trifluoro-4,4-dimethylheptan-2-yl)-1,1'-biphenyl (5h).

General Procedure B. NaI (0.5 equiv) instead of FeCl$_3$ (0.25 equiv) was used. The product (39.6 mg, 54% yield) was purified with silica gel chromatography (Petroleum ether) as a white solid. $[\alpha]_D^{20}$ = -20.24 (c = 0.51, CHCl$_3$) for a sample with 88% ee. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.64 – 7.52 (m, 4 H), 7.49 – 7.31 (m, 5 H), 3.43 – 3.21 (m, 3 H), 2.05 – 1.87 (m, 2 H), 1.75 – 1.62 (m, 1 H), 1.61 – 1.56 (m, 1 H), 1.34 – 1.24 (m, 1 H), 1.23 – 1.11 (m, 1 H), 0.82 (s, 3 H), 0.81 (s, 3 H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 141.0, 140.4, 135.5, 129.7, 128.8, 127.5, 127.3, 127.2 (q, C-F, $^1$J$_{C-F} = 280.1$ Hz), 127.1, 46.3 (q, C-F, $^2$J$_{C-F} = 26.6$ Hz), 45.5, 39.8, 39.1, 33.1, 27.6, 27.4, 27.4. $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -70.17 (d, $J = 9.5$ Hz, 3 F). MS (FT): m/z (%) 368 (100) [M]$^+$, 391 (51) [M+Na]$^+$. HRMS (DART) m/z: [M]$^+$ Calcd. for C$_{21}$H$_{24}$F$_3$Cl: 368.1513; Found: 368.1513. IR (thin film) $v_{\text{max}}$ 2958, 2875, 1489, 1442, 1372, 1257, 1162, 1106, 766 cm$^{-1}$. Enantiomeric purity (88% ee) was measured by chiral HPLC on ADH column (Hexane/iPrOH = 97:3, 0.7 mL/min, UV detection at 214 nm); retention time = 5.67 min (major), retention time = 5.35 min (minor).

(R)-5-(3-Acetylphenyl)-6,6,6-trifluoro-3,3-dimethylhexyl 6-bromohexanoate (5i). General Procedure B. NaI (0.5 equiv) instead of FeCl$_3$ (0.25 equiv) was used. The product (53.9 mg, 56% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 8:1) as a colorless oil. $[\alpha]_D^{20}$ = -11.88 (c = 0.35, CHCl$_3$) for a sample with 90% ee. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.96 – 7.88 (m, 2 H), 7.56 (d, $J = 7.7$ Hz, 1 H), 7.48 (t, $J = 7.6$ Hz, 1 H), 4.13 – 3.92 (m, 2 H), 3.51 – 3.34 (m, 3
H), 2.63 (s, 3 H), 2.27 (t, \( J = 7.4 \text{ Hz}, 2 \text{ H} \)), 2.07 – 1.94 (m, 2 H), 1.87 (p, \( J = 6.8 \text{ Hz}, 2 \text{ H} \)), 1.67 – 1.57 (m, 2 H), 1.55 – 1.38 (m, 4 H), 0.82 (s, 3 H), 0.79 (s, 3 H). 13C NMR (101 MHz, CDCl3) \( \delta \) 197.5, 173.4, 137.5, 137.3, 133.8, 129.1, 129.0, 128.3, 126.9 (q, C-F, \( J_{C,F} = 280.0 \text{ Hz} \)), 68.0, 61.1, 46.5 (q, C-F, \( J_{C,F} = 26.3 \text{ Hz} \)), 40.6, 40.1, 34.1, 33.4, 32.8, 32.4, 27.6, 27.6, 27.3, 26.7, 25.6, 24.0. 19F NMR (376 MHz, CDCl3) \( \delta \) -70.23 (d, \( J = 9.5 \text{ Hz}, 3 \text{ F} \)). MS (FT): m/z (%) 479 (98) [M+H]+, 481 (100) [M+H+2]+, 496 (88) [M+NH4]+, 498 (86) [M+NH4+2]+. HRMS (DART) m/z: [M+H]+ Calcd for C22H31O3F3Br: 479.1403; Found: 479.1397.

IR (thin film) \( v_{\text{max}} \) 2961, 2870, 1732, 1687, 1466, 1442, 1361, 1255, 1164, 701 cm\(^{-1}\). Enantiomeric purity (90% ee) was measured by chiral HPLC on IG column (Hexane/PrOH = 95:5, 0.7 mL/min, UV detection at 214 nm); retention time = 20.09 min (major), retention time = 22.03 min (minor).

(R)-6-((1,1'-Biphenyl)-4-yl)-7,7,7-trifluoro-4,4-dimethylheptyl 4-cyanobenzoate (5j). General Procedure B. No additive was used. The product (65.2 mg, 68% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 10:1) as a colorless oil. \([\alpha]_D^{20} = -22.36 \text{ (c = 0.73, CHCl3)}\) for a sample with 87% ee. 1H NMR (400 MHz, CDCl3) \( \delta \) 8.06 (d, \( J = 8.4 \text{ Hz}, 2 \text{ H} \)), 7.69 (d, \( J = 8.4 \text{ Hz}, 2 \text{ H} \)), 7.59 – 7.52 (m, 4 H), 7.46 – 7.32 (m, 5 H), 4.23 – 4.06 (m, 2 H), 3.45 – 3.28 (m, 1 H), 2.06 – 1.91 (m, 2 H), 1.76 – 1.62 (m, 1 H), 1.57 – 1.47 (m, 1 H), 1.34 – 1.13 (m, 2 H), 0.86 (s, 3 H), 0.83 (s, 3 H). 13C NMR (101 MHz, CDCl3) \( \delta \) 164.8, 140.9, 140.3, 135.5 (q, C-F, \( J_{C,F} = 1.8 \text{ Hz} \)), 134.1, 132.1, 123.0, 129.7, 128.8, 127.5, 127.2, 127.2 (q, C-F, \( J_{C,F} = 279.9 \text{ Hz} \)), 127.0, 118.0, 116.3, 66.2, 46.3 (q, C-F, \( J_{C,F} = 26.3 \text{ Hz} \)), 40.0, 38.0, 33.1, 27.4, 27.3, 23.3. 19F NMR (376 MHz, CDCl3) \( \delta \) -70.18 (d, \( J = 10.2 \text{ Hz}, 3 \text{ F} \)). MS (FT): m/z (%) 479 (100) [M]+ HRMS (DART) m/z: [M]+ Calcd for C29H28NO3F3: 479.2067; Found: 479.2059. IR (thin film) \( v_{\text{max}} \) 2960, 2853, 2228, 1721, 1474, 1311, 1179, 1106, 766 cm\(^{-1}\). Enantiomeric purity (87% ee) was measured by chiral HPLC on ADH column (Hexane/PrOH = 95:5, 0.7 mL/min, UV detection at 214 nm); retention time = 15.52 min (major), retention time = 13.37 min (minor).
(R)-6,6,6-Trifluoro-5-(3-formylphenyl)-3,3-dimethylhexyl 4-cyanobenzoate (5k). General Procedure B. No additive was used. The product (45.8 mg, 55% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 8:1) as a white solid (m.p. 79.1-80.6 °C). $[\alpha]_D^{20} = -15.74 (c = 0.47, \text{CHCl}_3)$ for a sample with 84% ee. $^1H$ NMR (400 MHz, CDCl$_3$) $\delta$ 10.02 (s, 1 H), 8.08 (d, $J = 8.5$ Hz, 2 H), 7.88 (s, 1 H), 7.83 (d, $J = 7.5$ Hz, 1 H), 7.75 (d, $J = 8.1$ Hz, 2 H), 7.63 (d, $J = 7.7$ Hz, 1 H), 7.55 (t, $J = 7.6$ Hz, 1 H), 4.40 – 4.31 (m, 1 H), 4.30 – 4.21 (m, 1H), 3.55 – 3.43 (m, 1 H), 2.13 – 2.01 (m, 2 H), 1.75 – 1.61 (m, 2 H), 0.90 (s, 3 H), 0.85 (s, 3 H). $^{13}C$ NMR (101 MHz, CDCl$_3$) $\delta$ 191.7, 164.8, 137.7 (q, C-F, $^3J_{C-F} = 1.7$ Hz), 136.8, 135.2, 133.9, 132.2, 130.0, 130.0, 129.6, 126.7 (q, C-F, $^1J_{C-F} = 279.9$ Hz), 117.9, 116.5, 62.4, 46.4 (q, C-F, $^2J_{C-F} = 26.3$ Hz), 40.7, 40.1, 32.9, 27.6, 27.2. $^{19}F$ NMR (376 MHz, CDCl$_3$) $\delta$ -70.23 (d, $J = 9.5$ Hz, 3 F). MS (FT): m/z (%) 440 (100) [M+Na$^+$], 462 (90) [M+NH$_4^+$]. HRMS (DART) m/z: [M+Na$^+$] Calcd. for C$_{23}$H$_{22}$NO$_3$F$_3$Na: 440.1444; Found: 440.1441. Enantiomeric purity (84% ee) was measured by chiral HPLC on ADH column (Hexane/iPrOH = 95:5, 0.7 mL/min, UV detection at 214 nm); retention time = 36.84 min (major), retention time = 34.36 min (minor).

(R)-7,7,7-Trifluoro-6-(4-formylphenyl)-4,4-dimethylheptyl 4-acetylbenzoate (5l). General Procedure B. The product (48.7 mg, 54% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 6:1) as a colorless oil. $[\alpha]_D^{20} = -27.20 (c = 0.82, \text{CHCl}_3)$ for a sample with 90% ee. $^1H$ NMR (400 MHz, CDCl$_3$) $\delta$ 10.00 (s, 1 H), 8.09 (d, $J = 8.2$ Hz, 2 H), 8.02 (d, $J = 8.3$ Hz, 2 H), 7.86 (d, $J = 8.0$ Hz, 2 H), 7.52 (d, $J = 7.8$ Hz, 2 H), 4.19 (t, $J = 6.5$ Hz, 2 H), 3.53 – 3.34 (m, 1 H), 2.66 (s, 3 H), 2.04 – 1.94 (m, 2 H), 1.79 – 1.66 (m, 1 H), 1.65 – 1.51 (m, 1 H), 1.36 – 1.15 (m, 2 H), 0.83 (s, 3 H), 0.78 (s, 3 H). $^{13}C$ NMR (101 MHz, CDCl$_3$) $\delta$ 197.5, 191.5, 165.6, 143.4 (q, C-F, $^3J_{C-F} = 2.3$ Hz), 140.2, 136.1, 134.0, 130.1, 129.9, 129.7, 128.2, 126.7 (q, C-F, $^1J_{C-F} = 280.0$ Hz), 65.7, 46.8 (q, C-F, $^2J_{C-F} = 26.3$ Hz), 40.1, 38.2, 33.1, 27.2, 27.2, 26.9, 23.3. $^{19}F$ NMR (376 MHz, CDCl$_3$) $\delta$ -69.86 (d, $J = 9.5$ Hz, 3 F). MS (FT): m/z (%) 449 (100) [M+H$^+$], 462 (90) [M+NH$_4^+$]. HRMS (DART) m/z: [M+H$^+$] Calcd. for C$_{25}$H$_{28}$O$_4$F$_3$: 449.1934; Found: 449.1929. IR (thin film) $\nu_{\text{max}}$ 3029, 2818, 2727, 1694, 1599, 1466, 1290, 1203, 1163, 783, 690 cm$^{-1}$.
2959, 2872, 1707, 1690, 1472, 1311, 1260, 1107, 770 cm\(^{-1}\). Enantiomeric purity (90% ee) was measured by chiral HPLC on OJH column (Hexane/iPrOH = 6:4, 0.7 mL/min, UV detection at 214 nm); retention time = 57.46 min (major), retention time = 29.73 min (minor).

\(\text{(R)}\)-6-\([1,1'\text{-Biphenyl}]\)-4-yl)-7,7,7-trifluoro-4,4-dimethylheptyl 1-naphthoate (5m). General Procedure B. The product (62.3 mg, 62% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 15:1) as a colorless oil. \([\alpha]_D^{20} = -19.91\) (c = 1.16, CHCl\(_3\)) for a sample with 87% ee. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.93 – 8.82 (m, 1 H), 8.18 – 8.08 (m, 1 H), 8.01 (d, \(J = 8.4\) Hz, 1 H), 7.88 (d, \(J = 7.9\) Hz, 1 H), 7.64 – 7.44 (m, 7 H), 7.44 – 7.29 (m, 5 H), 4.32 – 4.16 (m, 2 H), 3.46 – 3.29 (m, 1 H), 2.07 – 1.92 (m, 2 H), 1.82 – 1.69 (m, 1 H), 1.68 – 1.56 (m, 1 H), 1.43 – 1.21 (m, 2 H), 0.85 (s, 3 H), 0.84 (s, 3 H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 167.5, 140.9, 140.4, 135.6 (q, \(C\)-F, \(^3\)J\(_{C-F}\) = 1.9 Hz), 133.8, 133.3, 131.3, 130.0, 129.7, 128.7, 128.5, 127.7, 127.4, 127.4, 127.3, 127.2 (q, C-F, \(^1\)J\(_{C-F}\) = 279.9 Hz), 127.0, 126.2, 125.8, 124.5, 65.5, 46.3 (q, C-F, \(^2\)J\(_{C-F}\) = 26.1 Hz), 40.0, 38.2, 33.2, 27.5, 27.4, 23.5. \(^19\)F NMR (376 MHz, CDCl\(_3\)) \(\delta\) -70.16 (d, \(J = 9.5\) Hz, 3 F). MS (FT): m/z (%) 505 (60) [M+H]\(^+\), 522 (100) [M+NH\(_4\)]\(^+\). HRMS (DART) m/z: [M+H]\(^+\) Calcd. for C\(_{32}\)H\(_{32}\)O\(_2\)F\(_3\): 505.2349; Found: 505.2344. IR (thin film) \(\nu_{\text{max}}\) 3032, 2958, 2872, 1713, 1509, 1488, 1278, 1247, 1136, 1104, 784, 740 cm\(^{-1}\). Enantiomeric purity (87% ee) was measured by chiral HPLC on ODH column (Hexane/iPrOH = 95:5, 0.7 mL/min, UV detection at 214 nm); retention time = 11.96 min (major), retention time = 13.36 min (minor).

\(\text{(R)}\)-5-(4-Cyanophenyl)-6,6,6-trifluoro-3,3-dimethylhexyl 1-methyl-1H-indole-2-carboxylate (5n). General Procedure B. The product (44.6 mg, 53% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 8:1) as a colorless oil. \([\alpha]_D^{20} = -33.34\) (c = 0.76, CHCl\(_3\)) for a sample with 90% ee. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.67 (t, \(J = 8.6\) Hz, 3 H), 7.48 (d, \(J = 8.0\) Hz, 2 H), 7.42 – 7.33 (m, 2 H), 7.22 (s, 1 H), 7.16 (t, \(J = 7.2\) Hz, 1 H), 4.32 (dt, \(J = 11.2, 7.2\) Hz, 1 H), 4.23 (dt, \(J = 11.2, 7.3\) Hz, 1 H), 4.07 (s, 3 H), 3.54 – 3.40 (m, 1 H), 2.13 – 1.97 (m, 2 H), 1.74 – 1.59 (m, 2 H), 0.91 (s, 3 H), 0.84 (s, 3 H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 162.1, 141.9 (q, C-F, \(^3\)J\(_{C-F}\) = 2.3 Hz),
139.7, 132.5, 130.2, 127.6, 126.5 (q, C-F, $1J_{C,F} = 280.0$ Hz), 125.8, 125.1, 122.6, 120.6, 118.2, 112.4, 110.3, 110.2, 61.0, 46.7 (q, C-F, $2J_{C,F} = 26.8$ Hz), 40.7 (q, C-F, $3J_{C,F} = 1.8$ Hz), 40.3, 32.9, 31.6, 27.5, 27.2. $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -69.91 (d, $J = 9.5$ Hz, 3 F). MS (ESI): m/z (%) 465 (100) [M+Na]$^+$. HRMS (ESI) m/z: [M+Na]$^+$ Calcd. for C$_{25}$H$_{30}$O$_2$F$_3$Na: 465.1760; Found: 465.1768.

IR (thin film) $\nu$ max 2961, 2874, 2231, 1709, 1518, 1470, 1404, 1252, 1166, 1107, 749 cm$^{-1}$. Enantiomeric purity (90% ee) was measured by chiral HPLC on OJH column (Hexane/iPrOH = 7:3, 0.7 mL/min, UV detection at 214 nm); retention time = 52.13 min (major), retention time = 72.32 min (minor).

Ethyl (R)-(1,1,1-trifluoro-3-(1-methyl-4-phenylcyclohexyl)propan-2-yl)benzoate (5o). General Procedure B. FeBr$_2$ (0.25 equiv) instead of FeCl$_3$ (0.25 equiv) was used. The product (43.7 mg, 52% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 50:1) as a mixture of cis and trans isomer (colorless oil).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.09 – 7.98 (m, 4 H), 7.45 (t, $J = 8.4$ Hz, 4 H), 7.32 – 7.24 (m, 4 H), 7.22 – 7.12 (m, 6 H), 4.43 – 4.32 (m, 4 H), 3.58 – 3.46 (m, 1 H), 3.45 – 3.32 (m, 1 H), 2.49 – 2.27 (m, 2 H), 2.22 – 2.09 (m, 2 H), 2.04 – 1.93 (m, 2 H), 1.78 – 1.49 (m, 8 H), 1.42 – 1.06 (m, 14 H), 0.87 (s, 3 H), 0.75 (s, 3 H). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 166.2, 166.1, 147.1, 147.0, 142.0, 141.7, 130.3, 130.2, 129.8, 129.4, 129.4, 128.3, 128.3, 127.0 (q, C-F, $1J_{C,F} = 279.8$ Hz), 126.9 (q, C-F, $1J_{C,F} = 279.8$ Hz), 126.7, 126.7, 126.0, 125.9, 61.0, 46.5 (q, C-F, $2J_{C,F} = 26.4$ Hz), 46.0 (q, C-F, $2J_{C,F} = 26.4$ Hz), 44.3, 44.2, 43.9, 38.2, 38.1, 38.1, 38.0, 34.5, 32.9, 32.5, 29.8, 29.5, 29.4, 29.2, 29.1, 21.6, 14.3, 14.3.

$^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -69.89 (d, $J = 10.2$ Hz), -70.00 (d, $J = 9.5$ Hz). MS (FT): m/z (%) 436 (100) [M+NH$_4$]$^+$. HRMS (DART) m/z: [M+H]$^+$ Calcd. for C$_{25}$H$_{30}$O$_2$F$_3$: 419.2192; Found: 419.2193. IR (thin film) $\nu$ max 3027, 2926, 2850, 1720, 1614, 1493, 1452, 1368, 1279, 1157, 1106, 712, 700 cm$^{-1}$. Enantiomeric purity (one isomer 90% ee, the other isomer 89% ee) was measured by chiral HPLC on ODH column (Hexane/iPrOH = 98:2, 0.7 mL/min, UV detection at 214 nm); One isomer: retention time (isomer 1) = 8.50 min (major), retention time = 7.94 min (minor); The other isomer: retention time (isomer 2) = 9.41 min (major), retention time = 14.21 min (minor).
6. Transformations of compound 5b

6.1 Phthalimide deprotection

(R)-5-((1,1'-Biphenyl)-4-yl)-6,6,6-trifluoro-3,3-dimethylhexan-1-amine (6). To a suspension of 5b (465.5 mg, 1 mmol, 1 equiv) in 10 mL ethanol was added hydrazine monohydrate (0.25 mL, 4 mmol, 4 equiv) at room temperature. The mixture was heated under reflux and monitored by TLC. After completion, the reaction was cooled to room temperature, and the resulting precipitates were filtered off and washed with ethanol. The filtrate was concentrated and dried under vacuum to give compound 6 as a yellow solid (328.1 mg, 98% yield, m.p. 113.0-115.0 °C) without further purification.

**1H NMR** (400 MHz, CDCl₃) δ 7.66 – 7.49 (m, 4 H), 7.47 – 7.27 (m, 5 H), 3.37 (p, J = 9.8, 2.6 H, 1 H), 2.60 (td, J = 11.5, 5.5 Hz, 1 H), 2.50 (td, J = 11.5, 5.0 Hz, 1 H), 2.05 – 1.87 (m, 2 H), 1.40 – 1.18 (m, 2 H), 1.04 (br, 2 H), 0.79 (s, 6 H).

**13C NMR** (101 MHz, CDCl₃) δ 140.9, 140.3, 135.6 (q, C-F, J_C-F = 2.3 Hz), 129.7, 128.8, 127.4, 127.2, 127.2 (q, C-F, J_C-F = 279.9 Hz), 127.0, 46.2 (q, C-F, J_C-F = 26.1 Hz), 45.7, 40.2, 37.4, 32.9, 27.7, 27.5. **19F NMR** (376 MHz, CDCl₃) δ -70.12 (d, J = 9.9 Hz, 3 F). MS (ESI): m/z (%) 336 (100) [M+H]^+. HRMS (ESI) m/z: [M+H]^+ Calcd. for C₂₀H₂₅NF₃: 336.1934; Found: 336.1937. IR (thin film) v_max 3363, 2958, 2872, 1653, 1489, 1393, 1255, 1152, 1104 cm⁻¹.

6.2 Synthesis of compound 7a

(R)-4-(6-Azido-1,1,1-trifluoro-4,4-dimethylhexan-2-yl)-1,1'-biphenyl (7a). Compound 6 (33.5 mg, 0.1 mmol, 1.0 equiv), FSO₂N₃ (0.17 M in DMF/MTBE 1:1, 0.6 mL, 0.1 mmol, 1.0 equiv), and aqueous KHCO₃ (3 M in H₂O, 0.14 mL, 0.4 mmol, 4.0 equiv) were added to a 15 mL vial. The mixture was stirred at room temperature for 10 min, then 30 mL of EtOAc was added and the mixture was washed sequentially with brine (60 mL x 6), water (60 mL x 2) and brine (60 mL), dried over Na₂SO₄ and concentrated. The product 7a (28.2 mg, 78% yield) was purified with silica gel chromatography.
(Petroleum ether/EtOAc = 100:1) as a colorless oil. 1H NMR (400 MHz, CDCl₃) δ 7.65 – 7.50 (m, 4 H), 7.48 – 7.30 (m, 5 H), 3.36 (pd, J = 9.9, 3.2 Hz, 1 H), 3.17 (ddd, J = 12.1, 9.3, 6.8 Hz, 1 H), 3.08 (ddd, J = 12.1, 9.2, 6.8 Hz, 1 H), 2.04 – 1.91 (m, 2 H), 1.46 (ddd, J = 9.4, 6.6, 2.7 Hz, 2 H), 0.86 (s, 3 H), 0.84 (s, 3 H). 13C NMR (101 MHz, CDCl₃) δ 141.1, 140.4, 135.3 (q, J_C-F = 2.3 Hz), 129.6, 128.8, 127.5, 127.4, 127.1 (q, J_C-F = 280.0 Hz), 127.1, 47.3, 46.2 (q, J_C-F = 26.6 Hz), 40.4 (q, J_C-F = 1.8 Hz), 40.0, 32.8, 27.4, 27.3. 19F NMR (376 MHz, CDCl₃) δ -70.23 (d, J_F = 9.5 Hz, 3 F). MS (ESI): m/z (%) 379 (4) [M+NH₄]⁺, 334 (100) [M-N₃+NH₃]⁺. HRMS (ESI) m/z: [M+NH₄]⁺ Calcd. for C₂₀H₂₆N₄F₃: 379.2104; Found: 379.2101.

6.3 Synthesis of compound 7b

tert-Butyl (R)-4-((5-((1,1'-biphenyl)-4-yl)-6,6,6-trifluoro-3,3-dimethylhexyl)amino)-2-oxoethyl)piperidine-1-carboxylate (7b). To a mixture of 2-((1-(tert-butoxycarbonyl)piperidin-4-yl)acetic acid (0.12 mmol, 1.2 equiv) and 4-(dimethylamino)pyridine (0.2 mmol, 2 equiv) in 0.5 mL anhydrous CH₂Cl₂ were added N-(3-dimethylaminopropyl)-N'-ethyldiisocyanamide hydrochloride (EDCI-HCl) (0.12 mmol, 1.2 equiv) and the amine 6 (0.1 mmol, 1 equiv) at room temperature. The mixture was stirred at room temperature for 20 h. The resulting solution was diluted with ethyl acetate and washed with water and brine. The organic layer was dried over anhydrous Na₂SO₄, filtered, and concentrated. The product 7b (39.4 mg, 71% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 3:2) as a colorless oil. 1H NMR (400 MHz, CDCl₃) δ 7.57 – 7.47 (m, 4 H), 7.40 – 7.31 (m, 4 H), 7.28 (t, J = 7.3 Hz, 1 H), 5.00 (s, 1 H), 3.96 (d, J = 13.5 Hz, 2 H), 3.32 (p, J = 9.6 Hz, 1 H), 3.32 – 3.19 (m, 1 H), 3.03 – 2.87 (m, 1 H), 2.66 – 2.50 (m, 2 H), 2.02 – 1.99 (m, 1 H), 1.98 – 1.76 (m, 4 H), 1.59 – 1.46 (m, 2 H), 1.38 (s, 9 H), 1.35 – 1.26 (m, 1 H), 1.24 – 1.09 (m, 1 H), 1.03 – 0.87 (m, 2 H), 0.79 (s, 3 H), 0.77 (s, 3 H). 13C NMR (101 MHz, CDCl₃) δ 171.3, 154.8, 140.9, 140.1, 135.5, 129.8, 128.8, 127.6, 127.2, 127.1 (q, J_C-F, J_C-F = 280.0 Hz), 126.9, 79.3, 46.2 (q, J_C-F,
$J_{C,F} = 26.8$ Hz), 43.6, 41.2, 39.8, 35.4, 33.3, 32.9, 31.8, 28.4, 27.5, 27.4. 19F NMR (376 MHz, CDCl₃) δ -70.18 (d, $J = 10.2$ Hz, 3 F). MS (FT): m/z (%) 505 (100) [M-C₄H₈+H]^+, 561 (17) [M+H]^+, 583 (48) [M+Na]^+. HRMS (ESI) m/z: [M+Na]^+ Calcd. for C₃₂H₄₃N₂F₃Na: 583.3118; Found: 583.3117. IR (thin film) $ν_{max}$ 3316, 2934, 2870, 1690, 1548, 1472, 1366, 1163, 1105 cm⁻¹.

6.4 Synthesis of compound 7c

(R)-N-(5-[[1,1'-Biphenyl]-4-yl]-6,6,6-trifluoro-3,3-dimethylhexyl)pyrimidin-2-amine (7c). A mixture of 6 (0.19 mmol, 1.9 equiv) and 2-chloropyrimidine (0.1 mmol, 1 equiv) in 1.0 mL anhydrous EtOH was heated under reflux for 18 h. After cooling to room temperature, the reaction mixture was concentrated under reduced pressure. The resulting residue was purified with silica gel chromatography (Petroleum ether/EtOAc = 3:1) to afford 7c (27.8 mg, 67% yield) as a colorless oil.

1H NMR (400 MHz, CDCl₃) δ 8.24 (d, $J = 4.9$ Hz, 2 H), 7.62 – 7.49 (m, 4 H), 7.47 – 7.30 (m, 5 H), 6.48 (t, $J = 4.8$ Hz, 1 H), 5.07 – 4.92 (m, 1 H), 3.51 (pd, $J = 9.6, 3.2$ Hz, 1 H), 3.45 – 3.34 (m, 1 H), 3.29 – 3.14 (m, 1 H), 2.09 – 1.97 (m, 2 H), 1.55 (ddd, $J = 13.4, 11.3, 5.3$ Hz, 1 H), 1.40 (ddd, $J = 13.3, 11.3, 5.1$ Hz, 1 H), 0.87 (s, 3 H), 0.86 (s, 3 H). 13C NMR (126 MHz, CDCl₃) δ 162.1, 157.9, 140.9, 140.3, 135.5, 129.7, 128.7, 127.4, 127.3, 127.2 (q, C-F, $J_{C,F} = 279.9$ Hz), 127.1, 110.4, 46.1 (q, C-F, $J_{C,F} = 26.6$ Hz), 41.2, 40.1, 37.3, 32.9, 27.7, 27.6. 19F NMR (376 MHz, CDCl₃) δ -70.14 (d, $J = 10.2$ Hz, 3 F). MS (FT): m/z (%) 414 (100) [M+H]^+. HRMS (ESI) m/z: [M+H]^+ Calcd. for C₂₄H₂₇N₃F₃: 414.2152; Found: 414.2153.
III. Supplementary Discussion

7. Mechanistic studies

7.1 Radical inhibition experiments

To a 25 mL of Schlenk tube were added Zn dust (39.2 mg, 0.6 mmol, 1.5 equiv), 1,4-dinitrobenzene (67.2 mg, 0.4 mmol, 1.0 equiv) or TEMPO (62.5 mg, 0.4 mmol, 1.0 equiv), L6 (10.0 mg, 0.04 mmol, 10 mol%). The tube was then transferred to a glovebox, and NiBr₂·DME (12.4 mg, 0.04 mmol, 10 mol%) was added. The tube was then taken out of the glovebox and purge with Ar for three times, evacuated and backfilled with Ar (3 times). tert-Butyl iodide 2a (110.4 mg, 0.6 mmol, 1.5 equiv), ethyl 4-iodobenzoate 3a (110.4 mg, 0.4 mmol, 1.0 equiv), anhydrous DME and TFP solution (0.54 mL, 1.2 M in DMA, 1.6 equiv) were added under Ar. The Schlenk tube was screw capped and stirred (800 rpm) for 12 h at room temperature. The yield was determined by ¹⁹F NMR using benzotrifluoride as an internal standard.

7.2 Radical clock experiment

To a 25 mL of Schlenk tube were added Zn dust (39.2 mg, 0.6 mmol, 1.5 equiv), L6 (10.0 mg, 0.04 mmol, 10 mol%). The tube was then transferred to a glovebox, NiBr₂·DME (12.4 mg, 0.04 mmol, 10 mol%) was added. The tube was then taken out of the glovebox, evacuated and backfilled with Ar (3 times). tert-Butyl iodide 2a (110.4 mg, 0.6 mmol, 1.5 equiv), ethyl 4-iodobenzoate 3a (110.4 mg, 0.4 mmol, 1.0 equiv), 10 (92.2 mg, 0.64 mmol, 1.6 equiv), anhydrous DME and TFP solution (0.54 mL, 1.2 M in DMA, 1.6 equiv) were added under Ar. The tube was sealed with a Teflon cap. After the reaction mixture was stirred at 800 rpm for 12 h at room temperature, 24 μL benzotrifluoride was
added. The yields of 4a was determined by $^{19}$F NMR using benzotri fluoride as an internal standard. The reaction mixture was filtered through a pad of Celite. The filtrate was extracted with EtOAc and washed with brine. The organic layer was dried over Na$_2$SO$_4$, filtered and concentrated. The residue was purified with silica gel chromatography to give the corresponding products as a mixture. The mixture was further purified with reverse-phase HPLC to give the corresponding products 4a, 11a and 11b.

**Ethyl (E)-4-(6,6-dimethyl-4-phenylhept-3-en-1-yl)benzoate (11a).**

Colorless oil (13.1 mg, 9% yield). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.97 (d, $J = 8.2$ Hz, 2 H), 7.31 – 7.23 (m, 6 H), 7.23 – 7.16 (m, 1 H), 5.63 (t, $J = 7.2$ Hz, 1 H), 4.37 (q, $J = 7.1$ Hz, 2 H), 2.79 (t, $J = 7.8$ Hz, 2 H), 2.51 (q, $J = 7.7$ Hz, 2 H), 2.42 (s, 2 H), 1.39 (t, $J = 7.1$ Hz, 3 H), 0.74 (s, 9 H). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 166.7, 147.4, 145.9, 140.0, 130.8, 129.7, 128.5, 128.2, 128.0, 126.7, 126.3, 60.8, 42.7, 36.0, 33.0, 31.2, 30.3, 14.4. MS (FI): m/z (%) 350 (17) [M]$^+$. HRMS (FI) m/z: [M]$^+$ Calcd. for C$_{24}$H$_{30}$O$_2$: 350.2240; Found: 350.2247. IR (thin film) $\nu$ max 2954, 2927, 2866, 1720, 1611, 1465, 1365, 1275, 1106 cm$^{-1}$.

**Supplementary Figure 3. NOE spectrum of compound 11a**
Ethyl (E)-4-(8,8-dimethyl-4-phenyl-6-(trifluoromethyl)non-3-en-1-yl)benzoate (11b). Colorless oil (13.5 mg, 7% yield). \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 8.00 – 7.97 (m, 2 H), 7.35 – 7.23 (m, 8 H), 5.69 (t, \(J = 7.3\) Hz, 1 H), 4.37 (q, \(J = 7.1\) Hz, 2 H), 2.86 – 2.76 (m, 3 H), 2.62 – 2.47 (m, 3 H), 2.06 – 1.96 (m, 1 H), 1.59 (dd, \(J = 14.7, 4.2\) Hz, 1 H), 1.39 (t, \(J = 7.1\) Hz, 3 H), 1.12 (dd, \(J = 14.9, 4.3\) Hz, 1 H), 0.74 (s, 9 H). \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 166.7, 147.1, 141.8, 137.7, 130.1, 129.7, 128.6 (q, C-F, \(^1\)J\(_{C-F}\) = 280.2 Hz), 128.5, 128.3, 128.3, 127.1, 126.8, 60.8, 42.1, 37.5 (q, C-F, \(^2\)J\(_{C-F}\) = 24.3 Hz), 35.9, 31.3 (q, C-F, \(^3\)J\(_{C-F}\) = 3.1 Hz), 30.5, 30.3, 29.4, 14.3. \(^{19}\)F NMR (376 MHz, CDCl\(_3\)) \(\delta\) –69.79 (d, \(J = 8.9\) Hz). MS (FI): m/z (%) 446 (8) [M]+. HRMS (FI) m/z: [M]+ Calcd. for C\(_{27}\)H\(_{33}\)O\(_2\)F\(_3\): 446.2439; Found: 446.2432. IR (thin film) \(\nu_{\text{max}}\) 2959, 2868, 1719, 1611, 1466, 1368, 1278, 1179, 1156, 1106 cm\(^{-1}\).

Supplementary Figure 4. NOE spectrum of compound 11b

7.3 EPR experiments

7.3.1 Reaction of 1 with 2a and 3a in the presence of PBN under standard reaction conditions
To a 25 mL of Schlenk tube were added Zn dust (39.2 mg, 0.6 mmol, 1.5 equiv), L6 (10.0 mg, 0.04 mmol, 10 mol%) in the air. The tube was then moved to a glovebox. NiBr2-DME (12.3 mg, 0.04 mmol, 10 mol%) and PBN (106.3 mg, 0.6 mmol, 1.5 equiv) were added to the tube in a glovebox. The tube was then taken out from the glovebox and purge with Ar for three times. tert-Butyl iodide 2a (110.4 mg, 0.6 mmol, 1.5 equiv), ethyl 4-iodobenzoate 3a (110.4 mg, 0.4 mmol, 1.0 equiv), anhydrous DME and TFP solution (0.54 mL, 1.2 M in DMA, 1.6 equiv) were added under Ar. The tube was sealed with a Teflon cap. After stirring at 800 rpm for 12 h at room temperature, the resulting mixture was analyzed by EPR. The EPR showed an e.p.r. spectrum of nitroxides.

Supplementary Figure 5. The EPR spectrum of a mixture of PBN, 1, 2a and 3a under standard reaction conditions.

7.3.2 Reaction of 1 with 2a and 3a in the presence of PBN without 2a.

To a 25 mL of Schlenk were added L6 (10.0 mg, 0.04 mmol, 10 mol%) in the air. The tube was then moved to a glovebox. NiBr2-DME (12.3 mg, 0.04 mmol, 10 mol%) and PBN (106.3 mg, 0.6 mmol, 1.5 equiv) were added to the tube in a glovebox. The tube was then taken out from the glovebox and purge with Ar for three times. Ethyl 4-iodobenzoate 3a (110.4 mg, 0.4 mmol, 1.0 equiv), anhydrous DME and TFP solution (0.54 mL, 1.2 M in DMA, 1.6 equiv) were added under Ar. The tube was sealed with a Teflon cap. After stirring at 800 rpm for 12 h at room temperature, the resulting mixture was analyzed by EPR. The EPR showed no e.p.r. signal of nitroxide.
Supplementary Figure 6. The EPR spectrum of a mixture of PBN, 1 and 3a under standard reaction conditions.

7.3.3 Reaction of 1 with 2a and 3a in the presence of PBN without Zn dust.

\[
\begin{align*}
&\text{CF}_3 &+ &\text{tBu-I} &+ &\text{EtO}_2\text{C} \quad \text{standard conditions}^* \\
&1 &\text{(1.5 equiv)} &2a &\text{(1.5 equiv)} &3a &\text{(1.0 equiv)} \\
&\text{PBN} &\text{(1.5 equiv)}
\end{align*}
\]

To a 25 mL of Schlenk were added L6 (10.0 mg, 0.04 mmol, 10 mol%) in the air. The tube was moved to a glovebox. NiBr$_2$-DME (12.3 mg, 0.04 mmol, 10 mol%) and PBN (106.3 mg, 0.6 mmol, 1.5 equiv) were added to the tube in a glovebox. The tube was then taken out from the glovebox and purge with Ar for three times. tert-Butyl iodide 2a (110.4 mg, 0.6 mmol, 1.5 equiv), ethyl 4-iodobenzoate 3a (110.4 mg, 0.4 mmol, 1.0 equiv), anhydrous DME and TFP solution (0.54 mL, 1.2 M in DMA, 1.6 equiv) were added under Ar. The tube was sealed with Teflon cap. After stirring at 800 rpm for 12 h at room temperature, the resulting mixture was analyzed by EPR. The EPR showed no e.p.r. signal of nitroxide.

Supplementary Figure 7. The EPR spectrum of a mixture of PBN, 1, 2a and 3a without Zn dust.
8. Crystal data and structure refinement for compounds 4i and 5b.

**Compound 4i:** (The crystal structure of compound 4i has been deposited at the Cambridge Crystallographic Data Centre (CCDC 2191969). The data is available free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html.)

**Supplementary Table 11. Crystal data and structure refinement for compound 4i.**

| Parameter                                      | Value                        |
|------------------------------------------------|------------------------------|
| Identification code                            | mj22213_0m                   |
| Empirical formula                              | C19 H28 B F3 O2              |
| Formula weight                                 | 356.22                       |
| Temperature                                    | 213.00 K                     |
| Wavelength                                     | 1.34139 Å                    |
| Crystal system                                 | Orthorhombic                 |
| Space group                                    | P2₁2₁2₁                      |
| Unit cell dimensions                           | a = 12.1099(2) Å, α= 90°.    |
|                                               | b = 12.4495(2) Å, β= 90°.    |
|                                               | c = 26.6762(5) Å, γ = 90°.   |
| Volume                                         | 4021.76(12) Å³               |
| Z                                              | 8                            |
| Density (calculated)                           | 1.177 Mg/m³                  |
| Absorption coefficient                         | 0.491 mm⁻¹                   |
| F(000)                                         | 1520                         |
| Crystal size                                   | 0.07 x 0.07 x 0.05 mm³       |
| Theta range for data collection                | 3.408 to 54.944°             |
| Index ranges                                   | -14<=h<=14, -15<=k<=11, -32<=l<=32 |
| Reflections collected                          | 31897                        |
| Independent reflections                        | 7590 [R(int) = 0.0449]        |
| Completeness to theta = 53.594°                | 99.4 %                       |
| Absorption correction                          | Semi-empirical from equivalents |
| Max. and min. transmission                     | 0.7508 and 0.6026            |
| Refinement method                              | Full-matrix least-squares on F² |
| Data / restraints / parameters                  | 7590 / 0 / 465               |
| Goodness-of-fit on F²                           | 1.034                        |
| Final R indices [I>2sigma(I)]                  | R1 = 0.0753, wR2 = 0.2116    |
|                                               | R1 = 0.0961, wR2 = 0.2347    |
| Absolute structure parameter                   | 0.22(7)                      |
| Extinction coefficient                         | n/a                          |
| Largest diff. peak and hole                    | 0.696 and -0.323 e.Å⁻³       |
Compound 5b: (The crystal structure of compound 5b has been deposited at the Cambridge Crystallographic Data Centre (CCDC 2191970). The data is available free of charge at [www.ccdc.cam.ac.uk/conts/retrieving.html](http://www.ccdc.cam.ac.uk/conts/retrieving.html).

**Supplementary Table 12. Crystal data and structure refinement for compound 5b**

| Identification code | mj22251_0m          |
|---------------------|---------------------|
| Empirical formula   | C28 H26 F3 N O2     |
| Formula weight      | 465.50              |
| Temperature         | 213.00 K            |
| Wavelength          | 1.34139 Å           |
| Crystal system      | Monoclinic          |
| Space group         | P 1 2 1 1           |
| Unit cell dimensions| a = 7.88550(10) Å, α = 90°. |
|                     | b = 5.67580(10) Å, β = 95.6380(10)°. |
|                     | c = 26.4362(4) Å, γ = 90°. |
| Volume              | 1177.47(3) Å³      |
| Z                   | 2                   |
| Density (calculated)| 1.313 Mg/m³         |
| Absorption coefficient | 0.520 mm⁻¹      |
| F(000)              | 488                 |
| Crystal size        | 0.07 x 0.07 x 0.05 mm³ |
| Theta range for data collection| 4.386 to 54.900°. |
| Index ranges        | -9≤h≤8, -6≤k≤6, -32≤l≤32 |
| Reflections collected| 16216            |
| Independent reflections| 4419 [R(int) = 0.0308] |
| Completeness to theta = 53.594° | 99.6 %       |
| Absorption correction| Semi-empirical from equivalents |
| Max. and min. transmission| 0.7508 and 0.6305 |
| Refinement method   | Full-matrix least-squares on F² |
| Data / restraints / parameters | 4419 / 2 / 309 |
| Goodness-of-fit on F² | 1.062            |
| Final R indices [I>2sigma(I)] | R1 = 0.0354, wR2 = 0.1182 |
| R indices (all data) | R1 = 0.0385, wR2 = 0.1242 |
| Absolute structure parameter| 0.09(5)       |
| Extinction coefficient| n/a                |
| Largest diff. peak and hole | 0.115 and -0.182 e.Å⁻³ |
IV. Supplementary Figures

9. Copies of $^1$H, $^{13}$C, $^{19}$F NMR and HPLC Spectra

Supplementary Figure 8. $^1$H NMR spectrum of compound 2e

Supplementary Figure 9. $^{13}$C NMR spectrum of compound 2e
Supplementary Figure 10. $^1$H NMR spectrum of compound 2f

Supplementary Figure 11. $^{13}$C NMR spectrum of compound 2f
Supplementary Figure 12. $^1$H NMR spectrum of compound 2g

Supplementary Figure 13. $^{13}$C NMR spectrum of compound 2g
Supplementary Figure 14. \(^1\)H NMR spectrum of compound 2h

Supplementary Figure 15. \(^{13}\)C NMR spectrum of compound 2h
Supplementary Figure 16. $^1$H NMR spectrum of compound 2i

Supplementary Figure 17. $^{13}$C NMR spectrum of compound 2i
Supplementary Figure 18. \(^1\)H NMR spectrum of compound 2j

Supplementary Figure 19. \(^{13}\)C NMR spectrum of compound 2j
Supplementary Figure 20. $^1$H NMR spectrum of compound 2k

Supplementary Figure 21. $^{13}$C NMR spectrum of compound 2k
Supplementary Figure 22. $^1$H NMR spectrum of compound 3q

Supplementary Figure 23. $^{13}$C NMR spectrum of compound 3q
Supplementary Figure 24. $^1$H NMR spectrum of compound 4a

Supplementary Figure 25. $^{13}$C NMR spectrum of compound 4a
Supplementary Figure 26. $^{19}$F NMR spectrum of compound 4a
Supplementary Figure 27. Chiral HPLC analysis of compound 4a
Supplementary Figure 28. Chiral HPLC analysis of compound 4a using ethyl 4-bromobenzoate instead of ethyl 4-iodobenzoate.
Supplementary Figure 29. \(^{1}H\) NMR spectrum of compound 4b

Supplementary Figure 30. \(^{13}C\) NMR spectrum of compound 4b
Supplementary Figure 31. $^{19}\text{F}$ NMR spectrum of compound 4b
Supplementary Figure 32. Chiral HPLC analysis of compound 4b
Supplementary Figure 33. $^1$H NMR spectrum of compound 4c

Supplementary Figure 34. $^{13}$C NMR spectrum of compound 4c
Supplementary Figure 35. $^{19}$F NMR spectrum of compound 4c
Supplementary Figure 36. $^1$H NMR spectrum of compound 4d

Supplementary Figure 37. $^{13}$C NMR spectrum of compound 4d
Supplementary Figure 38. $^1$H NMR spectrum of compound 4d
Supplementary Figure 39. Chiral HPLC analysis of compound 4d
Supplementary Figure 40. $^1$H NMR spectrum of compound 4e

Supplementary Figure 41. $^{13}$C NMR spectrum of compound 4e
Supplementary Figure 42. $^{19}$F NMR spectrum of compound 4e
### Supplementary Figure 43. Chiral HPLC analysis of compound 4e

#### Table 1: Chiral HPLC analysis results for compound 4e

| No. | Ret.Time (min) | Peak Name | Height (mAU) | Area (mAU*min) | Rel.Area (%) | Amount | Type |
|-----|---------------|-----------|--------------|---------------|--------------|--------|------|
| 1   | 4.46          | n.a.      | 1282.809     | 128.108       | 49.73        | n.a.   | BM*  |
| 2   | 4.76          | n.a.      | 1132.410     | 129.502       | 50.27        | n.a.   | MB*  |
| **Total:** |                |            | **2415.219** | **257.610**  | **100.00**   | **0.000** |      |

### Table 2: Additional Chiral HPLC analysis results for compound 4e

| No. | Ret.Time (min) | Peak Name | Height (mAU) | Area (mAU*min) | Rel.Area (%) | Amount | Type |
|-----|---------------|-----------|--------------|---------------|--------------|--------|------|
| 1   | 4.45          | n.a.      | 95.842       | 9.605         | 5.16         | n.a.   | BMb* |
| 2   | 4.72          | n.a.      | 1376.813     | 176.652       | 94.84        | n.a.   | bMB* |
| **Total:** |                |            | **1472.655** | **186.257**   | **100.00**   | **0.000** |      |
Supplementary Figure 44. $^1$H NMR spectrum of compound 4f

Supplementary Figure 45. $^{13}$C NMR spectrum of compound 4f
Supplementary Figure 46. $^{19}$F NMR spectrum of compound 4f
**Supplementary Figure 47. Chiral HPLC analysis of compound 4e**

| No. | Ret.Time (min) | Peak Name | Height (mAU) | Area (mAU*min) | Rel.Area (%) | Amount | Type |
|-----|---------------|-----------|--------------|----------------|--------------|--------|------|
| 1   | 6.41          | n.a.      | 155.631      | 26.167         | 49.32        | n.a.   | BM*  |
| 2   | 6.80          | n.a.      | 143.989      | 26.889         | 50.68        | n.a.   | MB*  |
| **Total:** |            |           | 299.620      | 53.056         |              | 100.00 | 0.000|

| No. | Ret.Time (min) | Peak Name | Height (mAU) | Area (mAU*min) | Rel.Area (%) | Amount | Type |
|-----|---------------|-----------|--------------|----------------|--------------|--------|------|
| 1   | 6.35          | n.a.      | 12.869       | 2.009          | 4.89         | n.a.   | BM*  |
| 2   | 6.72          | n.a.      | 222.571      | 39.073         | 95.11        | n.a.   | MB*  |
| **Total:** |            |           | 235.440      | 41.082         |              | 100.00 | 0.000|
Supplementary Figure 48. $^1$H NMR spectrum of compound 4g

Supplementary Figure 49. $^{13}$C NMR spectrum of compound 4g
Supplementary Figure 50. $^{19}$F NMR spectrum of compound 4g

Supplementary Figure 51. $^1$H NMR spectrum of compound 4g'
Supplementary Figure 52. $^{13}$C NMR spectrum of compound 4g'

Supplementary Figure 53. $^{19}$F NMR spectrum of compound 4g'
Supplementary Figure 54. Chiral HPLC analysis of compound 4g'
Supplementary Figure 55. $^1$H NMR spectrum of compound 4h

Supplementary Figure 56. $^{13}$C NMR spectrum of compound 4h
Supplementary Figure 57. $^{19}$F NMR spectrum of compound 4h

Supplementary Figure 58. $^1$H NMR spectrum of compound 4h'
Supplementary Figure 59. $^{13}$C NMR spectrum of compound 4h'

Supplementary Figure 60. $^{19}$F NMR spectrum of compound 4h'
Supplementary Figure 61. Chiral HPLC analysis of compound 4h'
Supplementary Figure 62. $^1$H NMR spectrum of compound 4i

Supplementary Figure 63. $^{13}$C NMR spectrum of compound 4i
Supplementary Figure 64. $^{19}$F NMR spectrum of compound 4i
Supplementary Figure 65. Chiral HPLC analysis of compound 4i
Supplementary Figure 66. $^1$H NMR spectrum of compound 4j

Supplementary Figure 67. $^{13}$C NMR spectrum of compound 4j
Supplementary Figure 68. $^{19}$F NMR spectrum of compound 4j
Supplementary Figure 69. Chiral HPLC analysis of compound 4j
Supplementary Figure 70. $^1$H NMR spectrum of compound 4k

Supplementary Figure 71. $^{13}$C NMR spectrum of compound 4k
Supplementary Figure 72. $^{19}$F NMR spectrum of compound 4k
Supplementary Figure 73. Chiral HPLC analysis of compound 4k
Supplementary Figure 74. $^1$H NMR spectrum of compound 4l

Supplementary Figure 75. $^{19}$F NMR spectrum of compound 4l
Supplementary Figure 76. $^{19}$F NMR spectrum of compound 4l
Supplementary Figure 77. Chiral HPLC analysis of compound 4l
Supplementary Figure 78. $^1$H NMR spectrum of compound 4m

Supplementary Figure 79. $^{13}$C NMR spectrum of compound 4m
Supplementary Figure 80. $^{19}$F NMR spectrum of compound 4m
Supplementary Figure 81. Chiral HPLC analysis of compound 4m
Supplementary Figure 82. $^1$H NMR spectrum of compound 4n

Supplementary Figure 83. $^{13}$C NMR spectrum of compound 4n
Supplementary Figure 84. $^{19}\text{F}$ NMR spectrum of compound 4n
Supplementary Figure 85. Chiral HPLC analysis of compound 4n
Supplementary Figure 86. $^1$H NMR spectrum of compound 4o

Supplementary Figure 87. $^{13}$C NMR spectrum of compound 4o
Supplementary Figure 88. $^{19}$F NMR spectrum of compound 4o
### Supplementary Figure 89. Chiral HPLC analysis of compound 4o

| No. | Ret.Time (min) | Peak Name | Height (mAU) | Area (mAU*min) | Rel.Area (%) | Amount | Type |
|-----|----------------|-----------|--------------|----------------|--------------|--------|------|
| 1   | 4.85           | n.a.      | 1548.056     | 252.800        | 49.01        | n.a.   | BM*  |
| 2   | 5.22           | n.a.      | 1115.188     | 263.054        | 50.99        | n.a.   | MB*  |
| **Total:** |               |           | 2663.243     | 515.854        | 100.00       | 0.000  |      |

| No. | Ret.Time (min) | Peak Name | Height (mAU) | Area (mAU*min) | Rel.Area (%) | Amount | Type |
|-----|----------------|-----------|--------------|----------------|--------------|--------|------|
| 1   | 4.86           | n.a.      | 51.999       | 5.010          | 4.70         | n.a.   | M*   |
| 2   | 5.24           | n.a.      | 711.538      | 162.457        | 95.30        | n.a.   | MB*  |
| **Total:** |               |           | 763.537      | 170.467        | 100.00       | 0.000  |      |
Supplementary Figure 90. $^1$H NMR spectrum of compound 4p

Supplementary Figure 91. $^{13}$C NMR spectrum of compound 4p
Supplementary Figure 92. $^{19}$F NMR spectrum of compound 4p
Supplementary Figure 93. Chiral HPLC analysis of compound 4p
Supplementary Figure 94. $^1$H NMR spectrum of compound 4q

Supplementary Figure 95. $^{13}$C NMR spectrum of compound 4q
Supplementary Figure 96. $^{19}$F NMR spectrum of compound 4q
Supplementary Figure 97. $^1$H NMR spectrum of compound 4q'

Supplementary Figure 98. $^{13}$C NMR spectrum of compound 4q'
Supplementary Figure 99. $^{19}$F NMR spectrum of compound 4q'
Supplementary Figure 100. Chiral HPLC analysis of compound 4q'
Supplementary Figure 101. $^1$H NMR spectrum of compound 4r

Supplementary Figure 102. $^{13}$C NMR spectrum of compound 4r
Supplementary Figure 103. $^{19}$F NMR spectrum of compound 4r
### Supplementary Figure 104. Chiral HPLC analysis of compound 4r

| No. | Ret.Time (min) | Peak Name | Height (mAU) | Area (mAU*min) | Rel.Area (%) | Amount | Type |
|-----|----------------|-----------|--------------|----------------|--------------|--------|------|
| 1   | 18.56          | n.a.      | 245.918      | 101.449        | 48.14        | n.a.   | BM   |
| 2   | 19.58          | n.a.      | 241.688      | 109.278        | 51.86        | n.a.   | MB   |
| Total|                |           |              |                |              | 487.606 | 210.727 | 100.00 | 0.000 |

| No. | Ret.Time (min) | Peak Name | Height (mAU) | Area (mAU*min) | Rel.Area (%) | Amount | Type |
|-----|----------------|-----------|--------------|----------------|--------------|--------|------|
| 1   | 18.64          | n.a.      | 12.883       | 5.017          | 4.92         | n.a.   | BM   |
| 2   | 19.59          | n.a.      | 217.623      | 97.026         | 95.08        | n.a.   | MB   |
| Total|                |           |              |                |              | 230.706 | 102.043 | 100.00 | 0.000 |
Supplementary Figure 105. $^1$H NMR spectrum of compound 4s

Supplementary Figure 106. $^{13}$C NMR spectrum of compound 4s
Supplementary Figure 107. $^{19}\text{F}$ NMR spectrum of compound 4s
Supplementary Figure 108. Chiral HPLC analysis of compound 4s
Supplementary Figure 109. $^1$H NMR spectrum of compound 5a

Supplementary Figure 110. $^{13}$C NMR spectrum of compound 5a
Supplementary Figure 111. $^{19}$F NMR spectrum of compound 5a
Supplementary Figure 112. Chiral HPLC analyses of compound 5a
Supplementary Figure 113. $^1$H NMR spectrum of compound 5b

Supplementary Figure 114. $^{13}$C NMR spectrum of compound 5b
Supplementary Figure 115. $^{19}$F NMR spectrum of compound 5b
Supplementary Figure 116. Chiral HPLC analysis of compound 5b
Supplementary Figure 117. $^1$H NMR spectrum of compound 5c

Supplementary Figure 118. $^{13}$C NMR spectrum of compound 5c
Supplementary Figure 119. $^{19}$F NMR spectrum of compound 5c
Supplementary Figure 120. Chiral HPLC analysis of compound 5c
Supplementary Figure 121. $^1$H NMR spectrum of compound 5d

Supplementary Figure 122. $^{13}$C NMR spectrum of compound 5d
Supplementary Figure 123. $^{19}F$ NMR spectrum of compound 5d
Supplementary Figure 124. Chiral HPLC analysis of compound 5d
Supplementary Figure 125. $^1$H NMR spectrum of compound 5e

Supplementary Figure 126. $^{13}$C NMR spectrum of compound 5e
Supplementary Figure 127. $^{19}$F NMR spectrum of compound 5e
Supplementary Figure 128. Chiral HPLC analysis of compound 5e
Supplementary Figure 129. $^1$H NMR spectrum of compound 5f

Supplementary Figure 130. $^{13}$C NMR spectrum of compound 5f
Supplementary Figure 131. $^{19}$F NMR spectrum of compound 5f
Supplementary Figure 132. Chiral HPLC analysis of compound 5f
Supplementary Figure 133. $^1$H NMR spectrum of compound 5g

Supplementary Figure 134. $^{13}$C NMR spectrum of compound 5g
Supplementary Figure 135. $^{19}$F NMR spectrum of compound 5g
Supplementary Figure 136. Chiral HPLC analysis of compound 5g
Supplementary Figure 137. $^1$H NMR spectrum of compound 5h

Supplementary Figure 138. $^{13}$C NMR spectrum of compound 5h
Supplementary Figure 139. $^{19}$F NMR spectrum of compound 5h
### Supplementary Figure 140. Chiral HPLC analysis of compound 5h

| No. | Ret.Time (min) | Peak Name | Height (mAU) | Area (mAU*min) | Rel.Area (%) | Amount | Type |
|-----|----------------|-----------|--------------|----------------|--------------|--------|------|
| 1   | 5.35           | n.a.      | 739.550      | 91.118         | 49.55        | n.a.   | BM   |
| 2   | 5.67           | n.a.      | 732.919      | 92.777         | 50.45        | n.a.   | MB   |
| **Total:** |                |           | **1472.468** | **183.885**    | **100.00**   |        |      |

| No. | Ret.Time (min) | Peak Name | Height (mAU) | Area (mAU*min) | Rel.Area (%) | Amount | Type |
|-----|----------------|-----------|--------------|----------------|--------------|--------|------|
| 1   | 5.35           | n.a.      | 34.159       | 3.707          | 6.16         | n.a.   | BMB  |
| 2   | 5.67           | n.a.      | 470.595      | 56.523         | 93.84        | n.a.   | BMB  |
| **Total:** |                |           | **504.755**  | **60.230**     | **100.00**   |        |      |
Supplementary Figure 141. $^1$H NMR spectrum of compound 5i

Supplementary Figure 142. $^{13}$C NMR spectrum of compound 5i
Supplementary Figure 143. $^{19}$F NMR spectrum of compound 5i
Supplementary Figure 144. Chiral HPLC analysis of compound 5i
Supplementary Figure 145. $^1$H NMR spectrum of compound 5j

Supplementary Figure 146. $^{13}$C NMR spectrum of compound 5j
Supplementary Figure 147. $^{19}$F NMR spectrum of compound 5j
Supplementary Figure 148. Chiral HPLC analysis of compound 5j
Supplementary Figure 149. $^1$H NMR spectrum of compound 5k

Supplementary Figure 150. $^{13}$C NMR spectrum of compound 5k
Supplementary Figure 151. $^{19}$F NMR spectrum of compound 5k
Supplementary Figure 152. Chiral HPLC analysis of compound 5k
Supplementary Figure 153. $^1$H NMR spectrum of compound 5l

Supplementary Figure 154. $^{13}$C NMR spectrum of compound 5l
Supplementary Figure 155. $^{19}$F NMR spectrum of compound 51
Supplementary Figure 156. Chiral HPLC analysis of compound 51
Supplementary Figure 157. $^1$H NMR spectrum of compound 5m

Supplementary Figure 158. $^{13}$C NMR spectrum of compound 5m
Supplementary Figure 159. $^{19}$F NMR spectrum of compound 5m
Supplementary Figure 160. Chiral HPLC analysis of compound 5m
Supplementary Figure 161. $^1$H NMR spectrum of compound 5n

Supplementary Figure 162. $^{13}$C NMR spectrum of compound 5n
Supplementary Figure 163. $^{19}$F NMR spectrum of compound 5n
Supplementary Figure 164. Chiral HPLC analysis of compound 5n
Supplementary Figure 165. $^1$H NMR spectrum of compound 5o

Supplementary Figure 166. $^{13}$C NMR spectrum of compound 5o
Supplementary Figure 167. $^{19}$F NMR spectrum of compound 50
### Table 1

| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|-----|--------------|-----------|------------|--------------|------------|--------|------|
| 1   | 7.76         | n.a.      | 114.939    | 27.627       | 26.43      | n.a.   | BM   * |
| 2   | 8.33         | n.a.      | 105.911    | 28.443       | 27.21      | n.a.   | M    * |
| 3   | 9.25         | n.a.      | 81.760     | 24.090       | 23.04      | n.a.   | MB*  |
| 4   | 13.98        | n.a.      | 52.989     | 24.385       | 23.32      | n.a.   | BMB* |
|     | **Total:**    |           | **355.600**| **104.546**  |            | **0.000** |      |

### Table 2

| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|-----|--------------|-----------|------------|--------------|------------|--------|------|
| 1   | 7.95         | n.a.      | 39.534     | 8.197        | 5.08       | n.a.   | BM   * |
| 2   | 8.50         | n.a.      | 606.556    | 153.271      | 94.92      | n.a.   | MB*  |
|     | **Total:**    |           | **646.090**| **161.468**  |            | **100.00** | **0.000** |
Supplementary Figure 168. Chiral HPLC analysis of compound 5o
Supplementary Figure 169. $^1$H NMR spectrum of compound 6

Supplementary Figure 170. $^{13}$C NMR spectrum of compound 6
Supplementary Figure 171. $^{19}$F NMR spectrum of compound 6

Supplementary Figure 172. $^1$H NMR spectrum of compound 7a
Supplementary Figure 173. $^{13}$C NMR spectrum of compound 7a

Supplementary Figure 174. $^{19}$F NMR spectrum of compound 7a
Supplementary Figure 175. $^1$H NMR spectrum of compound 7b

Supplementary Figure 176. $^{13}$C NMR spectrum of compound 7b
Supplementary Figure 177. $^{19}$F NMR spectrum of compound 7b

Supplementary Figure 178. $^1$H NMR spectrum of compound 7c
Supplementary Figure 179. $^{13}$C NMR spectrum of compound 7c

Supplementary Figure 180. $^{19}$F NMR spectrum of compound 7c
Supplementary Figure 181. $^1$H NMR spectrum of compound 11a

Supplementary Figure 182. $^{13}$C NMR spectrum of compound 11b
Supplementary Figure 183. NOE spectrum of compound 11a

Supplementary Figure 184. $^1$H NMR spectrum of compound 11b
Supplementary Figure 185. $^{13}$C NMR spectrum of compound 11b

Supplementary Figure 186. $^{19}$F NMR spectrum of compound 11b
Supplementary Figure 187. NOE spectrum of compound 11b
V. Supplementary References

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