Supporting Information
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Supporting Information

Synthesis of cis-4,5-diarylazepanes

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S-1
A representative procedure of skeleton 4 from skeleton 3 is as follows:

**Table 1, entry 10:** Methanesulfonyl chloride (172 mg, 1.5 mmol) was added to a solution of skeleton 3 (0.5 mmol) in pyridine (6 mL) and 1,2-dichloroethane (6 mL) at rt. The reaction mixture was stirred at rt for 5 h. Dichloromethane (10 mL) was added to the reaction mixture and then hydrogen chloride solution (2N, 10 mL) was also added to the reaction mixture. The reaction mixture was extracted with dichloromethane (3 x 15 mL). The combined organic layers were washed with brine, dried, filtered and evaporated to afford crude product. Purification on silica gel (hexane/ethyl acetate = 4/1~2/1) afforded skeleton 4. For **compound 4b**: HRMS (ESI, M⁺+1) calcd for C_{25}H_{28}NO_5S_2 486.1409, found 486.1412; ¹H NMR (400 MHz): δ 7.68-7.65 (m, 2H), 7.58-7.44 (m, 1H), 7.30-7.16 (m, 10H), 7.07-7.04 (m, 2H), 5.35 (dd, J = 2.0, 6.4 Hz, 1H), 3.60 (ddd, J = 2.8, 6.4, 14.0 Hz, 1H), 3.50-3.38 (m, 2H), 3.30 (dt, J = 6.4, 9.6 Hz, 1H), 2.75 (ddd, J = 3.2, 9.2, 15.6 Hz, 1H), 2.62 (ddd, J = 2.8, 6.8, 15.6 Hz, 1H), 2.46-2.35 (m, 2H), 1.93 (s, 3H); ¹³C NMR (100 MHz): δ 144.66, 143.37, 138.73, 132.37, 129.05 (2x), 128.64 (2x), 128.35 (2x), 128.19 (2x), 127.45 (2x), 126.88, 126.86 (2x), 126.77, 86.50, 53.54, 42.80, 40.46, 36.65, 32.88, 32.45; Anal. Calcd for C_{25}H_{27}NO_5S_2: C, 61.83; H, 5.60; N, 2.88. Found: C, 62.11; H, 5.84; N, 3.01. For **compound 4c**: HRMS (ESI, M⁺+1) calcd for C_{26}H_{30}NO_5S_2 500.1565, found 500.1566; ¹H NMR (400 MHz): δ 7.54-7.52 (m, 2H), 7.31-7.17 (m, 10H), 7.07-7.04 (m, 2H), 5.34 (dd, J = 2.0, 6.4 Hz, 1H), 3.59 (ddd, J = 2.8, 6.4, 14.0 Hz, 1H), 3.50-3.25 (m, 3H), 2.76 (ddd, J = 3.2, 9.2, 15.6 Hz, 1H), 2.62 (ddd, J = 2.8, 6.8, 15.6 Hz, 1H), 2.50-2.34 (m, 2H), 2.43 (s, 3H), 1.93 (s, 3H); ¹³C NMR (100 MHz): δ 144.69, 143.53, 143.12, 135.79, 129.68 (2x), 128.64 (2x), 128.38 (2x), 128.29 (2x), 127.51 (2x), 126.97 (2x), 126.89, 126.80, 86.67, 53.64, 42.81, 40.49, 36.70, 33.02, 32.60, 21.46; Anal. Calcd for C_{26}H_{29}NO_5S_2: C, 62.50; H, 5.85; N, 2.80. Found: C, 62.82; H, 6.01; N, 3.11. For **compound 4f**: HRMS (ESI, M⁺+1) calcd for C_{20}H_{24}F_2NO_5S_2 460.1064, found 460.1067; ¹H NMR (400 MHz): δ 7.26-7.21 (m, 2H), 7.13-7.08 (m, 2H), 7.05-6.98 (m, 4H), 5.35 (dd, J = 3.2, 5.6 Hz, 1H), 3.64-3.55 (m, 2H), 3.54-3.40 (m, 1H), 3.33-3.27 (m, 1H), 2.87-2.80 (m, 1H), 2.69-2.62 (m, 1H), 2.59 (s, 3H), 2.58-2.51 (m, 2H), 2.15 (s, 3H); ¹³C NMR (100 MHz): δ 162.58, 160.12, 139.81, 139.38, 129.99, 129.92, 129.19, 129.12, 115.74, 115.53, 115.44, 115.23, 86.20, 52.76, 42.60, 40.40, 37.14, 36.98, 32.70, 33.32.

A representative procedure of skeleton 5 from skeleton 4 is as follows:

Boron trifluoride etherate (285 mg, 1.0 mmol) was added to a stirring solution of the skeleton 4 (0.5 mmol) in dichloromethane (10 mL) at rt. The reaction mixture was stirred at reflux temperature for 40 h. The total procedure was monitored by TLC until the reaction was completed. Saturated sodium bicarbonate solution (1 mL) was added to the reaction mixture and the solvent was concentrated under reduced pressure. The residue was extracted with ethyl acetate (3 x 20 mL). The combined organic layers were washed with brine, dried, filtered and evaporated to afford crude product under reduced pressure. Purification on silica gel (hexane/ethyl acetate = 8/1~4/1) afforded skeleton 5. For **compound 5a**: HRMS (ESI, M⁺+1) calcd for C_{19}H_{22}NO_2S 328.1371, found 328.1374; ¹H NMR (400 MHz): δ 7.13-7.04 (m, 6H), 6.95-6.92 (m, 4H), 3.56-3.53 (m, 4H), 2.95-2.92 (m, 4H), 2.85-2.82 (m, 4H), 2.69-2.62 (m, 4H), 2.59 (s, 3H), 2.58-2.51 (m, 2H), 2.15 (s, 3H); ¹³C NMR (100 MHz): δ 162.58, 160.12, 139.81, 139.38, 129.99, 129.92, 129.19.
2.85 (s, 3H); $^{13}$C NMR (100 MHz): $\delta$ 143.73 (2x), 139.66 (2x), 128.84 (4x), 127.83 (4x), 126.12 (2x), 46.87 (2x), 37.33 (2x), 36.61; Anal. Calcd for C$_{19}$H$_{21}$NO$_2$S: C, 69.69; H, 6.46; N, 4.28. Found: C, 69.93; H, 6.69; N, 4.48. For compound 5b: HRMS (ESI, M$^+$+1) calcd for C$_{24}$H$_{24}$NO$_2$S 390.1528, found 390.1532; $^1$H NMR (400 MHz): $\delta$ 7.83-7.80 (m, 2H), 7.63-7.53 (m, 3H), 7.09-7.00 (m, 6H), 6.89-6.86 (m, 4H), 3.43-3.41 (m, 4H), 2.91-2.88 (m, 4H); $^{13}$C NMR (100 MHz): $\delta$ 143.65 (2x), 139.60 (2x), 132.55, 129.12 (2x), 128.81 (4x), 128.08, 127.74 (4x), 127.20 (2x), 126.05 (2x), 47.19 (2x), 36.92 (2x); Anal. Calcd for C$_{24}$H$_{23}$NO$_2$S: C, 74.00; H, 5.95; N, 3.60. Found: C, 74.13; H, 5.79; N, 3.83. For compound 5c: HRMS (ESI, M$^+$+1) calcd for C$_{25}$H$_{26}$NO$_2$S 404.1684, found 404.1682; $^1$H NMR (400 MHz): $\delta$ 7.68 (d, $J$ = 8.0 Hz, 2H), 7.33 (d, $J$ = 8.0 Hz, 2H), 7.09-7.00 (m, 6H), 6.88-6.85 (m, 4H), 3.40-3.37 (m, 4H), 2.89-2.87 (m, 4H), 2.44 (s, 3H); $^{13}$C NMR (100 MHz): $\delta$ 143.71 (2x), 143.31, 139.66 (2x), 135.10, 129.74 (2x), 128.84 (4x), 127.74 (4x), 127.29 (2x), 126.05 (2x), 47.23 (2x), 36.92 (2x), 21.51; Anal. Calcd for C$_{25}$H$_{25}$NO$_2$S: C, 74.41; H, 6.24; N, 3.47. Found: C, 74.72; H, 6.48; N, 3.68. For compound 5d: HRMS (ESI, M$^+$+1) calcd for C$_{19}$H$_{20}$F$_2$NO$_2$S 364.1183, found 364.1182; $^1$H NMR (400 MHz): $\delta$ 6.91-6.86 (m, 4H), 6.83-6.78 (m, 4H), 3.54-3.51 (m, 4H), 2.90-2.87 (m, 4H), 2.85 (s, 3H); $^{13}$C NMR (100 MHz): $\delta$ 162.35, 159.91, 139.50, 139.46, 138.89 (2x), 130.44 (2x), 130.37 (2x), 115.01 (2x), 114.80 (2x), 46.62 (2x), 37.29 (2x), 36.79; Anal. Calcd for C$_{19}$H$_{19}$F$_2$NO$_2$S: C, 62.79; H, 5.27; N, 3.85. Found: C, 62.91; H, 5.49; N, 4.03. For compound 5e: HRMS (ESI, M$^+$+1) calcd for C$_{21}$H$_{26}$NO$_4$S 388.1583, found 388.1587; $^1$H NMR (400 MHz): $\delta$ 6.86 (d, $J$ = 8.8 Hz, 4H), 6.66 (d, $J$ = 8.8 Hz, 4H), 3.73 (s, 6H), 3.51-3.49 (m, 4H), 2.90-2.87 (m, 4H), 2.85 (s, 3H); $^{13}$C NMR (100 MHz): $\delta$ 157.65 (2x), 138.35 (2x), 136.22 (2x), 130.00 (4x), 113.24 (4x), 55.06 (2x), 46.82 (2x), 37.30 (2x), 36.46; Anal. Calcd for C$_{21}$H$_{25}$NO$_4$S: C, 65.09; H, 6.50; N, 3.61. Found: C, 64.88; H, 6.78; N, 3.82. For compound 5f: HRMS (ESI, M$^+$+1) calcd for C$_{20}$H$_{24}$NO$_3$S 358.1477, found 358.1478; $^1$H NMR (400 MHz): $\delta$ 7.14-7.05 (m, 3H), 6.83-6.87 (m, 4H), 6.81-6.75 (m, 2H), 3.72 (s, 3H), 3.54-3.50 (m, 4H), 2.90-2.86 (m, 4H), 2.84 (s, 3H); $^{13}$C NMR (100 MHz): $\delta$ 162.28, 159.79, 157.87, 139.49, 137.82, 135.82, 130.50, 129.99 (2x), 113.34 (2x), 55.10, 46.76 (2x), 37.36, 37.29, 36.64. Anal. Calcd for C$_{20}$H$_{22}$FNO$_3$S: C, 63.98; H, 5.91; N, 3.73. Found: C, 64.32; H, 5.80; N, 3.86.

A representative procedure of skeleton 6 from skeleton 5 is as follows:

10% Palladium on activated carbon (10 mg) was added to a stirred solution of skeleton 5 (0.3 mmol) in ethyl acetate (10 mL). Hydrogen was bubbled into the mixture for 20 min, and the reaction
mixture was continued to stir for 10 h at rt. The catalyst was filtered through a short plug of Celite and washing with ethyl acetate (2 x 20 mL). The combined organic layers were evaporated under reduced pressure to afford crude product. Purification on silica gel (hexane/ethyl acetate = 6/1~4/1) afforded skeleton 6. For compound 6a: HRMS (ESI, M⁺+1) cálculd for C₁₉H₂₄NO₂S 330.1528, found 330.1530; ¹H NMR (400 MHz): δ 7.14-7.09 (m, 6H), 6.84-6.80 (m, 4H), 3.84 (ddd, J = 4.0, 6.4, 13.6 Hz, 2H), 3.42-3.38 (m, 2H), 3.33 (ddd, J = 3.6, 9.6, 13.6 Hz, 2H), 2.88 (s, 3H), 2.43-2.34 (m, 2H), 2.21-2.13 (m, 2H); ¹³C NMR (100 MHz): δ 143.09 (2x), 128.83 (4x), 127.67 (4x), 126.07 (2x), 48.48 (2x), 47.20 (2x), 36.23, 32.33 (2x); Anal. Caled for C₁₉H₂₃NO₂S: C, 69.27; H, 7.04; N, 4.25. Found: C, 69.51; H, 7.32; N, 4.54. For compound 6b: HRMS (ESI, M⁺+1) cálculd for C₂₄H₂₆NO₂S 392.1684, found 392.1683; ¹H NMR (400 MHz): δ 7.89-7.86 (m, 2H), 7.65-7.53 (m, 3H), 7.10-7.07 (m, 6H), 6.78-6.74 (m, 4H), 3.85 (ddd, J = 4.0, 6.4, 13.6 Hz, 2H), 2.46-2.31 (m, 2H), 2.25-2.09 (m, 2H); ¹³C NMR (100 MHz): δ 143.09, 138.88, 132.45 (2x), 129.12 (2x), 128.79 (4x), 127.60 (4x), 127.08 (2x), 126.00 (2x), 48.44 (2x), 47.33 (2x), 32.05 (2x); Anal. Caled for C₂₄H₂₅NO₂S: C, 73.62; H, 6.44; N, 3.58. Found: C, 73.87; H, 6.67; N, 3.84. For compound 6c: HRMS (ESI, M⁺+1) cálculd for C₂₅H₂₈NO₂S 406.1841, found 406.1845; ¹H NMR (400 MHz): δ 7.75 (d, J = 8.4 Hz, 2H), 7.37-7.03 (m, 8H), 6.78-6.74 (m, 4H), 3.84 (ddd, J = 3.6, 9.6, 13.6 Hz, 2H), 2.46 (s, 3H), 2.41-2.30 (m, 2H), 2.17-2.08 (m, 2H); ¹³C NMR (100 MHz): δ 143.12, 129.68 (2x), 128.78 (4x), 128.56 (2x), 127.56 (4x), 127.11 (2x), 125.95 (2x), 48.42 (2x), 47.31 (2x), 31.99 (2x); Anal. Caled for C₂₅H₂₇NO₂S: C, 74.04; H, 6.71; N, 3.45. Found: C, 74.38; H, 6.97; N, 3.80. For compound 6d: HRMS (ESI, M⁺+1) cálculd for C₁₉H₂₂F₂NO₂S 366.1339, found 366.1340; ¹H NMR (400 MHz): δ 6.84-6.73 (m, 8H), 3.84 (ddd, J = 3.6, 9.6, 13.6 Hz, 2H), 2.87 (s, 3H), 2.35-2.25 (m, 2H), 2.16-2.08 (m, 2H); ¹³C NMR (100 MHz): δ 162.48, 160.04, 138.54, 138.51, 130.20 (2x), 130.12 (2x), 114.61 (2x), 114.40, 114.22, 48.80 (2x), 47.07 (2x), 36.11, 32.39 (2x); Anal. Caled for C₁₉H₂₁F₂NO₂S: C, 62.45; H, 5.79; N, 3.83. Found: C, 62.57; H, 6.02; N, 4.09. For compound 6e: HRMS (ESI, M⁺+1) cálculd for C₂₁H₂₈NO₄S 390.1739, found 390.1742; ¹H NMR (400 MHz): δ 7.74 (d, J = 8.8 Hz, 4H), 6.67 (d, J = 8.8 Hz, 4H), 3.84 (ddd, J = 4.0, 6.4, 13.6 Hz, 2H), 3.36-3.32 (m, 2H), 3.28 (ddd, J = 3.6, 9.6, 13.6 Hz, 2H), 2.87 (s, 3H), 2.35-2.25 (m, 2H), 2.16-2.08 (m, 2H); ¹³C NMR (100 MHz): δ 157.73 (2x), 135.26 (2x), 127.56 (4x), 127.11 (2x), 125.95 (2x), 48.42 (2x), 47.31 (2x), 31.99 (2x); Anal. Caled for C₂₁H₂₇NO₄S: C, 64.75; H, 6.99; N, 3.60. Found: C, 64.90; H, 7.30; N, 3.91. For compound 6f: HRMS (ESI, M⁺+1) cálculd for C₁₉H₂₃FNO₂S 348.1435, found 348.1434; ¹H NMR (400 MHz): δ 7.15-7.09 (m, 3H), 6.82-6.74 (m, 6H), 3.87-3.81 (m, 2H), 3.40-3.27 (m, 4H), 2.88 (s, 3H), 2.35-2.29 (m, 2H), 2.19-2.11 (m, 2H); ¹³C NMR (100 MHz): δ 162.48, 160.06, 142.95, 130.30, 130.21, 128.74 (2x), 127.80 (2x), 126.21, 114.52, 114.30, 48.52, 47.88, 47.28, 47.06, 36.20, 32.60, 32.16. For compound 6g: HRMS (ESI, M⁺+1) cálculd for C₂₀H₂₆NO₃S 360.1633, found 360.1632; ¹H NMR (400 MHz): δ 7.13-7.10 (m, 3H), 6.85-6.80 (m, 2H), 6.75-6.72 (m, 2H), 6.68-6.64 (m, 2H), 3.88-3.79 (m, 2H), 3.74 (s, 3H), 3.37-3.27 (m, 4H), 2.88 (m, 3H), 2.39-2.29 (m, 2H), 2.19-2.08 (m, 2H); ¹³C NMR (100 MHz): δ 157.83, 142.40, 135.00, 130.21, 128.87 (2x), 128.82 (2x), 127.70, 126.03, 113.04 (2x), 55.13, 48.57, 47.78, 47.26, 47.10,
36.18, 32.77, 32.09. For **compound 6h**: HRMS (ESI, M^+1) calcd for C_{20}H_{25}FNO_{3}S 378.0539, found 378.0540; ^1H NMR (400 MHz): δ 6.83-6.65 (m, 8H), 3.85-3.79 (m, 2H), 3.74 (s, 3H), 3.36-3.26 (m, 4H), 2.87 (s, 3H), 2.36-2.25 (m, 2H), 2.17-2.07 (m, 2H); ^13C NMR (100 MHz): δ 162.48, 160.05, 157.93, 134.84, 130.27, 130.19, 129.80 (2x), 114.54, 114.33, 113.17 (2x), 55.15, 47.99, 47.83, 47.16, 47.10, 36.17, 32.61, 32.38; Anal. Calcd for C_{20}H_{24}FNO_{3}S: C, 63.64; H, 6.41; N, 3.71. Found: C, 63.79; H, 6.66; N, 3.92.

**A representative procedure of skeleton 7 from skeleton 2 is as follows:**

Triethylamine (500 mg, 5.0 mmol), skeleton 2 (1.0 mmol) and dichloromethane (6 mL) were added to a sealed tube at rt. The reaction mixture was stirred at reflux temperature for 25 h and then cooled to rt. Dichloromethane (10 mL) was added to the reaction mixture and then hydrogen chloride solution (1 N, 10 mL) was also added to the reaction mixture. The reaction mixture was extracted with dichloromethane (3 x 15 mL). The combined organic layers were washed with brine, dried, filtered and evaporated to afford crude product. Purification on silica gel (hexane/ethyl acetate = 4/1~2/1) afforded skeleton 7. For **compound 7b**: HRMS (ESI, M^+1) calcd for C_{26}H_{28}NO_{4}S 450.1739, found 450.1744; ^1H NMR (300 MHz): δ 7.61 (d, J = 8.1 Hz, 2H), 7.42-7.26 (m, 12H), 5.28 (s, 2H), 6.66 (dt, J = 2.1, 11.4 Hz, 2H), 2.55 (dt, J = 1.8, 13.8 Hz, 2H), 2.44 (s, 3H), 1.83 (dt, J = 4.5, 13.5 Hz, 2H), 1.55 (d, J = 12.9 Hz, 2H); ^13C NMR (75 MHz): δ 143.71, 140.88 (2x), 133.57, 129.92, 128.23 (4x), 127.86, 127.69 (4x), 127.46 (4x), 92.54, 89.31, 82.92, 43.21 (2x), 31.46 (2x), 21.79; Anal. Calcd for C_{26}H_{27}NO_{4}S: C, 69.46; H, 6.05; N, 3.12. Found: C, 69.81; H, 6.40; N, 3.34.

**Synthesis of skeleton 8 is as follows:**

Skeleton 5 (0.13 mmol) was dissolved in ethyl acetate (10 mL) free of oxygen was irradiated under a nitrogen atmosphere with a lamp (λ = 3060 Å), using a pyrex glass filter at rt for 80 h. The solvent was evaporated to afford crude product. Purification on silica gel (hexane/AcOEt = 4/1~2/1) afforded skeleton 8. For **compound 8b**: HRMS (ESI, M^+1) calced for C_{24}H_{22}NO_{2}S 388.1371, found 388.1374; ^1H NMR (400 MHz): δ 8.73-8.70 (m, 2H), 8.09-8.05 (m, 2H), 7.69-7.59 (m, 6H), 7.42-7.30 (m, 3H), 3.56-3.53 (m, 4H), 3.49-3.46 (m, 4H); ^13C NMR (75 MHz): δ 137.60, 134.28, 132.33 (2x), 130.27 (2x), 129.75 (2x), 128.83 (2x), 127.02 (2x), 126.84 (2x), 125.98 (2x), 123.35 (2x), 123.13 (2x), 46.57 (2x), 28.48 (2x).
**Compound 4f**

![NMR spectrum of Compound 4f](image)

**Compound 5a**

![NMR spectrum of Compound 5a](image)
Compound 5b

Compound 5c
Compound 5d

Compound 5e
Compound 6b

Compound 6c
Compound 6h

Compound 7b
Compound 8b