SUPPORTING INFORMATION

Palladium-Catalysed Ligand-Free Reductive Heck Cycloisomerisation of 1,6-En-α-Chloro-Enamides

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1. General information

Reactions were performed in the presence of nitrogen applying Schlenk line technique unless otherwise statement. Commercially available reagents were used throughout without further purification other than those detailed below. THF (AR) and toluene were distilled over sodium benzophenone ketyl under nitrogen, 1,4-dioxane was distilled over calcium hydride, i-PrOH (HPLC) was used directly without further purification. \(^1\)H NMR and \(^{13}\)C NMR spectra were recorded using Bruker Advance 400 operating at 400 MHz for \(^1\)H NMR and \(^{13}\)C NMR at 100 MHz, or using Bruker Advance 500 spectrometer at 500 MHz for \(^1\)H NMR and \(^{13}\)C NMR at 125 MHz. CDCl\(_3\) and (CD\(_3\))\(_2\)CO were used as the solvents for all samples. \(^1\)H NMR chemical shifts are reported using residual proton on non-deuterated solvent (CDCl\(_3\): 7.26 ppm), whereas \(^{13}\)C NMR spectra are reported using the carbon signals of the deuterated solvent (CDCl\(_3\): 77.16 ppm). Product spots were visualized by UV light at 254 nm, and subsequently developed using potassium permanganate solution as appropriate. All chromatography was carried out using silica gel (300-400 mesh) obtained from Qingdao Puke company. The removal of solvent was performed on a rotary evaporator in vacuum. IR spectra were recorded in the range of 4000-400 cm\(^{-1}\), on Perkin-Elmer Spectrum FT/IR spectrometer using a KBr pellet. Melting points were determined using an Electrothermal melting point apparatus. High resolution mass spectrometry was carried out on a New ultraflextreme equipped with TOF/TOF/Ultimate 3000 Nano HPLC.

2. Experimental procedures and characterisation data
Heck coupling for preparation of o-(4-substituted styryl)aniline

To a solution of 2-iodoaniline (6.57 g, 30 mmol) in Et$_3$N (30 mL, 1.0 M) in a flame-dried 100 mL sealed tube was charged Pd(PPh$_3$)$_4$ (1.7 mg, 1.5 mmol), and substituted styrene (36 mmol) was injected under nitrogen protection. After being stirred at 120 °C in sealed tube overnight in nitrogen atmosphere, the reaction mixture was poured into water and then was extracted with CH$_2$Cl$_2$ (three times). The combined organic layer was washed with brine, dried over MgSO$_4$, and concentrated in vacuo. The residue was purified by column chromatography on silica gel to afford corresponding o-(substituted styryl)aniline products Aa, Ab, Ac, Ad, Al, Al, and Am.

Procedure: To a 100 mL one-neck round-bottom flask was charged 2-(2-aminophenyl)ethanol (13.1 mL, 100 mmol, 1.0 equiv.) and KOH (5.6 g, 100 mmol, 1 equiv.) at room temperature. The mixture was stirred at 180 °C for 4 hours until full consumption of the starting material monitored by TLC. The reaction mixture was diluted with water and extracted with ethyl acetate for three times. The combined organic layer was dried by MgSO$_4$, filtered, and was evaporated in vacuo and the residue was purified by column chromatography to afford 2-vinylaniline (4.7 g, 40 %). To a 100 mL flame-dried Schlenk flask was charged Pd(PPh$_3$)$_4$ (0.87 g, 0.75 mmol, 5 mol%) under nitrogen atmosphere, followed by injection of aryl iodide (15 mmol, 1.0 equiv.), 2-aminostyrene (2.14 g, 18 mmol, 1.2 equiv.) and Et$_3$N (5 mL, 30 mmol, 2.0 equiv.) in toluene. The mixture was stirred at 120 °C and monitored by TLC until the feedstock has been...
consumed. The reaction mixture was extracted with ethyl acetate. The combined organic layer was dried by MgSO₄, filtered, and was evaporated in vacuo and the residue was purified by column chromatography to afford the o-(substituted styryl)aniline products Aj and Ak.¹d

![Aj 44%](image1)

![Ak 7%](image2)

(E)-2-(2-Methoxystyryl)aniline (Aj)

Prepared according to Heck coupling procedure from 2-idoanisole (4.21 g, 18 mmol) and 2-aminostyrene (2.57 g, 21.6 mmol); silica gel purification (5.5 cm x 14 cm, EtOAc: petroleum ether = 1:70, then 1:50, Rf(EtOAc/petroleum ether (1:5)) = 0.6); yield: 44% (1.8 g, yellow solid); m.p. 114.3  ºC; ¹H NMR (500 MHz, CDCl₃) δ 3.77 (brs, 2 H), 3.93 (s, 3 H), 6.75 (d, J = 8.0 Hz, 1 H), 6.88 (t, J = 7.5 Hz, 1 H), 6.96 (d, J = 8.2 Hz, 1 H), 7.04 (t, J = 7.5 Hz, 1 H), 7.16 (t, J = 7.4 Hz, 1 H), 7.24 (d, J = 16.3 Hz, 1 H), 7.32 (t, J = 7.6 Hz, 1 H), 7.43 (dd, J₁ = 16.3 Hz, J₂ = 1.7 Hz, 1 H), 7.52 (d, J = 7.6 Hz, 1 H), 7.65 (d, J = 7.6 Hz, 1 H); ¹³C NMR (125 MHz, CDCl₃) δ 55.6, 111.0, 116.2, 119.1, 120.8, 124.5, 124.8, 125.2, 126.6, 126.8, 127.4, 128.5, 128.7, 144.0, 156.9; FT-IR (KBr) δ 3385, 3025, 2940, 1631, 1595, 1577, 1493, 1458, 1337, 1292, 1242, 1105, 1021, 974, 743, 483 cm⁻¹; HRMS (ESI⁺) m/z calcd for C₁₅H₁₆NO⁺ [M+H]⁺ 226.1226 found 226.1217.

(E)-2-(2-(Furan-3-yl)vinyl)aniline (Ak)

Prepared according to Heck reaction procedure from 3-bromofuran (1.3 mL, 15 mmol) and 2-aminostyrene (2.14 g, 18 mmol); silica gel purification (5.5 cm x 14 cm, ethyl acetate/petroleum ether = 1:70, then 1:50, Rf(EtOAc/PE = 1:5) = 0.6); yield: 11% (0.3 g, brown oil); Its spectroscopic data is consistent with a literature report.¹d

4-Fluoro-2-styrylaniline (An)

Prepared according to Heck coupling procedure from 4-fluoro-2-iodoaniline (4.17 g, 17.6 mmol) and styrene (2.5 mL, 21 mmol); silica gel purification (5.5 cm x 14 cm, EtOAc: petroleum ether = 1:70, then 1:50, Rf(EtOAc/petroleum ether (1:5)) = 0.60); yield: 27% (1.0 g, brown oil); ¹H NMR (500 MHz, CDCl₃) δ 3.68 (brs, 2 H), 6.66 (dd,
\(J_1 = 8.7 \text{ Hz}, J_2 = 4.9 \text{ Hz}, 1 \text{ H})\), 6.83 (td, \(J_1 = 8.4 \text{ Hz}, J_2 = 2.9 \text{ Hz}, 1 \text{ H})\), 6.99 (d, \(J = 16.1 \text{ Hz}, 1 \text{ H})\), 7.11-7.16 (m, 2 H), 7.29 (t, \(J = 7.4 \text{ Hz}, 1 \text{ H})\), 7.38 (t, \(J = 7.5 \text{ Hz}, 2 \text{ H})\), 7.52 (d, \(J = 7.4 \text{ Hz}, 2 \text{ H})\); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 113.0 (d, \(J_{CF} = 23 \text{ Hz})\), 115.3 (d, \(J_{CF} = 23 \text{ Hz})\), 117.4 (d, \(J_{CF} = 8 \text{ Hz})\), 123.4 (d, \(J_{CF} = 3 \text{ Hz})\), 125.2 (d, \(J_{CF} = 8 \text{ Hz})\), 126.7, 128.1, 128.9, 131.4, 137.3, 140.1 (d, \(J_{CF} = 1 \text{ Hz})\), 156.9 (d, \(J_{CF} = 235 \text{ Hz})\); FT-IR (KBr) \(\tilde{\nu}\) 3028, 1607, 1497, 1263, 1153, 960, 809, 755, 691, 498 cm\(^{-1}\); HRMS (ESI\(^+\)) m/z calcld for \(\text{C}_{14}\text{H}_{13}\text{FN}^+\) [M+H]\(^+\) found 214.1017.

\((E+Z)-5\)-Fluoro-2-styrylaniline (Ao)

![Image](image.png)

Prepared according to Heck coupling procedure from 2-bromo-5-fluoroaniline (5 g, 26.4 mmol) and styrene (3.64 mL, 31.7 mmol); silica gel purification (5.5 cm x 14 cm, EtOAc: petroleum ether = 1:70; then 1:50, \(R_t\) (EtOAc/petroleum ether (1:5)) = 0.60); yield: 15% (0.85 g, white solid); m.p. 84.0 \(^\circ\)C; \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 3.95 (brs, 2 H), 4.21 (brs, 0.6 H), 6.39 (td, \(J_1 = 8.5 \text{ Hz}, J_2 = 2.8 \text{ Hz}, 0.3 \text{ H})\), 6.45 (dd, \(J_1 = 10.5 \text{ Hz}, J_2 = 2.5 \text{ Hz}, 1 \text{ H})\), 6.50 (dd, \(J_1 = 10.3 \text{ Hz}, J_2 = 2.8 \text{ Hz}, 0.3 \text{ H})\), 6.54 (td, \(J_1 = 8.5 \text{ Hz}, J_2 = 2.4 \text{ Hz}, 1 \text{ H})\), 6.95 (d, \(J = 16.1 \text{ Hz}, 1 \text{ H})\), 7.09 (d, \(J = 16.1 \text{ Hz}, 1 \text{ H})\), 7.30 (t, \(J = 7.4 \text{ Hz}, 1 \text{ H})\), 7.35 (d, \(J = 7.4 \text{ Hz}, 0.5 \text{ H})\), 7.40 (t, \(J = 7.5 \text{ Hz}, 3 \text{ H})\), 7.53 (d, \(J = 7.6 \text{ Hz}, 2 \text{ H})\); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) (major isomer) 102.7 (d, \(J_{CF} = 24.3 \text{ Hz})\), 106.0 (d, \(J_{CF} = 21 \text{ Hz})\), 120.0 (d, \(J_{CF} = 2.7 \text{ Hz})\), 123.5, 126.5, 127.8, 128.9, 130.4, 133.5, 137.6, 145.6, 163.4; FT-IR (KBr) \(\tilde{\nu}\) 3363, 1634, 1605, 1584, 1501, 1438, 1342, 1284, 1262, 1170, 1143, 965, 842, 797, 754, 713, 691, 511 cm\(^{-1}\); HRMS (ESI\(^+\)) m/z calcld for \(\text{C}_{14}\text{H}_{13}\text{FN}^+\) [M+H]\(^+\) found 214.1018.

\((E)-2,4\)-Dichloro-6-styrylaniline (Ap)

![Image](image.png)

Prepared according to Heck coupling procedure from 2,4-dichloro-6-iodoaniline (3.7 g, 13 mmol) and styrene (1.8 mL, 15.6 mmol); silica gel purification (5.5 cm x 14 cm, EtOAc: petroleum ether = 1:500; then 1:200, \(R_t\) (EtOAc/petroleum ether (1:30)) = 0.60); yield: 18% (0.60 g, yellowish solid); m.p. 73.0 \(^\circ\)C; \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 4.00 (brs, 2 H), 6.99 (d, \(J = 16.0 \text{ Hz}, 1 \text{ H})\), 7.04 (d, \(J = 16.0 \text{ Hz}, 1 \text{ H})\), 7.22 (d, \(J = 2.4 \text{ Hz}, 1 \text{ H})\), 7.29 (d, \(J = 2.1 \text{ Hz}, 1 \text{ H})\), 7.32 (tt, \(J_1 = 7.4 \text{ Hz}, J_2 = 1.2 \text{ Hz}, 1 \text{ H})\), 7.40 (td, \(J_1 = 7.3 \text{ Hz}, J_2 = 1.7 \text{ Hz}, 2 \text{ H})\), 7.51-7.52 (m, 2 H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 120.6, 122.6, 123.1, 125.5, 126.2, 126.8, 127.9, 128.4, 128.9, 132.9, 136.8, 139.4; FT-IR (KBr) \(\tilde{\nu}\) 3386, 1631, 1612, 1453, 1073, 955, 855, 835, 718, 789, 540, 479 cm\(^{-1}\); HRMS (ESI\(^+\)) m/z calcld for \(\text{C}_{14}\text{H}_{10}\text{Cl}_2\text{N}^+\) [M-H]\(^-\) found 262.0190 found 262.0197.

\((E)-3\)-Methyl-2-styrylaniline (Aq)
Prepared according to Heck coupling procedure from 2-bromo-3-methylaniline (3.72 g, 15 mmol) and styrene (2.1 mL, 18 mmol); silica gel purification (5.5 cm x 14 cm, EtOAc: petroleum ether = 1:70, then 1:30, Rf (EtOAc/petroleum ether (1:5)) = 0.70); yield: 29% (0.92 g, brown oil); 1H NMR (500 MHz, CDCl₃) δ 2.36 (s, 3 H), 3.70 (brs, 2 H), 6.66 (d, J = 7.9 Hz, 1 H), 6.71 (d, J = 7.4 Hz, 1 H), 6.90 (d, J = 16.7 Hz, 1 H), 7.04 (t, J = 7.7 Hz, 1 H), 7.09 (d, J = 16.7 Hz, 1 H), 7.33 (t, J = 7.3 Hz, 1 H), 7.42 (t, J = 7.5 Hz, 2 H), 7.56 (d, J = 7.4 Hz, 2 H); 13C NMR (125 MHz, CDCl₃) δ 20.9, 113.6, 120.6, 123.2, 124.9, 126.4, 127.8, 127.9, 128.8, 134.0, 137.5, 137.5, 144.3; FT-IR (KBr) ν 2987, 2902, 1609, 1466, 1407, 1394, 1251, 1066, 1056, 775, 752, 692 cm⁻¹; HRMS (ESI⁺) m/z calcd for C₁₃H₁₆N⁺ [M+H]⁺ 210.1277 found 210.1271.

Tosyl protection of o-(4-substituted styryl)aniline

To a solution of o-(substituted styryl)aniline (26.7 mmol) and pyridine (2.8 mL, 34.7 mmol, 1.3 equiv.) in CH₂Cl₂ (60 mL, 0.5 M) in a flame-dried 250 mL Schlenk flask was added p-toluenesulfonyl chloride (5.8 g, 29.37 mmol, 1.1 equiv.) at 0 °C and the reaction mixture was heating under reflux for 12 hours until TLC monitored complete consumption of the starting material. Cooled to room temperature, then the product was extracted with CH₂Cl₂ (three times), dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography on silica gel to give the corresponding product B.

(E)-4-Methyl-N-(2-styrylphenyl)benzenesulfonamide (Ba)¹b

Prepared according to Ts protection general procedure from Aa o-styrylaniline (5.2 g, 26.7 mmol); silica gel purification (EtOAc: petroleum ether = 1:15, Rf (EtOAc/petroleum ether (1:5)) = 0.60); yield: 83% (7.7 g, white solid); m.p. 137.4 °C; 1H NMR (400 MHz, CDCl₃) δ 2.24 (s, 3 H), 6.59 (s, 1 H), 6.72 (d, J = 16.1 Hz, 1 H), 6.78 (d, J = 16.1 Hz, 1 H), 7.10 (d, J = 7.2 Hz, 2 H), 7.16-7.20 (m, 2 H), 7.21-7.23 (m, 1 H), 7.23-7.26 (m, 1 H), 7.27 (s, 1 H), 7.27-7.28 (m, 2 H), 7.31-7.34 (m, 1 H), 7.42-7.45 (m, 1 H), 7.56 (d, J = 8.3 Hz, 2 H); 13C NMR (100 MHz, CDCl₃) δ 21.6, 122.8, 126.7, 126.8, 126.9, 127.2, 127.3, 128.2, 128.5, 128.8, 129.8, 132.3, 133.37, 133.39, 136.7, 136.8, 144.0; FT-IR (KBr) ν 2924, 1595, 1494, 1453, 1386, 1326, 1157, 1089, 917, 890,
813, 759, 684, 567, 536 cm\(^{-1}\); HRMS (ESI\(^+\)) m/z calcd for C\(_{21}\)H\(_{20}\)NO\(_2\)S\(^+\) [M+H]\(^+\) 351.1272 found 351.1272. Its spectroscopic data is consistent with a literature report.\(^{1b}\)

\((E)-4\)-Methyl-N-(2-(4-methylstyryl)phenyl)benzenesulfonamide (Bb)\(^{1b}\)

![Chemical Structure](image)

Prepared according to Ts protection general procedure from Ab (E)-2-(4-methylstyryl)aniline (0.52 g, 2.48 mmol); silica gel purification (EtOAc: petroleum ether = 1:15, R\(_f\) (EtOAc/petroleum ether (1:5)) = 0.59); yield: 91% (0.82 g, white solid); m.p. 159.0 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 2.30 (s, 3 H), 2.37 (s, 3 H), 6.77 (dd, \(J\_1 = 16.1\) Hz, \(J\_2 = 5.2\) Hz, 3 H), 7.15 (td, \(J\_1 = 6.4\) Hz, \(J\_2 = 1.5\) Hz, 4 H), 7.20-7.22 (m, 2 H), 7.22-7.24 (m, 2 H), 7.38-7.40 (m, 1 H), 7.47-7.49 (m, 1 H), 7.62 (dt, \(J\_1 = 8.3\) Hz, \(J\_2 = 1.6\) Hz, 2 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 21.4, 21.6, 121.7, 126.6, 126.7, 126.8, 127.1, 127.3, 128.3, 129.4, 129.8, 132.3, 133.3, 133.4, 134.1, 136.7, 138.2, 144.0; FT-IR (KBr) \(\delta\) 3275, 1595, 1513, 1484, 1456, 1328, 1160, 1093, 966, 908, 804, 667 cm\(^{-1}\); HRMS (ESI\(^+\)) m/z calcd for C\(_{22}\)H\(_{22}\)NO\(_2\)S\(^+\) [M+H]\(^+\) 364.1366 found 364.1368; Its spectroscopic data is consistent with a literature report.\(^{1b}\)

\((E)-N-(2-(4-Methoxystyryl)phenyl)-4-methylbenzenesulfonamide (Be)\(^{1b}\)

![Chemical Structure](image)

Prepared according to Ts protection general procedure from Ac (E)-2-(4-methoxystyryl)aniline (0.71 g, 3.15 mmol); silica gel purification (EtOAc: petroleum ether = 1:5, R\(_f\) (EtOAc/petroleum ether (1:5)) = 0.41); yield: 79% (0.94 g, white solid); m.p. 191.0 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 2.19 (s, 3 H), 3.74 (s, 3 H), 6.63 (s, 2 H), 6.75 (t, \(J\_1 = 2.9\) Hz, 1 H), 6.87 (t, \(J\_1 = 2.0\) Hz, 1 H), 7.05 (d, \(J\_1 = 8.0\) Hz, 2 H), 7.09-7.14 (m, 2 H), 7.16 (t, \(J\_1 = 2.8\) Hz, 1 H), 7.19 (d, \(J\_1 = 2.0\) Hz, 1 H), 7.26-7.31 (m, 1 H), 7.34-7.39 (m, 1 H), 7.53 (dt, \(J\_1 = 8.3\) Hz, \(J\_2 = 1.6\) Hz, 2 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 21.6, 55.4, 114.1, 120.5, 126.4, 126.8, 127.1, 127.3, 128.1, 129.70, 129.73, 131.7, 133.2, 133.6, 136.7, 143.9, 159.7 (one carbon signal is missing due to the overlapping); FT-IR (KBr) \(\delta\) 3275, 1597, 1514, 1484, 1456, 1327, 1160, 1087, 917, 829, 672 cm\(^{-1}\); HRMS (ESI\(^+\)) m/z calcd for C\(_{22}\)H\(_{22}\)NO\(_2\)S\(^+\) [M+H]\(^+\) 380.1315 found 380.1314; Its spectroscopic data is consistent with a literature report.\(^{1b}\)

\((E)-N-(2-(4-Chlorostyryl)phenyl)-4-methylbenzenesulfonamide (Bd)\(^{1b}\)

![Chemical Structure](image)

Prepared according to Ts protection general procedure from Ad
(E)-2-(4-chlorostyryl)aniline (0.946 g, 4.12 mmol); silica gel purification (EtOAc: petroleum ether = 1:15, Rf (EtOAc/petroleum ether (1:5)) = 0.60); yield: 84% (1.33 g, white solid); m.p. 194.0 °C; ℎ NMR (400 MHz, d<sub>6</sub>-DMSO) δ 2.16 (s, 3 H), 6.93 (d, J = 16.3 Hz, 1 H), 7.10 (d, J = 16.3 Hz, 1 H), 7.12-7.17 (m, 1 H), 7.20 (d, J = 8.0 Hz, 2 H), 7.23-7.27 (m, 2 H), 7.40 (d, J = 8.7 Hz, 2 H), 7.46 (dt, J<sub>1</sub> = 8.6 Hz, J<sub>2</sub> = 1.8 Hz, 2 H), 7.49 (d, J = 8.2 Hz, 2 H), 7.66-7.68 (m, 1 H), 9.82 (s, 1 H); ℜ C NMR (100 MHz, d<sub>6</sub>-DMSO) δ 20.8, 124.3, 125.5, 126.5, 127.0, 128.0, 128.1, 128.2, 128.29, 129.6, 132.0, 132.2, 134.0, 136.0, 137.1, 143.0; FT-IR (KBr) ν 3277, 1595, 1513, 1484, 1456, 1328, 1160, 1087, 956, 908, 823, 667 cm<sup>-1</sup>; HRMS (ESI<sup>+</sup>) m/z calcd for C<sub>21</sub>H<sub>18</sub>ClNO<sub>2</sub>S<sup>+</sup> [M+H]<sup>+</sup> 384.0820 found 384.0824. Its spectroscopic data is consistent with a literature report.<sup>1b</sup>

(E)-N-(2-Styrylphenyl)methanesulfonamide (Bh)<sup>1b</sup>

![Chemical Structure](image)

Prepared according to Ts protection general procedure from Aa o-styrylaniline (1.4 g, 7.18 mmol), replacing p-TsCl by MsCl as a sulfonylation reagent; silica gel purification (EtOAc: n-hexane = 1:5, Rf (EtOAc/petroleum ether (1:5)) = 0.47); yield: 92% (1.80 g, yellowish oil); ℎ NMR (400 MHz, CDCl<sub>3</sub>) δ 2.97 (s, 3 H), 6.97 (brs, 1 H), 7.04 (d, J = 15.9 Hz, 1 H), 7.23-7.26 (m, 1 H), 7.27-7.30 (m, 2 H), 7.33-7.37 (m, 2 H), 7.39 (d, J = 11.8 Hz, 1 H), 7.46-7.48 (m, 1 H), 7.54 (d, J = 7.3 Hz, 2 H), 7.62-7.65 (m, 1 H); ℜ C NMR (100 MHz, CDCl<sub>3</sub>) δ 40.0, 122.8, 125.36, 125.37, 127.0, 127.1, 128.4, 128.8, 128.9, 132.6, 132.8, 133.5, 136.8; FT-IR (KBr) ν 3287, 3013, 2928, 2856, 1328, 1164, 960, 762, 672, 549, 521 cm<sup>-1</sup>; HRMS (ESI<sup>+</sup>) m/z calcd for C<sub>15</sub>H<sub>16</sub>ClNO<sub>2</sub>S<sup>+</sup> [M+H]<sup>+</sup> 274.0896 found 274.0898; Its spectroscopic data is consistent with a literature report.<sup>1b</sup>

(E)-4-Nitro-N-(2-styrylphenyl)benzenesulfonamide (Bi)<sup>1b</sup>

![Chemical Structure](image)

Prepared according to Ts protection general procedure from Aa o-styrylaniline (1.4 g, 7.18 mmol), replacing p-TsCl by NsCl as a sulfonylation reagent to yield 69% (1.88 g) Bi; Its spectroscopic data is consistent with a literature report.<sup>1b</sup>

(E)-N-(2-(2-Methoxystyryl)phenyl)-4-methylbenzenesulfonamide (Bj)

![Chemical Structure](image)

Prepared according to Ts protection general procedure from Aj (1.80 g, 7.9 mmol); silica gel purification (3.5 cm × 14 cm, ethyl acetate/petroleum ether = 1:50, then 1:20, Rf = 0.5 (EtOAc/PE = 1:5); yield: 70% (2.1 g, white solid); m.p. 159.0 °C; ℎ NMR
(500 MHz, CDCl₃) δ 2.31 (s, 3 H), 3.87 (s, 3 H), 6.65 (brs, 1 H), 6.83 (d, J = 16.3 Hz, 1 H), 6.90 (d, J = 8.3 Hz, 1 H), 6.95 (t, J = 7.5 Hz, 1 H), 7.14-7.17 (m, 3 H), 7.21-7.24 (m, 2 H), 7.29 (td, J₁ = 7.7 Hz, J₂ = 1.5 Hz, 2 H), 7.40 (dd, J₁ = 7.8 Hz, J₂ = 2.1 Hz, 1 H), 7.51 (dd, J₁ = 7.0 Hz, J₂ = 2.1 Hz, 1 H), 7.62 (d, J = 8.3 Hz, 2 H); ¹³C NMR (125 MHz, CDCl₃) δ 21.6, 55.6, 111.0, 120.8, 123.1, 125.9, 126.9, 126.9, 127.0, 127.3, 127.5, 128.3, 129.3, 129.7, 133.3, 133.6, 136.8, 143.9, 157.1 (one carbon signal is missing due to the overlapping); FT-IR (KBr) ν 2925, 2853, 1666, 1493, 1330, 1245, 1161, 1091, 752, 663, 568 cm⁻¹; HRMS (ESI) m/z calcd for C₂₂H₂₆NO₅S²⁻ [M-H]⁻: 378.1169 found 378.1164.

**(E)-N-(2-(2-(Furan-3-yl)vinyl)phenyl)-4-methylbenzenesulfonamide (Bk)***

![Image](image.jpg)

Prepared from Ak (0.3 g, 1.7 mmol) and TsCl (0.2 g, 2.6 mmol); silica gel purification (3.5 cm × 14 cm, ethyl acetate/petroleum ether = 1:50, then 1:20, Rf = 0.5 (EtOAc/PE = 1:5); yield: 69% (0.4 g, yellow solid); m.p. 159 °C; ¹H NMR (400 MHz, CDCl₃) δ 2.33 (s, 3 H), 6.45 (d, J = 1.8 Hz, 1 H), 6.50 (d, J = 16.0 Hz, 1 H), 6.57 (s, 1 H), 6.65 (d, J = 16.0 Hz, 1 H), 7.18-7.23 (m, 4 H), 7.35-7.38 (m, 1 H), 7.41-7.45 (m, 3 H), 7.61 (d, J = 8.3 Hz, 2 H); ¹³C NMR (125 MHz, CDCl₃) δ 21.6, 107.4, 122.2, 122.4, 124.4, 126.5, 126.7, 127.1, 127.3, 128.3, 129.8, 133.1, 133.3, 136.7, 141.5, 143.9, 144.1; FT-IR (KBr) ν 2926, 2854, 1759, 1669, 1493, 1335, 1160, 1091, 964, 759, 665, 564 cm⁻¹; HRMS (ESI) m/z calcd for C₁₉H₁₈NO₅S⁻ [M-H]⁻: 338.0856 found 338.0865. Its spectroscopic data is consistent with a literature report.***

***(E)-4-Methyl-N-(4-methyl-2-styrylphenyl)benzenesulfonamide (Bl)***

![Image](image.jpg)

Prepared according to Ts protection general procedure from Al (1.23 g, 5.9 mmol); silica gel purification (3.5 cm × 14 cm, ethyl acetate/petroleum ether = 1:50, then 1:20, Rf = 0.5 (EtOAc/PE = 1:5); yield: 87% (1.86 g, yellow oil); ¹H NMR (500 MHz, CDCl₃) δ 2.19 (s, 3 H), 2.27 (s, 3 H), 6.62 (brs, 1 H), 6.69 (d, J = 16.2 Hz, 1 H), 6.77 (d, J = 16.2 Hz, 1 H), 6.97 (d, J = 8.2 Hz, 1 H), 7.06 (d, J = 8.0 Hz, 2 H), 7.14-7.21 (m, 2 H), 7.24-7.25 (m, 5 H), 7.54 (d, J = 8.1 Hz, 2 H); ¹³C NMR (125 MHz, CDCl₃) δ 21.2, 21.5, 123.0, 126.8, 126.9, 127.3, 127.7, 128.0, 128.7, 129.3, 129.7, 130.7, 131.6, 133.6, 136.7, 136.9, 137.2, 143.9; FT-IR (KBr) ν 3271, 3027, 2924, 1599, 1496, 1394, 1330, 1162, 1092, 907, 813, 692, 666, 600, 552, 528 cm⁻¹; HRMS (ESI) m/z calcd for C₂₂H₂₀NO₅S⁻ [M-H]⁻: 362.1220 found 362.1216.

***(E+Z)-N-(4-Methoxy-2-styrylphenyl)-4-methylbenzenesulfonamide (Bm)***

![Image](image.jpg)
Prepared according to Ts protection general procedure from **Am** (2.06 g, 9.1 mmol); silica gel purification (3.5 cm × 14 cm, ethyl acetate/petroleum ether = 1:50, then 1:20, \( R_f = 0.5 \) (EtOAc/PE = 1:5); yield: 32 % (1.13 g, yellow solid); m.p. 141.1 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) (major isomer) 2.18 (s, 3 H), 3.76 (s, 3 H), 6.58 (bs, 1 H), 6.66-6.73 (m, 2 H), 6.74-6.79 (m, 1 H), 6.95 (d, \( J = 2.9 \) Hz, 1 H), 7.04 (d, \( J = 8.0 \) Hz, 2 H), 7.15 (d, \( J = 8.7 \) Hz, 1 H), 7.17-7.19 (m, 1 H), 7.18-7.25 (m, 4 H), 7.51 (d, \( J = 8.3 \) Hz, 2 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 21.5, 55.6, 110.9, 114.1, 123.1, 126.1, 126.8, 127.3, 128.1, 128.7, 129.7, 130.3, 131.6, 136.1, 136.6, 136.8, 143.9, 158.9; FT-IR (KBr) \( \tilde{\nu} \) 3267, 2927, 1599, 1495, 1326, 1290, 1206, 1159, 1091, 1033, 962, 812, 756, 664, 549 cm\(^{-1}\); HRMS (ESI) m/z calcd for C\(_{22}\)H\(_{20}\)NO\(_3\)S [M-H] 378.1169 found 378.1163.

\[(E)-N-(4-Fluoro-2-styrylphenyl)-4-methylbenzenesulfonamide (Bn)\]

Prepared according to Ts protection general procedure from **An** (1.00 g, 4.5 mmol); silica gel purification (3.5 cm × 14 cm, ethyl acetate/petroleum ether = 1:50, then 1:20, \( R_f = 0.5 \) (EtOAc/PE = 1:5); yield: 63 % (1.04 g, white solid); m.p. 150.2 °C; \(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta \) 2.16 (s, 3 H), 6.65 (d, \( J = 16.1 \) Hz, 1 H), 6.75 (d, \( J = 16.2 \) Hz, 1 H), 6.79 (s, 1 H), 6.84 (td, \( J_1 = 8.2 \) Hz, \( J_2 = 2.9 \) Hz, 1 H), 7.03 (d, \( J = 8.2 \) Hz, 2 H), 7.11 (dd, \( J_1 = 9.7 \) Hz, \( J_2 = 2.9 \) Hz, 1 H), 7.17-7.25 (m, 6 H), 7.50 (d, \( J = 8.2 \) Hz, 2 H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \( \delta \) 21.5, 112.4 (d, \( J_{CF} = 23 \) Hz), 115.2 (d, \( J_{CF} = 23 \) Hz), 121.9 (d, \( J_{CF} = 2 \) Hz), 126.9, 127.3, 128.5, 128.7, 129.1 (d, \( J_{CF} = 3 \) Hz), 129.8 (d, \( J_{CF} = 9 \) Hz), 130.3 (d, \( J_{CF} = 8.9 \) Hz), 132.7, 136.3, 136.4, 136.6 (d, \( J_{CF} = 8.4 \) Hz), 144.1, 161.8 (d, \( J_{CF} = 245.2 \) Hz); FT-IR (KBr) \( \tilde{\nu} \) 3272, 3062, 2927, 1599, 1489, 1328, 1160, 1092, 961, 813, 758, 665, 603, 550, 527 cm\(^{-1}\); HRMS (ESI) m/z calcd for C\(_{21}\)H\(_{17}\)FNO\(_2\)S\(_2\) [M-H] 366.0964 found 366.0959.

\[(E)-N-(5-Fluoro-2-styrylphenyl)-4-methylbenzenesulfonamide (Bo)\]

Prepared according to Ts protection general procedure from **Ao** (0.72 g, 3.4 mmol); silica gel purification (3.5 cm × 14 cm, ethyl acetate/petroleum ether = 1:50, then 1:20, \( R_f = 0.5 \) (EtOAc/PE = 1:5); yield: 42 % (0.52 g, brown solid); m.p. 78 °C; \(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta \) 2.31 (s, 3 H), 6.71 (d, \( J = 16.0 \) Hz, 1 H), 6.80 (d, \( J = 16.1 \) Hz, 1 H), 6.91 (td, \( J_1 = 8.3 \) Hz, \( J_2 = 2.5 \) Hz, 1 H), 7.03 (bs, 1 H), 7.17-7.21 (m, 3 H), 7.26-7.29 (m, 1 H), 7.33-7.34 (m, 4 H), 7.42 (dd, \( J_1 = 8.6 \) Hz, \( J_2 = 6.3 \) Hz, 1 H), 7.67 (d, \( J = 8.2 \) Hz, 2 H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \( \delta \) 21.6, 112.4 (d, \( J_{CF} = 25 \) Hz), 113.8 (d, \( J_{CF} = 21 \) Hz), 121.7, 126.8, 127.3, 128.2 (d, \( J_{CF} = 9 \) Hz), 128.3, 128.4 (d, \( J_{CF} = 4 \) Hz), 128.8, 129.9, 132.6, 134.8 (d, \( J_{CF} = 10 \) Hz), 136.3, 136.6, 144.4, 162.3 (d, \( J_{CF} = 246 \) Hz); FT-IR (KBr) \( \tilde{\nu} \) 3272, 3062, 2926, 1677, 1598, 1502, 1334, 1168, 1090, 984, 894, 812, 691, 666, 576, 546 cm\(^{-1}\); HRMS (ESI) m/z calcd for C\(_{21}\)H\(_{17}\)FNO\(_2\)S\(_2\) [M-H] 366.0964 found 366.0961.
(E)-N-(2,4-Dichloro-6-styrylphenyl)-4-methylbenzenesulphonamide (Bp)

Prepared according to Ts protection general procedure from Ap (0.60 g, 2.3 mmol); silica gel purification (3.5 cm × 14 cm, ethyl acetate/petroleum ether = 1:200, then 1:100, Rf = 0.5 (EtOAc/PE = 1:30); yield: 64 % (0.61 g, yellowish solid); m.p. 197.1 °C; 1H NMR (500 MHz, CDCl3) δ 2.30 (s, 3 H), 6.48 (s, 1 H), 6.99 (d, J = 16.3 Hz, 1 H), 7.15 (d, J = 8.0 Hz, 2 H), 7.23 (d, J = 2.3 Hz, 1 H), 7.29-7.30 (m, 1 H), 7.32-7.34 (m, 2 H), 7.35-7.37 (m, 1 H), 7.39-7.40 (m, 2 H), 7.60-7.62 (m, 3 H); 13C NMR (125 MHz, CDCl3) δ 21.7, 123.8, 124.8, 127.2, 127.7, 128.0, 128.5, 129.4, 129.7, 132.1, 134.0, 134.6, 136.5, 136.6, 139.9, 144.4; FT-IR (KBr) ʋ 3259, 2926, 1577, 1554, 1494, 1451, 1331, 1158, 1091, 965, 894, 813, 786, 751, 691, 670, 582, 549 cm−1; HRMS (ESI) m/z calcd for C21H16Cl2NO2S− [M-H]− 416.0279 found 416.0278.

(E)-4-Methyl-N-(3-methyl-2-styrylphenyl)benzenesulphonamide (Bq)

Prepared according to Ts protection general procedure from Aq (0.88 g, 4.2 mmol); silica gel purification (3.5 cm × 14 cm, ethyl acetate/petroleum ether = 1:50, then 1:20, Rf = 0.5 (EtOAc/PE = 1:5); yield: 72 % (1.1 g, white solid); m.p. 132.5 °C; 1H NMR (400 MHz, CDCl3) δ 2.23 (s, 3 H), 2.42 (s, 3 H), 6.29 (d, J = 16.8 Hz, 1 H), 6.62 (dd, J1 = 16.8, J2 = 2.6 Hz, 1 H), 6.96 (brs, 1 H), 7.02 (d, J = 7.6 Hz, 1 H), 7.18 (t, J = 7.9 Hz, 1 H), 7.23 (d, J = 8.0 Hz, 2 H), 7.31-7.43 (m, 5 H), 7.52 (d, J = 8.2 Hz, 1 H), 7.64 (d, J = 8.1 Hz, 2 H); 13C NMR (100 MHz, CDCl3) δ 20.8, 21.6, 119.9, 122.8, 126.5, 127.0, 127.2, 127.8, 128.5, 128.8, 129.7, 130.1, 134.1, 136.2, 136.3, 136.7, 137.5, 143.9; FT-IR (KBr) ʋ 3274, 3061, 2926, 2853, 1598, 1464, 1329, 1163, 1093, 970, 813, 755, 693, 665, 564 cm−1; HRMS (ESI) m/z calcd for C22H20NO2S− [M-H]− 362.1215 found 362.1215.

Phenyl(trimethylsilyl)ethynyl)iodonium triflate (C)2

Prepared according to a literature report.2 To a stirred mixture of diazotioxyiodo benzene (9.7 g, 30 mmol, 1 equiv.) in dry CH2Cl2 (20 mL) in a flame-dried 100 mL Schlenk flask was added trifluoromethanesulphonic anhydride (2.52 mL, 15 mmol, 0.5 equiv.) under nitrogen at -30 °C. The resulting mixture turned into a clear solution after 20 min stirring. Then bis(trimethylsilyl)acetylene (8.1 mL, 36 mmol, 1.2 equiv.) was injected via syringe under nitrogen atmosphere at 0 °C. The reaction was stirred at room temperature for 2 hours. Then anhydrous diethyl ether (30 mL) and petroleum ether (60
were added, and the resulting solution was left for several hours at 0 °C for crystallization of the product. Colorless crystals of C were filtered under nitrogen, washed with anhydrous ether, and dried in vacuum; yield 10.73 g (80%), white solid. Its spectroscopic data is consistent with a literature report.²

**Typical Witulski rearrangement to synthesize ynamide derivatives 6**

![Diagram](image)

To a solution of the substrate B (3 mmol, 1 equiv.) in THF (30 mL, 0.1 M) in a flame-dried 100 mL Schlenk flask was added LiHMDS (lithium bis(trimethylsilyl)amide) (3.6 mL, 3.6 mmol, 1.2 equiv.) under nitrogen at -78 °C. The resulting mixture was stirred at 0 °C for 30 min. Then phenyl(trimethylsilyl)ethynyl)iodonium triflate C (1.62 g, 3.6 mmol, 1.2 equiv.) in THF (5 mL) solution was added. After being stirred at 0 °C for 7 hours, the reaction mixture was poured into water and then concentrated in vacuo to remove THF, and extracted with CH₂Cl₂ (three times). The combined organic layer was washed with brine, and concentrated in vacuo to obtain the crude ynamide D. Tetra-butyl ammonium fluoride (0.78 g, 3 mmol, 1 equiv.) was added into a solution of D in CH₂Cl₂ (25 mL) and the reaction mixture was stirred at room temperature for 10-20 minutes until full conversion of ynamide D as monitored by TLC. Extraction of the reaction mixture with CH₂Cl₂ (three times), and the combined organic layer was washed with brine, dried over MgSO₄, and concentrated in vacuo. The residue was purified by column chromatography on silica gel to afford the corresponding product 6.

**(E)-N-Ethynyl-4-methyl-N-(2-styrylphenyl)benzenesulfonamide (6a)**

Prepared according to Witulski rearrangement general procedure from Ba

**(E)-4-methyl-N-(2-styrylphenyl)benzenesulfonamide (3.5 g, 10 mmol); silica gel purification (EtOAc: petroleum ether = 1:50, Rf(EtOAc/petroleum ether (1:5)) = 0.75); yield: 61% (2.28 g, yellow solid); m.p. 113.0 °C; ¹H NMR (400 MHz, CDCl₃) δ 2.26 (s, 3 H), 2.89 (s, 1 H), 6.94 (d, J = 16.2 Hz, 1 H), 7.02 (d, J = 16.3 Hz, 1 H), 7.21 (d, J = 8.1 Hz, 3 H), 7.25-7.26 (m, 1 H), 7.29 (dd, J₁ = 5.8 Hz, J₂ = 1.7 Hz, 1 H), 7.31-7.35 (m, 4 H), 7.39 (td, J₁ = 7.5 Hz, J₂ = 1.1 Hz, 1 H), 7.71 (d, J = 8.3 Hz, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 21.7, 58.9, 77.0, 123.0, 126.4, 127.0, 128.2, 128.38, 128.42, 128.7, 129.88, 129.89, 129.9, 131.2, 134.2, 135.5, 136.3, 137.0, 145.4; FT-IR (KBr) ν 3294, 2130, 1597, 1495, 1451, 1372, 1171, 1090, 963, 813, 761, 690, 586, 543 cm⁻¹; HRMS (ESI⁺) m/z calcd for C₂₃H₂₀NO₂S⁺ [M+H⁺] 374.1210 found 374.1209.

**(E)-N-Ethynyl-4-methyl-N-(2-(4-methylstyril)phenyl)benzenesulfonamide (6b)**
Prepared according to Witulski rearrangement general procedure from Bb (E)-4-methyl-N-(2-(4-methylstyril)phenyl)benzenesulfonylamide (1.01 g, 2.67 mmol); silica gel purification (EtOAc: petroleum ether = 1:50, Rf(EtOAc/petroleum ether (1:5)) = 0.68); yield: 24% (0.26 g, yellow oil); 1H NMR (400 MHz, CDCl3) δ 2.28 (s, 3 H), 2.38 (s, 3 H), 2.88 (s, 1 H), 6.92 (d, J = 16.3 Hz, 1 H), 6.96 (d, J = 16.3 Hz, 1 H), 7.13 (d, J = 8 Hz, 2 H), 7.19-7.22 (m, 4 H), 7.23-7.25 (m, 2 H), 7.39 (td, J1 = 7.5 Hz, J2 = 1.4 Hz, 1 H), 7.69-7.72 (m, 3 H); 13C NMR (100 MHz, CDCl3) δ 21.4, 21.7, 58.8, 76.9, 121.9, 126.3, 126.9, 128.2, 128.4, 129.4, 129.9, 131.2, 134.18, 134.20, 135.3, 136.4, 138.1, 145.4 (two carbon signals are missing due to the overlapping); FT-IR (KBr) ν 3297, 2925, 2130, 1373, 1172, 963, 804, 584 cm⁻¹; HRMS (ESI⁺) m/z calcd for C24H22NO2S⁺ [M+H]+ 388.1366 found 388.1362.

(E)-N-Ethynyl-N-(2-(4-methoxystyril)phenyl)-4-methylbenzenesulfonylamide (6c)

Prepared according to Witulski rearrangement general procedure from Bc (E)-N-(2-(4-methoxystyril)phenyl)-4-methylbenzenesulfonylamide (0.95 g, 2.49 mmol); silica gel purification (EtOAc: petroleum ether = 1:50, Rf(EtOAc/petroleum ether (1:5)) = 0.65); yield: 52% (0.52 g, yellow oil); 1H NMR (400 MHz, CDCl3) δ 2.28 (s, 3 H), 2.88 (s, 1 H), 3.84 (s, 3 H), 6.86 (dd, J1 = 6.8 Hz, J2 = 2 Hz, 2 H), 6.89 (d, J = 5.0 Hz, 2 H), 7.18 (dd, J1 = 8.0 Hz, J2 = 1.4 Hz, 1 H), 7.21-7.25 (m, 4 H), 7.25-7.26 (m, 1 H), 7.37 (td, J1 = 7.5 Hz, J2 = 1.4 Hz, 1 H), 7.70 (tt, J1 = 8.4 Hz, J2 = 1.6 Hz, 3 H); 13C NMR (100 MHz, CDCl3) δ 21.7, 55.5, 58.8, 77.0, 114.1, 120.8, 126.1, 128.0, 128.2, 128.4, 129.8, 130.7, 134.2, 135.2, 136.6, 145.3, 159.7 (three carbon signals are missing due to the overlapping); FT-IR (KBr) ν 2130, 1634, 1607, 1512, 1373, 1265, 1174, 1090, 1032, 764, 748, 585, 541 cm⁻¹; HRMS (ESI⁺) m/z calcd for C24H22NO2S⁺ [M+H]+ 404.1315 found 404.1313.

(E)-N-(2-(4-Chlorostyril)phenyl)-N-ethyl-4-methylbenzenesulfonylamide (6d)

Prepared according to Witulski rearrangement general procedure from Bd (E)-N-(2-(4-chlorostyril)phenyl)-4-methylbenzenesulfonylamide (1.37 g, 3.46 mmol); silica gel purification (EtOAc: petroleum ether = 1:50, Rf(EtOAc/petroleum ether (1:5)) = 0.63); yield: 32% (0.45 g, yellow solid); m.p. 119.0 °C; 1H NMR (400 MHz, CDCl3) δ 2.26 (s, 3 H), 2.85 (s, 1 H), 6.86 (d, J = 16.2 Hz, 1 H), 6.98 (d, J = 16.3 Hz, 1 H), 7.13
(dd, $J_1 = 7.9$ Hz, $J_2 = 1.0$ Hz, 1 H), 7.19 (d, $J = 8.4$ Hz, 3 H), 7.21-7.25 (m, 4 H), 7.35 (td, $J_1 = 7.9$ Hz, $J_2 = 1.0$ Hz, 1 H), 7.66 (d, $J = 8.3$ Hz, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 21.7, 58.9, 76.9, 123.6, 126.3, 128.1, 128.4, 128.7, 128.8, 129.7, 129.79, 129.85, 129.9, 133.7, 134.0, 135.5, 135.6, 135.9, 145.4; FT-IR (KBr) $\tilde{\nu}$ 3293, 3267, 3056, 2126, 1596, 1491, 1450, 1367, 1245, 1185, 1165, 1088, 971, 924, 815, 675, 583 cm$^{-1}$; HRMS (ESI$^+$) m/z calcd for C$_{23}$H$_{19}$ClNO$_2$S$^+$ [M+H]$^+$ 408.0820 found 408.0795.

(E)-N-Ethynyl-N-(2-styrylphenyl)methanesulfonamide (6h)

Prepared according to Witulski rearrangement general procedure from Bh (E)-N-(2-styrylphenyl)methanesulfonamide (1.75 g, 6.41 mmol); silica gel purification (EtOAc: petroleum ether = 1:50, R$_f$ (EtOAc/petroleum ether (1:5)) = 0.69); yield: 34% (0.65 g, white solid); m.p. 153.2 °C; $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 2.97 (s, 1 H), 3.24 (s, 3 H), 7.17 (d, $J = 16.3$ Hz, 1 H), 7.31 (t, $J = 7.3$ Hz, 1 H), 7.34-7.36 (m, 1 H), 7.37-7.41 (m, 2 H), 7.45 (d, $J = 7.9$ Hz, 2 H), 7.52 (d, $J = 16.3$ Hz, 1 H), 7.57 (d, $J = 7.4$ Hz, 2 H), 7.81 (d, $J = 8.1$ Hz, 1 H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 38.5, 59.3, 76.3, 123.0, 126.9, 127.0, 128.5, 128.8, 129.0, 130.2, 132.3, 135.3, 136.6, 136.9 (one carbon signal is missing due to the overlapping); FT-IR (KBr) $\tilde{\nu}$ 3280, 3013, 2928, 2854, 2129, 1352, 1164, 960, 762, 691, 549, 521 cm$^{-1}$; HRMS (ESI$^+$) m/z calcd for C$_{17}$H$_{16}$NO$_2$S$^+$ [M+H]$^+$ 298.0896 found 298.0894.

(E)-N-Ethynyl-4-nitro-N-(2-styrylphenyl)benzenesulfonamide (6i)

Prepared according to Witulski rearrangement general procedure from Bi (1.14 g, 3 mmol), silica gel purification (EtOAc: petroleum ether = 1:50, then 1:30, R$_f$ (EtOAc/petroleum ether (1:5)) = 0.57); yield: 57% (0.69 g, yellow solid); m.p. 164.3 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 2.98 (s, 1 H), 6.83 (d, $J = 16.2$ Hz, 1 H), 6.91 (d, $J = 16.2$ Hz, 1 H), 7.19-7.21 (m, 2 H), 7.22-7.27 (m, 4 H), 7.28-7.32 (m, 1 H), 7.38-7.44 (m, 1 H), 7.62-7.68 (m, 1 H), 7.94 (d, $J = 8.9$ Hz, 2 H), 8.12 (d, $J = 8.9$ Hz, 2 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 59.8, 75.8, 122.5, 124.3, 126.6, 126.8, 128.7, 128.8, 128.9, 129.5, 130.0, 130.5, 132.1, 134.6, 136.2, 136.4, 142.4, 150.6; FT-IR (KBr) $\tilde{\nu}$ 3276, 3104, 2255, 2131, 1528, 1372, 1349, 1256, 1172, 971, 857, 758, 740, 692, 581 cm$^{-1}$; HRMS (ESI$^+$) m/z calcd for C$_{22}$H$_{17}$N$_2$O$_2$S$^+$ [M+H]$^+$ 405.0904 found 405.0908.

(E)-N-Ethynyl-N-(2-(2-methoxystyryl)phenyl)-4-methylbenzenesulfonamide (6j)
Prepared according to Witulski rearrangement general procedure from Bj (1.07 g, 2.9 mmol); silica gel purification (3.5 cm × 14 cm, ethyl acetate/petroleum ether = 1:50, then 1:30, Rf = 0.5 (EtOAc/PE = 1:5); yield: 22% (0.25 g, yellow solid); m.p. 85.4 °C; 1H NMR (500 MHz, d6-acetone) δ 2.32 (s, 3 H), 3.52 (s, 1 H), 3.93 (s, 3 H), 7.00 (td, J1 = 7.5 Hz, J2 = 0.6 Hz, 1 H), 7.06 (d, J = 8.1 Hz, 1 H), 7.18 (d, J = 16.5 Hz, 1 H), 7.24 (dd, J1 = 8 Hz, J2 = 1.2 Hz, 1 H), 7.31-7.37 (m, 3 H), 7.39-7.41 (m, 2 H), 7.43 (d, J = 16.6 Hz, 1 H), 7.51 (t, J = 7.4 Hz, 1 H), 7.74-7.76 (m, 2 H), 7.86 (dd, J1 = 8.0 Hz, J2 = 1.4 Hz, 1 H); 13C NMR (125 MHz, d6-acetone) δ 21.5, 55.9, 60.2, 77.6, 112.0, 121.4, 123.8, 126.4, 126.8, 126.9, 127.5, 128.9, 129.0, 130.2, 130.4, 130.7, 130.8, 135.1, 136.4, 137.5, 146.5, 158.1; FT-IR (KBr) ν 2975, 1597, 1492, 1462, 1350, 1246, 1167, 1091, 1049, 971, 881, 813, 753, 686, 656, 583, 568, 540 cm−1; HRMS (ESI+) m/z calcd for C24H23N3O3S+ [M+H]+ 404.3120 found 404.3122.

(E)-N-Ethynyl-N-(2-(2-(furan-3-yl)vinyl)phenyl)-4-methylbenzenesulfonamide (6k)

Prepared according to Witulski rearrangement reaction procedure from Bk (0.4 g, 1.1 mmol); silica gel purification (3.5 cm × 14 cm, ethyl acetate/petroleum ether = 1:50, then 1:30, Rf = 0.5 (EtOAc/PE = 1:5); yield: 77% (312.2 mg, yellow solid); m.p. 85.4 °C; 1H NMR (500 MHz, CDCl3) δ 2.28 (s, 3 H), 2.93 (s, 1 H), 6.98 (d, J = 16.3 Hz, 1 H), 7.07 (d, J = 16.3 Hz, 1 H), 7.23-7.26 (m, 3 H), 7.28-7.32 (m, 2 H), 7.34-7.36 (m, 2 H), 7.42 (td, J1 = 7.4 Hz, J2 = 1.0 Hz, 1 H), 7.73-7.75 (m, 3 H); 13C NMR (125 MHz, CDCl3) δ 21.6, 58.9, 76.9, 122.9, 126.3, 126.9, 128.1, 128.3, 128.4, 128.6, 129.8, 129.9, 131.2, 134.1, 135.5, 136.2, 136.9, 145.4; FT-IR (KBr) ν 2923, 2853, 2130, 1641, 1597, 1371, 1171, 1089, 1023, 962, 871, 682, 581, 544 cm−1; HRMS (ESI+) m/z calcd for C21H18N3O3S− [M+H]− 364.1007 found 364.1003.

(E)-N-Ethynyl-4-methyl-N-(4-methyl-2-styrylphenyl)benzenesulfonamide (6l)

Prepared according to Witulski rearrangement general procedure from Bi (1.86 g, 5.1 mmol); silica gel purification (3.5 cm × 14 cm, ethyl acetate/petroleum ether = 1:50, then 1:30, Rf = 0.6 (EtOAc/PE = 1:5); yield: 22% (0.44 g, brown solid); m.p. 82.0 °C; 1H NMR (500 MHz, CDCl3) δ 2.20 (s, 3 H), 2.35 (s, 3 H), 2.83 (s, 1 H), 6.89 (d, J = 16.3 Hz, 1 H), 6.94 (d, J = 16.3 Hz, 1 H), 7.01-7.06 (m, 2 H), 7.16 (d, J = 8.0 Hz, 2 H), 7.21-7.24 (m, 1 H), 7.25-7.30 (m, 4 H), 7.46 (s, 1 H), 7.66 (d, J = 8.3 Hz, 2 H); 13C
NMR (125 MHz, CDCl₃) δ 21.5, 21.6, 58.6, 77.1, 122.9, 126.7, 126.9, 128.1, 128.3, 128.6, 129.3, 129.6, 129.8, 130.8, 133.0, 134.2, 135.7, 137.0, 139.9, 145.3; FT-IR (KBr) ν 2976, 2927, 2882, 2129, 1650, 1495, 1374, 1171, 1090, 1049, 881, 812, 671, 579, 545 cm⁻¹; HRMS (ESI⁺) m/z cale for C₂₄H₂₂NO₃S⁺ [M+H]⁺ 388.1371 found 388.1372.

(E)-N-ethynyl-N-(4-methoxy-2-styrylphenyl)-4-methylbenzenesulfonamide (6m)

Prepared according to Witulski rearrangement general procedure from Bn (1.10 g, 2.9 mmol); silica gel purification (3.5 cm × 14 cm, ethyl acetate/petroleum ether = 1:50, then 1:30, Rf = 0.6 (EtOAc/PE = 1:5); yield: 50% (0.59 g, yellow solid); m.p. 132.0 °C; ¹H NMR (500 MHz, CDCl₃) δ 2.20 (s, 3 H), 2.84 (s, 1 H), 3.82 (s, 3 H), 6.76 (dd, J₁ = 8.8 Hz, J₂ = 2.9 Hz, 1 H), 6.86 (d, J = 16.3 Hz, 1 H), 6.92 (d, J = 16.3 Hz, 1 H), 7.09 (d, J = 8.8 Hz, 1 H), 7.12 (d, J = 2.8 Hz, 1 H), 7.16 (d, J = 8.1 Hz, 2 H), 7.22-7.25 (m, 2 H), 7.27-7.30 (m, 3 H), 7.66 (d, J = 8.2 Hz, 2 H); ¹³C NMR (125 MHz, CDCl₃) δ 21.7, 55.7, 58.5, 77.4, 110.8, 114.2, 123.0, 127.0, 128.2, 128.4, 128.5, 128.7, 129.9, 131.1, 131.3, 134.2, 136.8, 137.4, 145.3, 160.4; FT-IR (KBr) ν 3285, 2974, 2923, 2129, 1597, 1492, 1372, 1170, 1089, 1048, 960, 881, 812, 755, 670, 568, 545 cm⁻¹; HRMS (ESI⁺) m/z cale for C₂₄H₂₂NO₃S⁺ [M+H]⁺ 404.1320 found 404.1322.

(E)-N-Ethynyl-N-(4-fluoro-2-styrylphenyl)-4-methylbenzenesulfonamide (6n)

Prepared according to Witulski rearrangement general procedure from Bn (0.49 g, 1.3 mmol); silica gel purification (3.5 cm × 14 cm, ethyl acetate/petroleum ether = 1:50, then 1:30, Rf = 0.6 (EtOAc/PE = 1:5); yield: 82% (0.42 g, brown oil); ¹H NMR (400 MHz, CDCl₃) δ 2.19 (s, 3 H), 2.85 (d, J = 0.9 Hz, 1 H), 6.88-6.92 (m, 3 H), 7.12-7.17 (m, 3 H), 7.23-7.29 (m, 4 H), 7.31 (dd, J₁ = 9.8 Hz, J₂ = 2.9 Hz, 2 H), 7.65 (d, J = 8.3 Hz, 2 H); ¹³C NMR (100 MHz, CDCl₃) δ 21.6, 58.9, 76.7, 112.6 (d, J_CF = 24 Hz), 115.4 (d, J_CF = 23 Hz), 121.9 (d, J_CF = 2 Hz), 127.1, 128.3, 128.5, 128.7, 129.9, 131.4 (d, J_CF = 3 Hz), 131.8 (d, J_CF = 9 Hz), 132.3, 133.9, 136.4, 138.5 (d, J_CF = 9 Hz), 145.6, 163.1 (d, J_CF = 248 Hz); FT-IR (KBr) ν 3300, 3061, 2131, 1605, 1581, 1485, 1373, 1089, 961, 813, 755, 691, 671, 568, 545 cm⁻¹; HRMS (ESI⁺) m/z cale for C₂₃H₁₀FNO₂S⁺ [M+H]⁺ 392.1121 found 392.1126.

(E)-N-Ethynyl-N-(5-fluoro-2-styrylphenyl)-4-methylbenzenesulfonamide (6o)
Prepared according to Witulski rearrangement reaction procedure from Bo (0.48 g, 1.3 mmol); silica gel purification (3.5 cm × 14 cm, ethyl acetate/petroleum ether = 1:50; then 1:30, Rf = 0.6 (EtOAc/PE = 1:5); yield: 40% (0.2 g, yellow solid); m.p. 111.0 °C; 1H NMR (500 MHz, CD2COCOD3) δ 2.28 (s, 3 H), 3.56 (s, 1 H), 6.92 (d, J = 16.3 Hz, 1 H), 7.06 (dd, J1 = 9.0 Hz, J2 = 2.7 Hz, 1 H), 7.10 (d, J = 16.3 Hz, 1 H), 7.29-7.39 (m, 6 H), 7.40 (d, J = 8.0 Hz, 2 H), 7.74 (d, J1 = 8.3 Hz, J2 = 1.7 Hz, 2 H), 7.91 (dd, J1 = 8.9 Hz, J2 = 6.2 Hz, 1 H); 13C NMR (125 MHz, CD2COCOD3) δ 21.5, 61.0, 77.0, 117.4 (d, JCF = 23 Hz), 118.2 (d, JCF = 21 Hz), 122.3, 127.5, 128.8 (d, JCF = 9 Hz), 129.0, 129.5, 131.0, 132.0, 133.5 (d, JCF = 3.7 Hz), 134.8, 137.2 (d, JCF = 9 Hz), 137.7, 146.9, 162.4 (d, JCF = 249 Hz) (one carbon signal is missing due to the overlapping); FT-IR (KBr) ν 2923, 2132, 1597, 1500, 1359, 1273, 1170, 1091, 965, 752, 683, 658, 577, 541 cm−1; HRMS (ESI+) m/z calcd for C23H19FNO2S+ [M+H]+ 392.1121 found 3921121.

(E)-N-(2,4-Dichloro-6-styrylphenyl)-N-ethylbenzenesulfonylamide (6p)

Prepared according to Witulski rearrangement general procedure from Bp (0.61 g, 1.5 mmol); silica gel purification (3.5 cm × 14 cm, ethyl acetate/petroleum ether = 1:100, then 1:50, Rf = 0.5 (EtOAc/PE = 1:10); yield: 63% (0.42 g, brown solid); m.p. 146.2 °C; 1H NMR (500 MHz, CDCl3) δ 2.21 (s, 3 H), 2.87 (s, 1 H), 6.81 (d, J = 16.2 Hz, 1 H), 6.96 (d, J = 16.2 Hz, 1 H), 7.14 (d, J = 8.0 Hz, 2 H), 7.18-7.21 (m, 2 H), 7.24-7.28 (m, 3 H), 7.34 (d, J = 2.3 Hz, 1 H), 7.55 (d, J = 2.3 Hz, 1 H), 7.77 (d, J = 8.3 Hz, 2 H); 13C NMR (125 MHz, CDCl3) δ 21.7, 59.3, 75.2, 121.8, 124.6, 127.2, 128.6, 128.7, 128.9, 129.0, 129.8, 131.8, 133.9, 134.7, 136.0, 136.1, 136.7, 140.1, 145.6; FT-IR (KBr) ν 2965, 2869, 2131, 155, 1152, 1451, 1377, 1171, 1087, 963, 812, 756, 661, 600, 578, 542 cm−1; HRMS (ESI+) m/z calcd for C23H18Cl2NO2S+ [M+H]+ 442.0435 found 442.0435.

(E)-N-Ethyl-4-methyl-N-(3-methyl-2-styrylphenyl)benzenesulfonylamide (6q)

Prepared according to Witulski rearrangement general procedure from Bq (1.0 g, 2.9 mmol); silica gel purification (3.5 cm × 14 cm, ethyl acetate/petroleum ether = 1:50; then 1:30, Rf = 0.6 (EtOAc/PE = 1:5); yield: 19% (0.21 g, brown oil); 1H NMR (400 MHz, CD2COCOD3) δ 2.34 (s, 3 H), 2.44 (s, 3 H), 3.42 (s, 1 H), 6.82 (d, J = 16.8 Hz, 1 H), 7.03 (d, J = 7.5 Hz, 1 H), 7.09 (d, J = 16.8 Hz, 1 H), 7.22 (t, J = 7.9 Hz, 1 H), 7.28-7.33 (m, 4 H), 7.35-7.39 (m, 2 H), 7.44-7.46 (m, 2 H), 7.72 (d, J = 8.4 Hz, 2 H); 13C NMR (100 MHz, CD2COCOD3) δ 21.4, 21.6, 60.1, 78.0, 123.8, 127.3, 128.3, 128.7, 128.9, 129.3, 130.6, 132.6, 135.5, 136.1, 137.3, 137.5, 138.1, 139.1, 146.1 (one carbon signal is missing due to the overlapping); FT-IR (KBr) ν 3032, 2974, 2926, 2860, 1708, 1598, 1496, 1472, 1352, 1167, 1092, 974, 814, 770, 748, 698, 669, 565, 541 cm−1;
HRMS (ESI⁺) m/z calcd for C₂₅H₂₂NO₂S⁺ [M+H]⁺ 388.1371 found 388.1369.

General procedure for copper-mediated Sonogashira coupling of terminal ynamide

A flame-dried 10-mL Schlenk tube was charged with 6a (149 mg, 0.4 mmol) and 2 mL of pyridine. The solution was cooled at -35 °C while 0.4 mL of LiHMDS solution (1 M in THF, 0.40 mmol) was added via syringe over 4 min. The reaction mixture was stirred at 0 °C for 30 min, before CuI (0.076 g, 0.4 mmol) was added in one portion under nitrogen purge. It was stirred at 0 °C for 2 h. A solution of iodoarene (0.4 mmol) and Pd(PPh₃)₄ (23 mg, 0.02 mmol) in THF solution (2 mL) was then added via syringe, and the resulting mixture was stirred at room temperature overnight. The reaction mixture was diluted with 50 mL of Et₂O and washed with three 50-mL portions of saturated NaCl. The combined organic layers were dried over MgSO₄, filtered, and concentrated. Column chromatography on silica gel provided the desired ynamides 6e-6g.

(E)-4-Methyl-N-(phenylethynyl)-N-(2-styrylphenyl)benzenesulfonamide (6e)

Prepared according to Sonogashira coupling general procedure from 6a (149 mg, 0.4 mmol); silica gel purification (EtOAc: petroleum ether = 1:60, Rf (EtOAc/petroleum ether (1:5)) = 0.77); yield: 57% (103 mg, yellow oil); ¹H NMR (400 MHz, CDCl₃) δ 2.28 (s, 3 H), 6.98 (d, J = 16.2 Hz, 1 H), 7.10 (d, J = 16.3 Hz, 1 H), 7.24 (d, J = 8.1 Hz, 2 H), 7.25-7.26 (m, 2 H), 7.27-7.29 (m, 4 H), 7.32-7.33 (m, 4 H), 7.34-7.35 (m, 1 H), 7.36-7.37 (m, 1 H), 7.41 (m, 1 H), 7.75 (t, J = 8.4 Hz, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 21.7, 70.4, 83.5, 122.9, 123.3, 126.4, 126.9, 128.08, 128.12, 128.38, 128.40, 128.5, 128.7, 129.7, 129.9, 130.0, 131.1, 131.7, 134.2, 136.25, 136.27, 137.1, 145.3; FT-IR (KBr) v 2247, 1705, 1654, 1598, 1495, 1452, 1359, 1170, 1087, 965, 815, 761, 692, 566, 536 cm⁻¹; HRMS (ESI⁺) m/z calcd for C₂₀H₂₄NO₂S⁺ [M+H]⁺ 450.1522 found 450.1521.

(E)-4-Methyl-N-(2-styrylphenyl)-N-(p-tolylethynyl)benzenesulfonamide (6f)

Prepared according to Sonogashira coupling general procedure from 6a (149 mg, 0.4 mmol); silica gel purification (EtOAc: petroleum ether = 1:60, Rf (EtOAc/petroleum ether (1:5)) = 0.78); yield: 52% (97 mg, yellow oil); ¹H NMR (500 MHz, CDCl₃) δ 2.22
(s, 3 H), 2.27 (s, 3 H), 6.92 (dd, J₁ = 16.3 Hz, J₂ = 4.1 Hz, 1 H), 7.02 (d, J = 7.9 Hz, 2 H), 7.06 (d, J = 16.3 Hz, 1 H), 7.17-7.19 (m, 3 H), 7.21-7.25 (m, 6 H), 7.27-7.28 (m, 3 H), 7.33-7.35 (m, 1 H), 7.71 (d, J₁ = 8.4 Hz, J₂ = 1.9 Hz, 2 H); ¹³C NMR (125 MHz, CDCl₃) δ 21.6, 21.7, 70.4, 82.8, 119.6, 123.4, 126.3, 126.9, 128.1, 128.4, 128.5, 128.6, 129.1, 129.6, 129.8, 131.0, 131.7, 131.8, 134.1, 136.2, 136.3, 137.1, 138.3, 145.2; FT-IR (KBr) 2238, 1597, 1495, 1451, 1372, 1261, 1173, 1090, 1069, 963, 815, 759, 691, 583 cm⁻¹; HRMS (ESI⁺) m/z calcd for C₃₀H₂₆NO₂S⁺ [M+H]+' 464.1679 found 464.1677.

(E)-N-((4-(tert-Butyl)phenyl)ethynyl)-4-methyl-N-(2-styrylphenyl)benzenesulfonamide (6g)

Prepared according to Sonogashira coupling general procedure from 6a (149 mg, 0.4 mmol); silica gel purification (EtOAc: petroleum ether = 1:60, Rf (EtOAc/petroleum ether (1:5)) = 0.78); yield: 42% (85 mg, yellow solid); m.p. 126.4 °C; ¹H NMR (400 MHz, CDCl₃) δ 1.30 (s, 9 H), 2.28 (s, 3 H), 6.97 (d, J = 16.2 Hz, 1 H), 7.11 (d, J = 16.3 Hz, 1 H), 7.23 (d, J = 8.0 Hz, 2 H), 7.27-7.28 (m, 2 H), 7.28-7.29 (m, 1 H), 7.29-7.30 (m, 4 H), 7.31-7.33 (m, 4 H), 7.38-7.42 (m, 1 H), 7.74 (tt, J₁ = 8.4 Hz, J₂ = 1.6 Hz, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 21.7, 31.3, 34.9, 70.4, 82.8, 119.7, 123.4, 125.4, 126.3, 127.0, 128.1, 128.4, 128.5, 128.7, 129.6, 129.8, 130.0, 131.0, 131.7, 134.2, 136.2, 136.4, 137.1, 145.2, 151.5; FT-IR (KBr) 2238, 1597, 1495, 1451, 1373, 1174, 1114, 1090, 962, 835, 813, 759, 691, 658, 581, 542 cm⁻¹; HRMS (ESI⁺) m/z calcd for C₃₃H₃₂NO₂S⁺ [M+H]+' 506.2148 found 506.2146.

Procedure of chlorotrimethylsilane-mediated hydrochlorination of ynamide (E)-N-(1-Chlorovinyl)-4-methyl-N-(2-styrylphenyl)benzenesulfonamide (7a)

![Chemical structure of 7a](Image)

To a solution of the substrate 6a (0.15 mmol, 1 equiv.) in moist THF (3 mL) was injected TMSCl (trimethyl chlorosilane) (16 μL, 0.18 mmol, 1.2 equiv) dropwise under nitrogen at -78 °C. The resulting mixture was warmed up gradually and stirred at 0 °C for 6 h until complete conversion of 6a monitored by TLC. The mixture was concentrated in rotavap to afford the crude 7a quantitatively. Column chromatography on silica gel (EtOAc: n-hexane = 1:50, Rf (EtOAc/petroleum ether (1:5)) = 0.78) provided the desired alkenyl chloro-ynamide 7a; yield 92% (56.4 mg, white solid); m.p. 97.7 °C; ¹H NMR (400 MHz, CDCl₃) δ 2.30 (s, 3 H), 5.35 (d, J = 1.9 Hz, 1 H), 5.51 (d, J = 1.9 Hz, 1 H), 6.93 (d, J = 16.3 Hz, 1 H), 7.13 (dd, J₁ = 8.0 Hz, J₂ = 1.2 Hz, 1 H), 7.16-7.22 (m, 5 H), 7.26 (t, J = 7.1 Hz, 2 H), 7.30-7.35 (m, 3 H), 7.66 (dt, J₁ = 8.4 Hz, J₂ = 1.5 Hz, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 21.7, 116.7, 124.0, 126.5, 126.9,
Notice: alkenyl chloro-enamides are sensitive in silica gel and moisture, it decomposed partially to acetamide after flash chromatography. Hence, except for isolation of 7a, all crude alkenyl chloro-enamides 7 were concentrated in rotavap and used directly for cyclisation without further purification. Crude 7a and purified 7a both gave reproducible yields of 8a.

**Procedure of synthesizing**

**N-****((E)-1,2-Dichlorovinyl)**-4-methyl-N-(2-**((E)-styryl)phenyl)**benzenesulfonamide 9r

\[
\text{Ba} \xrightarrow{\text{K}_2\text{CO}_3 (3 \text{ equiv.}) \text{ DMF, 70 °C, overnight}} 92\% \text{ Cl} \xrightarrow{\text{K}_2\text{CO}_3 (3 \text{ equiv.}) \text{ DMF, 70 °C, overnight}} 92\% \\
\]

To a stirring suspension of Ba (0.828 g, 2.5 mmol), powdered K₂CO₃ (1.04 g, 7.5 mmol, 3 equiv.) in DMF (3 mL) at 70 °C, was added trichloroethylene (0.65 mL, 7.5 mmol, 3 equiv.) dropwise over 10 minutes. The resulting mixture was stirred at 70 °C until reaction completion (8 h), as analysed by TLC. Upon cooling to room temperature, the mixture was partitioned between EtOAc and H₂O, the organic layer was separated and further washed with water (×3). The organic layer was then dried (Na₂SO₄), filtered and concentrated in vacuo. Column chromatography on silica gel (EtOAc: petroleum ether = 1:60, then 1:40, Rf (EtOAc/petroleum ether (1:5)) = 0.72) provided the desired dichloroenamide 9r; yield 92% (56.4 mg, yellow solid); m.p. 153.5 °C; ¹H NMR (500 MHz, CDCl₃) δ 2.23 (s, 3 H), 6.35 (s, 1 H), 6.82 (d, J = 16.3 Hz, 1 H), 7.11 (d, J = 8.1 Hz, 2 H), 7.15-7.20 (m, 2 H), 7.25 (t, J = 7.5 Hz, 2 H), 7.30 (d, J = 7.2 Hz, 2 H), 7.33 (t, J = 7.6 Hz, 1 H), 7.37 (d, J = 8.0 Hz, 1 H), 7.43 (d, J = 16.4 Hz, 1 H), 7.59 (d, J = 8.3 Hz, 2 H), 7.76 (dd, J₁ = 7.9 Hz, J₂ = 1.1 Hz, 1 H); ¹³C NMR (125 MHz, CDCl₃) δ 21.7, 119.3, 124.9, 126.4, 127.0, 127.8, 128.0, 128.7, 128.9, 129.6, 130.0, 130.9, 132.4, 134.9, 135.6, 137.1, 138.4, 145.0 (one carbon signal is missing due to the overlapping); FT-IR (KBr) ʋ 3024, 1597, 1494, 1480, 1449, 1365, 1168, 1075, 964, 812, 760, 661, 598, 544 cm⁻¹, HRMS (ESI⁺) m/z calcd for C_{23}H_{20}Cl₂NO₂S⁺ [M+H]⁺ 444.0586 found 444.0593.

**PdCl₂ catalyzed one-pot stepwise protocol for cascade cyclization of aromatic 1,6-enynamides**

\[
\text{6} \xrightarrow{\text{TMSCl, THF, 0 °C, 6 h}} \text{PdCl₂ (cat.) K₂CO₃ (2 equiv.) i-PrOH or 1,4-dioxane, 80 °C, 8 h}} \\
\]

To a solution of the substrate 6 (0.15 mmol, 1 equiv.) in moist THF (3 mL) in an round
bottom-flask was added TMSCl (trimethyl chlorosilane) (23 μL, 0.18 mmol, 1.2 equiv.) drop-wise under nitrogen at -78 °C. The resulting mixture was warmed up gradually and stirred at 0 °C for 6 h until complete conversion of 6 monitored by TLC. The crude 7 was then concentrated in rotavap, dissolved in i-PrOH (condition (A)) or 1,4-dioxane (condition (B)) and transferred into a flame-dried 10 mL Schlenk tube.

**Condition (A)** To a solution of crude 7 (0.15 mmol, 1 equiv.) in i-PrOH (1.5 mL, 0.1 M) were added PdCl₂ (5.4 mg, 0.030 mmol, 20 mol %), and K₂CO₃ (41.5 mg, 3 mmol, 2 equiv.) under a balloon pressure of nitrogen. After being stirred at 80 °C for 8 hours, the reaction mixture was concentrated in vacuo. The residue was purified by column chromatography on silica gel to afford the corresponding product. Yields are for the overall yields.

**Condition (B)** To a solution of crude 7 (0.15 mmol, 1 equiv.) in 1,4-dioxane (1.5 mL, 0.1 M) were added PdCl₂ (5.4 mg, 0.030 mmol, 20 mol %), and K₂CO₃ (41.5 mg, 3 mmol, 2 equiv.) under a balloon pressure of nitrogen. After being stirred at 80 °C for 8 hours, the reaction mixture was concentrated in vacuo. The residue was purified by column chromatography on silica gel to afford the corresponding product. Yields are for the overall yields.

### 3-Benzyl-2-methyl-1-tosyl-1H-indole (8a)

![3-Benzyl-2-methyl-1-tosyl-1H-indole](image)

Prepared according to one-pot stepwise protocol from 6a (56 mg, 0.15 mmol); silica gel purification (EtOAc: petroleum ether = 1:60, Rᵋ(EtOAc/petroleum ether (1:5)) = 0.87) to afford the product in condition (A) yield: 79% (44 mg, yellow oil), condition (B) yield: 50% (28 mg); ¹H NMR (400 MHz, CDCl₃) δ 2.34 (s, 3 H), 2.57 (s, 3 H), 3.96 (s, 2 H), 7.02 (dd, J₁ = 8.0 Hz, J₂ = 1.3 Hz, 2 H), 7.12-7.16 (m, 2 H), 7.17-7.20 (m, 4 H), 7.25 (t, J = 7.9 Hz, 2 H), 7.61 (d, J = 8.4 Hz, 2 H), 8.20 (dd, J₁ = 8.0 Hz, J₂ = 1.6 Hz, 1 H); ¹³C NMR (100 MHz, CDCl₃) δ 13.1, 21.7, 30.0, 114.9, 118.9, 119.3, 123.5, 124.2, 126.2, 126.4, 128.1, 128.5, 129.9, 130.8, 133.9, 136.3, 136.8, 139.6, 144.7; FT-IR (KBr) ν 1598, 1494, 1453, 1362, 1173, 1089, 989, 913, 811, 745, 690, 658, 576, 541 cm⁻¹; HRMS (ESI⁺) m/z calcd for C₂₃H₂₂NO₂S⁺ [M+H]⁺ 376.1366 found 376.1358.

### 2-Methyl-3-(4-methylbenzyl)-1-tosyl-1H-indole (8b)

![2-Methyl-3-(4-methylbenzyl)-1-tosyl-1H-indole](image)

Prepared according to one-pot stepwise protocol from 6b (58 mg, 0.15 mmol); silica gel purification (EtOAc: petroleum ether = 1:60, Rᵋ(EtOAc/petroleum ether (1:5)) = 0.87) to afford the product in condition (A) yield: 58% (34 mg, yellow oil); condition (B) yield: 18% (11 mg); ¹H NMR (400 MHz, CDCl₃) δ 2.29 (s, 3 H), 2.36 (s, 3 H), 2.58 (s,
3 H), 3.94 (s, 2 H), 6.93 (d, \( J = 8.0 \) Hz, 2 H), 7.01 (d, \( J = 7.9 \) Hz, 2 H), 7.16 (d, \( J = 7.4 \) Hz, 1 H), 7.20 (d, \( J = 8.6 \) Hz, 2 H), 7.24-7.27 (m, 1 H), 7.28-7.29 (m, 1 H), 7.63 (d, \( J = 8.3 \) Hz, 2 H), 8.21 (d, \( J = 8.3 \) Hz, 1 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 13.1, 21.1, 21.7, 29.6, 114.9, 118.9, 119.5, 123.5, 124.1, 124.6, 128.0, 129.2, 129.9, 130.8, 133.8, 135.7, 136.4, 136.5, 136.8, 144.7; FT-IR (KBr) \( \tilde{\nu} \) 2996, 2925, 2858, 1599, 1513, 1452, 1363, 1236, 1176, 1090, 810, 747 cm\(^{-1}\); HRMS (ESI) m/z calcd for C\(_{24}\)H\(_{22}\)NO\(_2\)S\(^{-}\) [M-H]\(^{-}\] 388.1377 found 388.1363.

3-(4-Methoxybenzyl)-2-methyl-1-tosyl-1H-indole (8c)

![Structure of 3-(4-Methoxybenzyl)-2-methyl-1-tosyl-1H-indole (8c)]

Prepared according to one-pot stepwise protocol from 6c (60 mg, 0.15 mmol); silica gel purification (EtOAc: petroleum ether = 1:80, then 1:60, R\(_f\) (EtOAc/petroleum ether (1:5)) = 0.81) to afford the product in condition (A) yield: 73% (44 mg, yellow solid); condition (B) yield: 42% (26 mg); m.p. 143 °C; \(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta \) 2.39 (s, 3 H), 2.60 (s, 3 H), 3.78 (s, 3 H), 3.94 (s, 2 H), 6.76 (d, \( J = 8.6 \) Hz, 2 H), 6.97 (d, \( J = 8.6 \) Hz, 2 H), 7.19 (t, \( J = 7.5 \) Hz, 1 H), 7.22 (d, \( J = 8.2 \) Hz, 2 H), 7.29 (d, \( J = 6.2 \) Hz, 2 H), 7.65 (d, \( J = 8.3 \) Hz, 2 H), 8.23 (d, \( J = 8.2 \) Hz, 1 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 13.1, 21.7, 29.1, 55.4, 113.9, 114.9, 118.9, 119.6, 123.5, 124.1, 126.4, 129.0, 129.9, 130.7, 131.6, 133.7, 136.3, 136.8, 144.7, 158.0; FT-IR (KBr) \( \tilde{\nu} \) 2957, 2928, 1611, 1511, 1454, 1362, 1246, 1175, 1120, 1090, 1034, 990, 812, 748, 706, 690, 660, 568, 542 cm\(^{-1}\); HRMS (ESI) m/z calcd for C\(_{24}\)H\(_{22}\)NO\(_2\)S\(^{-}\) [M-H]\(^{-}\] 404.1320 found 404.1327.

3-(4-Chlorobenzyl)-2-methyl-1-tosyl-1H-indole (8d)

![Structure of 3-(4-Chlorobenzyl)-2-methyl-1-tosyl-1H-indole (8d)]

Prepared according to one-pot stepwise protocol from 6d (61 mg, 0.15 mmol); silica gel purification (EtOAc: petroleum ether = 1:60, R\(_f\) (EtOAc/petroleum ether (1:5)) = 0.85) to afford the product in condition (A) yield: 56% (34 mg, yellow oil), condition (B): trace; \(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta \) 2.37 (s, 3 H), 2.57 (s, 3 H), 3.94 (s, 2 H), 6.96 (d, \( J = 8.5 \) Hz, 2 H), 7.15-7.17 (m, 2 H), 7.18-7.21 (m, 3 H), 7.23 (d, \( J = 7.5 \) Hz, 1 H), 7.28 (tt, \( J_1 = 8.5 \) Hz, \( J_2 = 1.3 \) Hz, 1 H), 7.64 (d, \( J = 8.4 \) Hz, 2 H), 8.23 (d, \( J = 8.4 \) Hz, 1 H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \( \delta \) 13.1, 21.7, 29.4, 114.9, 118.7, 118.8, 123.6, 124.3, 126.4, 128.6, 129.4, 129.9, 130.5, 131.9, 133.9, 136.2, 136.7, 138.0, 144.8; FT-IR (KBr) \( \tilde{\nu} \) 3049, 2963, 2927, 2856, 1911, 1725, 1598, 1491, 1453, 1364, 1237, 1175, 1091, 989, 748, 660 cm\(^{-1}\); HRMS (ESI) m/z calcd for C\(_{23}\)H\(_{19}\)ClNO\(_2\)S\(^{-}\) [M-H]\(^{-}\] 408.0825 found 408.0821.

3-Benzyl-2-phenyl-1-tosyl-1H-indole (8e)
Prepared according to one-pot stepwise protocol from 6e (67 mg, 0.15 mmol); silica gel purification (EtOAc: petroleum ether = 1:60, Rf (EtOAc/petroleum ether (1:5)) = 0.82); to afford the product in condition (A) yield: 77% (52 mg, yellow oil); condition (B) yield 70% (47 mg); ¹H NMR (500 MHz, CDCl₃) δ 2.32 (s, 3 H), 4.10 (s, 2 H), 4.55 (s, 2 H), 7.03-7.06 (m, 4 H), 7.15-7.16 (m, 2 H), 7.18-7.23 (m, 7 H), 7.31-7.38 (m, 4 H), 8.25 (d, J = 8.4 Hz, 1 H); ¹³C NMR (125 MHz, CDCl₃) δ 21.6, 30.1, 31.6, 115.4, 119.4, 121.3, 123.6, 124.5, 126.26, 126.29, 126.5, 128.2, 128.46, 128.50, 129.5, 130.7, 135.8, 136.1, 137.0, 138.7, 139.2, 144.4 (one carbon signal is missing due to the overlapping); FT-IR (KBr) ʋ 1599, 1494, 1453, 1365, 1256, 1170, 1150, 1122, 1090, 1028, 957, 812, 747, 701, 661, 581, 540 cm⁻¹; HRMS (ESI⁺) m/z calcd for C₂₀H₂₆NO₂S⁺ [M+H]⁺ 452.1679 found 452.1681.

3-Benzyl-2-(4-methylbenzyl)-1-tosyl-1H-indole (8f)

Prepared according to one-pot stepwise protocol from 6f (69 mg, 0.15 mmol); silica gel purification (EtOAc: petroleum ether = 1:60, Rf (EtOAc/petroleum ether (1:5)) = 0.81) to afford the product in condition (A) yield: 47% (33 mg, yellow oil), condition (B) yield: 50% (35 mg); ¹H NMR (400 MHz, CDCl₃) δ 2.18 (s, 3 H), 2.31 (s, 3 H), 4.07 (s, 2 H), 4.48 (s, 2 H), 6.79 (s, 1 H), 6.95-7.00 (m, 3 H), 7.02-7.05 (m, 3 H), 7.10 (t, J = 7.6 Hz, 1 H), 7.16-7.23 (m, 4 H), 7.30-7.34 (m, 4 H), 8.23 (d, J = 8.3 Hz, 1 H); ¹³C NMR (100 MHz, CDCl₃) δ 21.4, 21.6, 30.2, 31.5, 115.4, 119.4, 121.2, 123.6, 124.5, 125.7, 126.3, 126.6, 127.0, 128.3, 128.4, 128.5, 129.1, 129.5, 130.7, 136.0, 136.2, 137.1, 138.5, 139.3, 144.3; FT-IR (KBr) ʋ 1599, 1494, 1453, 1365, 1260, 1230, 1169, 1149, 1122, 1090, 1028, 956, 811, 746, 660, 582, 542 cm⁻¹; HRMS (ESI⁺) m/z calcd for C₃₀H₃₆NO₂S⁺ [M+H]⁺ 466.1835 found 466.1836.

3-Benzyl-2-(4-(tert-butyl)benzyl)-1-tosyl-1H-indole (8g)

Prepared according to one-pot stepwise protocol from 6g (76 mg, 0.15 mmol); silica gel purification (EtOAc: petroleum ether = 1:60, Rf (EtOAc/petroleum ether (1:5)) = 0.82) to afford the product in condition (A) yield: 70% (53 mg, yellow solid), condition (B) yield 43% (33 mg); m.p. 63.0 °C; ¹H NMR (500 MHz, CDCl₃) δ 1.32 (s, 9 H), 2.31 (s, 3 H), 4.09 (s, 2 H), 4.49 (s, 2 H), 7.00-7.03 (m, 4 H), 7.07 (d, J = 8.1 Hz, 2 H), 7.23 (d, J = 8.1 Hz, 2 H), 7.28-7.34 (m, 4 H), 8.21 (d, J = 8.3 Hz, 1 H); ¹³C NMR (125 MHz, CDCl₃) δ 21.6, 30.2, 31.1, 31.6, 34.5, 115.4, 119.4, 121.1, 123.6, 124.5, 125.4, 126.3, 126.6, 128.2, 128.3, 128.5, 129.5, 130.8, 135.6, 136.0, 136.5, 137.0, 139.3, 144.3, 149.2; FT-IR (KBr) ʋ 3734, 3648, 1598, 1494, 1365, 1177, 1151, 1120,
1089, 962, 811, 749, 704, 667, 580, 542 cm$^{-1}$; HRMS (ESI$^+$) m/z calcd for C$_{33}$H$_{34}$NO$_5$S$^+$ [M+H]$^+$ 508.2305 found 508.2299.

3-Benzyl-2-methyl-1-(methylsulfonyl)-1H-indole (8h)$^4$

![Chemical Structure](image)

Prepared according to one-pot stepwise protocol from 6h (45 mg, 0.15 mmol); silica gel purification (EtOAc: petroleum ether = 1:60, R$_f$(EtOAc/petroleum ether (1:5)) = 0.76) to afford the product in condition (A) yield: 49% (22 mg, white solid); Condition (B) yield 10% (5 mg); m.p. 76.0 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 2.58 (s, 3 H), 3.02 (s, 3 H), 4.05 (s, 2 H), 7.16-7.21 (m, 3 H), 7.23-7.28 (m, 4 H), 7.37 (d, $J$ = 7.5 Hz, 1 H), 8.02 (d, $J$ = 8.2 Hz, 1 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 31.0, 30.1, 40.6, 114.2, 119.0, 119.1, 123.7, 124.3, 126.4, 128.2, 128.7, 130.7, 133.7, 136.2, 139.6; FT-IR (KBr) $\bar{\nu}$ 1495, 1454, 1360, 1240, 1172, 1027, 991, 961, 769, 699, 543, 514 cm$^{-1}$; HRMS (ESI$^+$) m/z calcd for C$_{17}$H$_{16}$NO$_5$S$^+$ [M-H]$^-$ 298.0907 found 298.0915. Its spectroscopic data is consistent with a literature report.$^4$

4-Benzyl-2-methyl-1-((4-nitrophenyl)sulfonyl)-1H-indole (8i)

![Chemical Structure](image)

Prepared according to one-pot stepwise protocol from 6i (61 mg, 0.15 mmol); silica gel purification (EtOAc: petroleum ether = 1:70, then 1:50, R$_f$(EtOAc/petroleum ether (1:5)) = 0.72) to afford the product in condition (A) yield: 82% (50 mg, yellow oil); Condition (B) yield 37% (22 mg); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 2.59 (s, 3 H), 3.98 (s, 2 H), 7.03 (d, $J$ = 6.8 Hz, 2 H), 7.17-7.23 (m, 4 H), 7.30 (t, $J$ = 7.5 Hz, 2 H), 7.87 (dt, $J_I$ = 8.9 Hz, $J_2$ = 2.3 Hz, 2 H), 8.15-8.17 (m, 1 H), 8.22 (dt, $J_I$ = 8.9 Hz, $J_2$ = 2.0 Hz, 2 H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 13.2, 30.0, 114.9, 119.3, 121.2, 124.5, 124.5, 124.8, 126.5, 127.6, 128.0, 128.6, 131.1, 133.5, 136.6, 139.2, 144.1, 150.6; FT-IR (KBr) $\bar{\nu}$ 2945, 2254, 1531, 1452, 1378, 1348, 1180, 1019, 990, 854, 740, 615, 574, 463 cm$^{-1}$; HRMS (ESI$^+$) m/z calcd for C$_{22}$H$_{17}$N$_2$O$_4$S$^+$ [M-H]$^-$ 405.0915 found 405.0924.

3-(2-Methoxybenzyl)-2-methyl-1-tosyl-1H-indole (8j)

![Chemical Structure](image)

Condition (A): prepared from 6j (177.5 mg, 0.44 mmol); silica gel purification (2 cm × 14 cm, ethyl acetate/petroleum ether = 1:100, then 1:50, R$_f$ = 0.6 (EtOAc/PE = 1:5); yield: 23% (40.7 mg, white solid); Condition (B): prepared from 6j (48.4 mg, 0.12 mmol), yield: 10% (4.6 mg, white solid); m.p. 122.9 °C; $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 2.36 (s, 3 H), 2.56 (s, 3 H), 3.86 (s, 3 H), 3.94 (s, 2 H), 6.66 (dd, $J_1$ = 7.5 Hz, $J_2$ = 1.6 Hz, 3 H), 7.37 (d, $J$ = 7.5 Hz, 5 H), 7.43 (d, $J$ = 8 Hz, 2 H), 7.87 (t, $J$ = 7.5 Hz, 2 H), 8.17 (d, $J$ = 8 Hz, 2 H), 8.22 (d, $J$ = 8 Hz, 2 H), 11.24 (s, 1 H), 12.81 (s, 1 H), 13.91 (s, 1 H), 14.90 (s, 1 H), 15.70 (s, 1 H), 16.50 (s, 1 H).
Hz, 1 H), 6.71 (td, J₁ = 7.5 Hz, J₂ = 0.9 Hz, 1 H), 6.85 (d, J = 8.1 Hz, 1 H), 7.14-7.18 (m, 2 H), 7.18-7.20 (m, 2 H), 7.26 (td, J₁ = 7.3 Hz, J₂ = 1.2 Hz, 1 H), 7.31 (d, J = 7.8 Hz, 1 H), 7.63 (dt, J₁ = 8.4 Hz, J₂ = 1.7 Hz, 2 H), 8.22 (d, J = 8.4 Hz, 1 H); ¹³C NMR (125 MHz, CDCl₃) δ 13.1, 21.7, 24.0, 55.4, 110.1, 114.9, 119.0, 120.4, 123.5, 124.0, 126.4, 127.3, 127.7, 128.9, 129.9, 131.1, 134.1, 136.4, 136.8, 144.6, 157.3 (one carbon signal is missing due to the overlapping); FT-IR (KBr) ν 3066, 2933, 2837, 1599, 1494, 1454, 1362, 1240, 1175, 1029, 989, 751, 659, 572, 542 cm⁻¹; HRMS (ESI⁺) m/z calcd for C₂₃H₂₁NO₃S⁺ [M-H]⁺ 404.1320 found 404.1327.

3-(Furan-3-ylmethyl)-2-methyl-1-tosyl-1H-indole (8k)

Condition (A): prepared from 6k (138.1 mg, 0.38 mmol); silica gel purification (2 cm × 14 cm, ethyl acetate / petroleum ether = 1:100, then 1:50, Rₜ = 0.6 (EtOAc/PE = 1:5); yield: 24 % (34 mg, yellow oil); Condition (B): prepared from 6k (43.6 mg, 0.12 mmol), yield: 10 % (4.4 mg, yellow oil); ¹H NMR (500 MHz, CDCl₃) δ 2.35 (s, 3 H), 2.56 (s, 3 H), 3.73 (s, 2 H), 6.13 (d, J = 0.9 Hz, 1 H), 6.93 (s, 1 H), 7.18-7.22 (m, 3 H), 7.25-7.29 (m, 2 H), 7.34 (d, J = 7.7 Hz, 1 H), 7.62 (d, J = 8.4 Hz, 2 H), 8.20 (d, J = 8.3 Hz, 1 H); ¹³C NMR (125 MHz, CDCl₃) δ 129.0, 20.0, 21.7, 110.9, 114.9, 118.6, 118.8, 123.2, 123.5, 124.2, 126.4, 129.9, 130.5, 133.4, 136.4, 136.7, 139.4, 143.1, 144.7; FT-IR (KBr) ν 2928, 1760, 1598, 1454, 1362, 1236, 1174, 1089, 1022, 747, 688, 660, 576, 542; HRMS (ESI⁺) m/z calcd for C₂₁H₂₀NO₃S⁺ [M+H]⁺ 366.1164 found 366.1166.

3-Benzyl-2,5-dimethyl-1-tosyl-1H-indole (8l)

Condition (A): Prepared from 6l (100.7 mg, 0.26 mmol); silica gel purification (2 cm × 14 cm, ethyl acetate/petroleum ether = 1:100, then 1:50, Rₜ = 0.7 (EtOAc/PE = 1:5); yield: 67% (68 mg, yellow solid); Condition (B): Prepared from 6l (43.3 mg, 0.11 mmol); yield: 23% (10 mg, yellow solid); m.p. 129.9 °C; ¹H NMR (500 MHz, CDCl₃) δ 2.36 (s, 6 H), 2.57 (s, 3 H), 3.96 (s, 2 H), 7.04 (d, J = 7.2 Hz, 2 H), 7.07-7.10 (m, 2 H), 7.17-7.23 (m, 5 H), 7.62 (d, J = 8.3 Hz, 2 H), 8.10 (d, J = 8.5 Hz, 1 H); ¹³C NMR (125 MHz, CDCl₃) δ 13.1, 21.4, 21.7, 29.9, 114.6, 118.8, 119.2, 125.5, 126.2, 126.3, 128.0, 128.5, 129.8, 131.0, 133.1, 134.0, 135.0, 136.3, 139.6, 144.5; FT-IR (KBr) ν 3027, 2924, 1599, 1494, 1453, 1373, 1237, 1174, 1128, 1089, 1001, 877, 809, 681, 583, 566, 542 cm⁻¹; HRMS (ESI⁺) m/z calcd for C₂₃H₂₂NO₃S⁺ [M-H]⁺ 388.1377 found 388.1384.

3-Benzyl-5-methoxy-2-methyl-1-tosyl-1H-indole (8m)
Condition (A): Prepared from 6m (157.4 mg, 0.39 mmol); silica gel purification (2 cm × 14 cm, ethyl acetate/petroleum ether = 1:100, then 1:50, Rf = 0.7 (EtOAc/PE = 1:5); yield: 53% (84 mg, brown solid); m.p. 122.6 °C; Condition (B): Prepared from 6m (69.8 mg, 0.17 mmol); yield: 11% (8 mg); 1H NMR (500 MHz, CDCl3) δ 2.36 (s, 3 H), 2.55 (s, 3 H), 3.74 (s, 3 H), 3.94 (s, 2 H), 6.70 (d, J = 2.4 Hz, 1 H), 6.86 (dd, J1 = 9.0 Hz, J2 = 2.5 Hz, 1 H), 7.01 (d, J = 7.2 Hz, 2 H), 7.14-7.21 (m, 5 H), 7.59 (d, J = 8.2 Hz, 2 H), 8.10 (d, J = 9.1 Hz, 1 H); 13C NMR (125 MHz, CDCl3) δ 13.2, 21.7, 30.0, 55.7, 102.0, 112.2, 115.9, 119.6, 126.2, 126.3, 128.1, 128.5, 129.8, 131.4, 132.0, 134.8, 136.1, 139.4, 144.6, 156.6; FT-IR (KBr) ν 2976, 2930, 2871, 1600, 1494, 1475, 1453, 1374, 1355, 1212, 1173, 1133, 1089, 1035, 996, 881, 811, 683, 584, 543 cm⁻¹; HRMS (ESI) m/z calcd for C24H22NO3S [M-H]⁻ 404.1326 found 404.1331.

3-Benzyl-5-fluoro-2-methyl-1-tosyl-1H-indole (8n)

Condition (A): Prepared from 6n (122.1 mg, 0.30 mmol); silica gel purification (2 cm × 14 cm, ethyl acetate/petroleum ether = 1:100, then 1:50, Rf = 0.7 (EtOAc/PE = 1:5); yield: 51% (60.2 mg, yellow oil); Condition (B): Prepared from 6n (163.8 mg, 0.42 mmol), N.R.; 1H NMR (500 MHz, CDCl3) δ 2.38 (s, 3 H), 2.58 (s, 3 H), 3.93 (s, 2 H), 6.90 (dd, J1 = 8.7 Hz, J2 = 2.6 Hz, 1 H), 6.94-6.99 (m, 1 H), 6.99-7.02 (m, 2 H), 7.15-7.24 (m, 5 H), 7.60 (d, J = 8.3 Hz, 2 H), 8.15 (dd, J1 = 9.1 Hz, J2 = 4.5 Hz, 1 H); 13C NMR (125 MHz, CDCl3) δ 13.2, 21.7, 30.0, 104.6 (d, JCF = 23.8 Hz), 111.8 (d, JCF = 24.9 Hz), 116.0 (d, JCF = 9.1 Hz), 119.3 (d, JCF = 3.8 Hz), 126.4 (d, JCF = 3.7 Hz), 127.4, 128.1, 128.6, 129.8, 130.0, 132.0 (d, JCF = 9.5 Hz), 133.0, 135.9 (d, JCF = 41.8 Hz), 136.1, 139.1, 144.9, 159.9 (d, JCF = 238.9 Hz); FT-IR (KBr) ν 3063, 2931, 1599, 1494, 1469, 1454, 1261, 1174, 1117, 1090, 910, 888, 809, 682, 583, 564, 543 cm⁻¹; HRMS (ESI) m/z calcd for C25H19FNO3S⁻ [M-H]⁻ 392.1126 found 392.1134.

3-Benzyl-6-fluoro-2-methyl-1-tosyl-1H-indole (8o)

Condition (A): Prepared from 6o (165.7 mg, 0.4 mmol); silica gel purification (2 cm × 14 cm, ethyl acetate/petroleum ether = 1:100, then 1:50, Rf = 0.7 (EtOAc/PE = 1:5); yield: 49% (80.4 mg, white solid), m.p. 151.3 °C; Condition (B): Prepared from 6o (117.4 mg, 0.3 mmol), N.R.; 1H NMR (500 MHz, CDCl3) δ 2.39 (s, 3 H), 2.58 (s, 3 H), 3.96 (s, 2 H), 6.92 (td, J1 = 8.9 Hz, J2 = 2.3 Hz, 1 H), 7.04 (d, J = 7.2 Hz, 2 H),
7.16-7.19 (m, 2 H), 7.21-7.24 (m, 4 H), 7.65 (d, J = 8.3 Hz, 2 H), 7.99 (dd, J1 = 10.5 Hz, J2 = 2.2 Hz, 1 H); 13C NMR (125 MHz, CDCl3) δ 13.1, 21.7, 30.0, 102.5 (d, JCF = 28.9 Hz), 111.6 (d, JCF = 23.8 Hz), 118.8, 119.4 (d, JCF = 9.7 Hz), 126.3, 126.4, 127.0, 128.1, 128.6, 130.0, 134.0 (d, JCF = 4.0 Hz), 136.1, 136.8 (d, JCF = 12.4 Hz), 139.3, 145.0, 160.8 (d, JCF = 238.7 Hz); FT-IR (KBr) ν 2976, 2875, 1485, 1453, 1428, 1379, 1263, 1142, 1089, 1049, 881, 803, 703, 665, 583, 544 cm⁻¹; HRMS (ESI) m/z calced for C23H16FNO2S [M-H] 392.1126 found 392.1134.

3-Benzyl-5,7-dichloro-2-methyl-1-tosyl-1H-indole (8p)

Condition (A): prepared from 6p (159.2 mg, 0.36 mmol); silica gel purification (2 cm × 14 cm, ethyl acetate/petroleum ether = 1:200, then 1:100, Rf = 0.7 (EtOAc/PE = 1:10), yield: 39% (62 mg, brown solid); m.p. 128.0 °C; Condition (B): Prepared from 6p (137.1 mg, 0.31 mmol), yield: N.R.; 1H NMR (500 MHz, CDCl3) δ 2.42 (s, 3 H), 2.55 (s, 3 H), 3.84 (s, 2 H), 6.87-6.89 (m, 2 H), 7.07 (d, J = 1.9 Hz, 1 H), 7.18-7.21 (m, 5 H), 7.25 (d, J = 2.0 Hz, 1 H), 7.53 (d, J = 8.4 Hz, 2 H); 13C NMR (125 MHz, CDCl3) δ 14.4, 21.8, 30.0, 117.4, 121.9, 123.5, 126.6, 126.7, 126.8, 128.0, 128.7, 129.7, 130.6, 134.5, 135.9, 137.1, 138.3, 140.3, 144.8; FT-IR (KBr) ν 3029, 2926, 2853, 1594, 1557, 1494, 1441, 1415, 1373, 1175, 1090, 828, 811, 699, 666, 583, 543 cm⁻¹; HRMS (ESI) m/z calced for C23H18Cl2NO2S [M-H] 442.0441 found 442.0446.

3-Benzyl-2,4-dimethyl-1-tosyl-1H-indole (8q)

Condition (A): Prepared from 6q (147.3 mg, 0.38 mmol); silica gel purification (2 cm × 14 cm, ethyl acetate/petroleum ether = 1:100, then 1:50, Rf = 0.7 (EtOAc/PE = 1:5); yield: 20% (30 mg, brown solid), m.p. 128.3 °C; Condition (B): Prepared from 6q (69.8 mg, 0.18 mmol), N.R.; 1H NMR (500 MHz, CDCl3) δ 2.36 (s, 3 H), 2.38 (s, 3 H), 2.56 (s, 3 H), 4.16 (s, 2 H), 6.92 (d, J = 7.2 Hz, 3 H), 7.14-7.22 (m, 6 H), 7.64 (d, J = 8.3 Hz, 2 H), 8.15 (d, J = 8.5 Hz, 1 H); 13C NMR (125 MHz, CDCl3) δ 12.9, 20.1, 21.7, 31.1, 112.9, 119.2, 124.0, 125.9, 126.1, 126.4, 127.8, 128.6, 129.2, 129.9, 130.3, 134.3, 136.3, 137.3, 140.1, 144.6; FT-IR (KBr) ν 2962, 1599, 1494, 1373, 1260, 1179, 1090, 1019, 967, 801, 750, 726, 677, 579, 544 cm⁻¹; HRMS (ESI) m/z calced for C24H22NO2S [M-H] 388.1377 found 388.1379.

3-Benzyl-2-(isopropoxymethyl)-1-tosyl-1H-indole (10r)
Condition (A): Prepared from 9r (66.5 mg, 0.15 mmol); silica gel purification (2 cm × 14 cm, ethyl acetate/petroleum ether = 1:100, then 1:50, Rf = 0.7 (EtOAc/PE = 1:5); yield: 52% (34 mg, yellow oil); Condition (B): Prepared from 9r (66.5 mg, 0.15 mmol), yield: trace; 1H NMR (500 MHz, CDCl3) δ 1.22 (s, 3 H), 1.23 (s, 3 H), 2.33 (s, 3 H), 3.79-3.84 (m, 1 H), 4.11 (s, 2 H), 4.91 (s, 2 H), 7.11-7.18 (m, 6 H), 7.21 (d, J = 7.3 Hz, 2 H), 7.23-7.27 (m, 1 H), 7.30 (d, J = 7.7 Hz, 1 H), 7.91 (d, J = 8.4 Hz, 2 H), 8.09 (d, J = 8.4 Hz, 1 H); 13C NMR (125 MHz, CDCl3) δ 21.7, 22.2, 30.3, 60.0, 72.0, 115.1, 119.9, 123.0, 123.4, 125.2, 126.3, 127.3, 128.4, 128.5, 129.5, 130.1, 134.5, 136.2, 136.7, 139.4, 144.5; FT-IR (KBr) 2927, 1613, 1509, 1491, 1361, 1247, 1178, 1121, 1090, 991, 813, 748, 704, 691, 660, 568, 541 cm⁻¹; HRMS (ESI⁺) m/z calcd for C26H27NaO3S⁺ [M+Na]⁺ 456.1604 found 456.1607.

2-(Z / E), 3-(Z / E)-Dibenzyldiene-1-tosylinidoline (11e)

Procedure: To a 10 mL Schlenk tube was charged 6e (67 mg, 0.15 mmol) and Pd(PPh₃)₄ (9 mg, 0.015 mmol, 10 mol%) under nitrogen protection, toluene (1.5 mL, 0.1 M) was injected to dissolve the mixture. Upon stirring at 80 °C for 6 hours, the reaction mixture was concentrated in vacuo and purified by column chromatography on silica gel (petroleum ether / ethyl acetate = 70:1, then 50:1) to afford the corresponding product: Rf = 0.81 (EtOAc/PE = 1:5); yield: 11% (7 mg, yellow oil); 1H NMR (500 MHz, CDCl3) δ (major isomer) 2.27 (s, 3 H), 6.63 (d, J = 7.9 Hz, 1 H), 7.03 (t, J = 7.3 Hz, J₂ = 0.7 Hz, 1 H), 7.11 (d, J = 8.2 Hz, 2 H), 7.17-7.25 (m, 2 H), 7.37-7.44 (m, 4 H), 7.55-7.58 (m, 1 H), 7.59-7.63 (m, 4 H), 7.77 (d, J = 8.4 Hz, 2 H), 8.13 (d, J = 8.3 Hz, 1 H), 8.35 (d, J = 8.4 Hz, 1 H), 8.81 (s, 1 H); 13C NMR (125 MHz, CDCl3) δ (major isomer) 21.6, 111.8, 115.0, 123.1, 123.8, 125.1, 126.0, 126.2, 126.4, 126.6, 126.8, 128.0, 128.3, 128.4, 128.6, 128.8, 129.3, 129.8, 130.0, 132.8, 137.0, 138.1, 140.3, 145.0; FT-IR (KBr) 3059, 2925, 1621, 1597, 1494, 1368, 1295, 1189, 1172, 1151, 1090, 1014, 960, 761, 747, 703, 692, 581 cm⁻¹; HRMS (ESI⁺) m/z calcd for C29H25N2O2S⁺ [M-H]⁻ 448.1377 found 448.1380.

2-(1-Deuterated-2-phenylethenyl)-benzenamine (A12a)

To a solution of o-idoaniline (2.19 g, 10 mmol) and 4,4,5,5-tetramethyl-2-[(1E)-2-phenylethenyl-1-d]-1,3,2-dioxaborolane⁵ (2.31 g, 10 mmol) in 1,4-dioxane (30 mL) was added Pd(PPh₃)₄ (575.10 mg, 0.50 mmol) and Cs₂CO₃ (9.74 g, 29.89 mmol). The reaction mixture was stirred at 100 °C under N₂ until TLC indicated 2-idoaniline disappeared. The reaction was quenched with water and extracted three times with ethyl acetate. The combined organic extracts were washed with H₂O, brine, and dried over Na₂SO₄. The solvent was removed in vacuo and
purified by column chromatography on silica gel (petroleum ether / ethyl acetate = 100:1, then 60:1) to afford the corresponding product: $R_f = 0.82$ (EtOAc/PE = 1:10); yield: 89% (1.74 g, yellow oil); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.66 (s, 2 H), 6.76 (d, $J = 8.0$ Hz, 1 H), 6.87 (td, $J_1 = 8.2$ Hz, $J_2 = 0.8$ Hz, 1 H), 7.02-7.06 (m, 1 H), 7.16 (t, $J = 7.8$ Hz, 1 H), 7.31 (t, $J = 7.3$ Hz, 1 H), 7.41 (t, $J = 7.4$ Hz, 2 H), 7.46 (d, $J = 7.7$ Hz, 1 H), 7.56 (d, $J = 7.7$ Hz, 2 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 116.4, 119.3, 123.9, 126.5, 127.3, 127.6, 128.78, 128.80, 130.3, 130.4, 137.7, 144.0; FT-IR (KBr) $\tilde{\nu}$ 3434, 3358, 1620, 1488, 1456, 1319, 1354, 924, 755, 705, 689, 503 cm$^{-1}$; HRMS (ESI$^+$) m/z calcd for C$_{14}$H$_{13}$DN$^+$ [M+H]$^+$ 197.1184 found 197.1185.

5-Methyl-N-[2-(1-deuterated-2-phenylethenyl) phenyl] benzenesulfonamide (B12a)

![Chemical Structure]

Prepared according to Ts protection general procedure from A12a (1.57 g, 8 mmol); silica gel purification (petroleum ether : EtOAc = 1:40 then 1:15, $R_f$ (EtOAc/petroleum ether (1:5)) = 0.60); yield: 80% (2.24 g, white solid); m.p. 138 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 2.17 (s, 3 H), 6.66-6.70 (m, 1 H), 7.02-7.04 (m, 3 H), 7.11-7.19 (m, 3 H), 7.21-7.30 (m, 5 H), 7.41-7.43 (m, 1 H), 7.54 (d, $J = 7.9$ Hz, 2 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 21.5, 122.5 (t, $J = 23.5$ Hz), 126.4, 126.8, 127.12, 127.17, 127.23, 128.0, 128.4, 128.6, 129.7, 131.8, 133.3, 133.4, 136.5, 136.8, 143.9; FT-IR (KBr) $\tilde{\nu}$ 3278, 2924, 1595, 1494, 1453, 1386, 1326, 1157, 1089, 917, 890, 813, 759, 684, 567, 536 cm$^{-1}$; HRMS (ESI$^+$) m/z calcd for C$_{21}$H$_{19}$NOS$^+$ [M+H]$^+$ 351.1272 found 351.1272.

(Z)-N-(2-(1-Deuterated-2-phenylvinyl)phenyl)-N-ethynyl-4-methylbenzenesulfonamide (12a)

![Chemical Structure]

Prepared according to Witulski rearrangement general procedure from B12a (1 g, 3 mmol); silica gel purification (ethyl acetate/petroleum ether = 1:70, then 1:50, $R_f$ = 0.75 (EtOAc/PE = 1:5); yield: 27% (0.3 g, yellow solid); m.p. 113 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 2.17 (s, 3 H), 2.83 (s, 1 H), 6.87 (s, 1 H), 7.12-7.16 (m, 3 H), 7.16-7.19 (m, 1 H), 7.19-7.22 (m, 1 H), 7.23-7.28 (m, 4 H), 7.31 (td, $J_1 = 7.6$ Hz, $J_2 = 1.6$ Hz, 1 H), 7.64 (d, $J = 7.9$ Hz, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 21.6, 58.8, 76.9, 122.5 (t, $J = 23.6$ Hz), 122.8, 126.2, 126.9, 128.1, 128.3, 128.4, 128.6, 129.81, 129.84, 131.0, 134.0, 135.4, 136.0, 136.8, 145.4; FT-IR (KBr) $\tilde{\nu}$ 2921, 2861, 2129, 1506, 1449, 1374, 1174, 1170, 1125, 1090, 1042, 585 cm$^{-1}$; HRMS (ESI$^+$) m/z calcd for C$_{23}$H$_{19}$NOS$^+$ [M+H]$^+$ 375.1272 found 351.1273.

3-(Deuterated (phenyl)methyl)-2-methyl-1-tosyl-1H-indole (13a)
Prepared according to one-pot stepwise protocol from 12a (56 mg, 0.15 mmol); silica gel purification (EtOAc: petroleum ether = 1:80, then 1:60, Rf (EtOAc/petroleum ether (1:5)) = 0.87) to afford the product in condition (B) yield: 42% (24 mg, yellow oil); 1H NMR (500 MHz, CDCl3) δ 2.34 (s, 3 H), 2.56 (s, 3 H), 3.92-3.95 (m, 0.7 H), 3.96 (s, 0.5 H), 7.02 (d, J = 6.9 Hz, 2 H), 7.11-7.15 (m, 2 H), 7.17 (d, J = 7.7 Hz, 4 H), 7.25 (d, J = 7.6 Hz, 2 H), 7.61 (d, J = 8.3 Hz, 2 H), 8.19 (dd, J1 = 8.2 Hz, J2 = 0.8 Hz, 1 H); 13C NMR (100 MHz, CDCl3) δ 13.0, 21.7, 29.7 (t, J = 19.2 Hz), 30.0, 114.9, 118.9, 119.3, 123.6, 124.2, 126.2, 126.4, 128.1, 128.5, 129.9, 130.8, 133.9, 136.4, 136.8, 139.6, 144.7; FT-IR (KBr) ʋ 1595, 1492, 1458, 1361, 1176, 1089, 991, 915, 813, 749, 687, 658, 579, 539 cm⁻¹; HRMS (ESI⁻) m/z calcd for C23H19DNO2S⁻ [M-H]⁻ 375.1283 found 375.1279.

3-Benzyl-2-(deuterated methyl)-1-tosyl-1H-indole (14a)

Condition (A): Prepared from 6a (93 mg, 0.25 mmol) in 2-propanol-d8; silica gel purification (2 cm × 14 cm, ethyl acetate/petroleum ether = 1:80, then 1:60, Rf = 0.87 (EtOAc/PE = 1:5); yield: 36% (34 mg, yellow oil); 1H NMR (500 MHz, CDCl3) δ 2.38 (s, 3 H), 2.58 (t, J = 2.1 Hz, 1.6 H), 2.60 (s, 0.5 H), 4.0 (s, 2 H), 7.06 (d, J = 7.0 Hz, 2 H), 7.16-7.24 (m, 6 H), 7.28-7.30 (m, 2 H), 7.65 (d, J = 8.4 Hz, 2 H), 8.23 (d, J = 8.1 Hz, 1 H); 13C NMR (125 MHz, CDCl3) δ 12.9 (t, J = 19.8 Hz), 13.1, 21.7, 30.0, 114.9, 118.9, 119.3, 123.5, 124.2, 126.2, 126.4, 128.1, 128.5, 129.9, 130.8, 133.9, 136.3, 136.8, 139.6, 144.7; FT-IR (KBr) ʋ 1595, 1492, 1458, 1363, 1176, 1089, 991, 915, 813, 749, 709, 687, 658, 581, 541 cm⁻¹; HRMS (ESI⁻) m/z calcd for C23H19DNO2S⁻ [M-H]⁻ 375.1283 found 375.1280.

(E)-N-(Deuterated ethynyl)-4-methyl-N-(2-styrylphenyl)benzenesulfonamide (15a)

To a solution of 6a (298 mg, 0.8 mmol) in anhydrous THF solution (10 mL) was injected n-BuLi (384 μL, 2.5 M, 0.96 mmol, 1.2 equiv.) dropwise at -78 °C under nitrogen atmosphere. After stirring for 1 hour, it was quenched by D2O (48 μL, 2.4 mmol, 3 equiv.). The combined organic mixture was extracted with H2O, brine, and dried over Na2SO4. The solvent was removed in vacuo and purified by column chromatography on silica gel (petroleum ether / ethyl acetate = 70:1, then 50:1) to afford the corresponding product: Rf = 0.74 (EtOAc/PE = 1:5); yield: 79% (236 mg, yellow oil); 1H NMR (500 MHz, CDCl3) δ 2.26 (s, 3 H), 6.94 (d, J = 16.3 Hz, 1 H), 7.01
(d, J = 16.2 Hz, 1 H), 7.21 (d, J = 7.9 Hz, 3 H), 7.25-7.28 (m, 2 H), 7.30-7.34 (m, 4 H), 7.39 (t, J = 7.7 Hz, 1 H), 7.71 (d, J = 8.1 Hz, 3 H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 21.7, 58.9, 122.9, 126.4, 127.0, 128.2, 128.41, 128.44, 128.7, 129.2, 129.88, 129.90, 129.92, 131.2, 134.2, 135.5, 136.2, 145.4; FT-IR (KBr) \(\delta\) 3294, 2131, 1597, 1495, 1451, 1372, 1171, 1090, 963, 813, 761, 690, 586, 543 cm\(^{-1}\); HRMS (ESI\(^+\)) m/z calcd for C\(_{23}\)H\(_{19}\)DNO\(_2\)S\(^+\) [M+H\(^+\)] \(375.1272\) found 375.1273.

**\((E)-N-(2,2-Dideuterated-1-chlorovinyl)-4-methyl-N-(2-styrylphenyl)benzenesulfonamide (16a)\)**

![Chemical structure of 16a]

Procedure of chlorotrimethylsilane-mediated hydrochlorination of ynamide, prepared from 15a (0.15 mmol) and D\(_2\)O (9 \(\mu\)L, 0.45 mmol, 3 equiv.), concentrated in vacuo to afford the crude product, yield: 89\% (55 mg, yellow oil), used in the next step without further purification (highly unstable, decomposed in CDCl\(_3\)).

**\((E)-N-(2,2-Dideuterated-1-isopropoxyvinyl)-4-methyl-N-(2-styrylphenyl)benzenesulfonamide (17a)\)**

**Condition (A):** Prepared from 16a (0.15 mmol); silica gel purification (2 cm \(\times\) 14 cm, ethyl acetate/petroleum ether = 1:80, then 1:60, \(R_f = 0.72\) (EtOAc/PE = 1:5); yield: 27\% (18 mg, yellow oil); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 1.04 (d, \(J = 6.8\) Hz, 3 H), 1.09 (d, \(J = 6.7\) Hz, 3 H), 2.37 (s, 3 H), 4.61-4.66 (m, 1 H), 6.98 (s, 1 H), 7.00 (d, \(J = 8.3\) Hz, 1 H), 7.21-7.25 (m, 3 H), 7.27-7.28 (m, 1 H), 7.32-7.39 (m, 4 H), 7.40-7.42 (m, 2 H), 7.66 (d, \(J = 7.3\) Hz, 2 H), 7.80 (d, \(J = 7.9\) Hz, 1 H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 21.6, 22.0, 22.1, 45.8, 102.1, 102.6, 125.6, 126.9, 127.5, 127.7, 128.7, 129.1, 129.6, 130.1, 133.1, 133.7, 137.4, 138.5, 140.1, 143.3; FT-IR (KBr) \(\delta\) 2927, 1598, 1495, 1450, 1340, 1266, 1162, 1124, 1083, 1029, 967, 925, 815, 762, 710, 692, 656, 585, 545 cm\(^{-1}\); HRMS (ESI\(^+\)) m/z calcd for C\(_{26}\)H\(_{27}\)D\(_2\)NO\(_3\)S\(_2\)\(^+\) [M+2H\(^+\)] \(209.0380\) found 209.0355.

3. Unreactive substrates

![Chemical structures of 6r, 6s, 6t, 6u, 6v, 6w, 6x, 6y]
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**\((E)-N\text{-Ethynyl-N-(2-}(4\text{-fluorostyryl})\text{phenyl)-4-methylbenzenesulfonamide} (6r)\)**

Prepared according to Witulski rearrangement general procedure from \((E)-N-(2-}(4\text{-fluorostyryl})\text{phenyl)-4-methylbenzenesulfonamide} Br (1.1 g, 2.97 mmol); silica gel purification (ethyl acetate / petroleum ether = 1:70, then 1:50, Rf = 0.68 (EtOAc/PE = 1:5); yield 37% (0.43 g, yellow solid); m.p. 115.8 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 2.30 (s, 3 H), 2.89 (s, 1 H), 6.96 (d, \(J = 16.3\) Hz, 2 H), 7.01-7.06 (m, 2 H), 7.17 (dd, \(J_1 = 7.9\) Hz, \(J_2 = 1.2\) Hz, 1 H), 7.22-7.27 (m, 3 H), 7.28-7.33 (m, 2 H), 7.39 (dt, \(J_1 = 8.1\) Hz, \(J_2 = 0.9\) Hz, 1 H), 7.70-7.72 (m, 3 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 21.7, 58.8, 76.9, 115.6 (d, \(J_{CF} = 21.6\) Hz), 122.8 (d, \(J_{CF} = 2.4\) Hz), 126.2, 128.43, 128.45, 128.5, 129.7, 129.8, 129.9, 133.2 (d, \(J_{CF} = 3.3\) Hz), 134.1, 135.5, 136.1, 137.6, 145.4, 162.7 (d, \(J_{CF} = 246.4\) Hz); FT-IR (KBr) \(\bar{\nu}\) 3300, 2966, 2925, 2925, 2131, 1597, 1509, 1372, 1232, 1170, 1091, 817, 585 cm\(^{-1}\); HRMS (ESI\(^+\)) m/z calcd for C\(_{23}\)H\(_{19}\)FNO\(_2\)S\(^+\) [M+H]\(^+\) 392.1115 found 392.1111.

**\((E)-N-(2-(3,3-Dimethylbut-1-en-1-yl)phenyl)-N-ethynyl-4-methylbenzenesulfonamide} (6s)\)**

Prepared according to Witulski rearrangement general procedure from \((E)-N-(2-(3,3-dimethylbutenyl)phenyl)-4-methylbenzenesulfonamide} Bs (0.98 g, 2.98 mmol); silica gel purification (ethyl acetate / petroleum ether = 1:70, then 1:50, Rf = 0.73 (EtOAc/PE = 1:5); yield 37% (0.39 g, yellow oil); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 1.00 (s, 3 H), 2.46 (s, 3 H), 2.82 (s, 1 H), 6.20 (s, 1 H), 7.12 (dd, \(J_1 = 8.0\) Hz, \(J_2 = 1.3\) Hz, 1 H), 7.19 (td, \(J_1 = 8.0\) Hz, \(J_2 = 1.5\) Hz, 1 H), 7.31-7.36 (m, 4 H), 7.56 (dd, \(J_1 = 7.9\) Hz, \(J_2 = 1.3\) Hz, 1 H), 7.72 (d, \(J = 8.3\) Hz, 2 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 21.8, 29.4, 33.7, 58.5, 119.6, 126.4, 127.6, 128.5, 129.3, 129.5, 129.6, 129.9, 134.5, 134.9, 136.9, 144.8, 145.1; FT-IR (KBr) \(\bar{\nu}\) 3295, 2131, 1630, 1596, 1495, 1479, 1373, 1174, 1091, 813, 759, 702, 561, 535 cm\(^{-1}\); HRMS (ESI\(^+\)) m/z calcd for C\(_{21}\)H\(_{24}\)NO\(_2\)S\(^+\) [M+H]\(^+\) 354.1522 found 354.1522.
\((E)\)-N-(2-(2-Cyclohexylvinyl)phenyl)-N-ethynl-4-methylbenzenesulfonamide (6t)

Prepared according to Witulski rearrangement general procedure from \((E)\)-N-(2-(2-cyclohexylvinyl)phenyl)-4-methylbenzenesulfonamide \(\text{Bt}\) (1.06 g, 2.98 mmol); silica gel purification (ethyl acetate / petroleum ether = 1:70, then 1:50, \(R_t = 0.71\) (EtOAc/PE = 1:5); yield 23% (0.26 g, yellow oil); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 1.01-1.10 (m, 2 H), 1.19 (tt, \(J_1 = 12.1\) Hz, \(J_2 = 3.2\) Hz, 1 H), 1.25-1.28 (m, 2 H), 1.68-1.78 (m, 5 H), 1.97-2.04 (m, 1 H), 2.47 (s, 3 H), 2.82 (s, 1 H), 6.15 (dd, \(J_1 = 15.9\) Hz, \(J_2 = 6.7\) Hz, 1 H), 6.32 (d, \(J = 16.0\) Hz, 1 H), 7.03 (dd, \(J_1 = 8.0\) Hz, \(J_2 = 1.2\) Hz, 1 H), 7.16 (td, \(J_1 = 7.9\) Hz, \(J_2 = 1.4\) Hz, 1 H), 7.30 (dd, \(J_1 = 7.7\) Hz, \(J_2 = 0.6\) Hz, 1 H), 7.34 (d, \(J = 7.9\) Hz, 2 H), 7.56 (dd, \(J_1 = 8.0\) Hz, \(J_2 = 1.4\) Hz, 1 H), 7.72 (d, \(J = 8.3\) Hz, 2 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 21.8, 26.1, 26.3, 32.7, 41.3, 58.3, 77.0, 121.9, 126.4, 127.6, 128.6, 129.1, 129.7, 129.8, 134.4, 134.9, 137.0, 139.8, 145.1; FT-IR (KBr) \(\bar{\nu}\) 3257, 2130, 1595, 1495, 1479, 1373, 1173, 1114, 1090, 813, 759, 529 cm\(^{-1}\); HRMS (ESI\(^+\)) m/z calcd for C\(_{32}\)H\(_{26}\)O\(_2\)N\(_2\)S\(_2\) [M+H]\(^+\) 380.1679 found 380.1683.

\((E)-4\)-Methyl-N-(2-styrylphenyl)-N-((4-(trifluoromethyl)phenyl)ethynyl)benzenesulfonamide (6u)

Prepared according to Sonogashira general procedure from 6a (0.15 g, 0.40 mmol) and 1-iodo-4-(trifluoromethyl)benzene; silica gel purification (ethyl acetate / petroleum ether = 1:70, then 1:50, \(R_t = 0.78\) (EtOAc/PE = 1:5); yield 66% (0.14 g, yellow oil); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 2.25 (s, 3 H), 6.97 (qd, \(J_1 = 16.3\) Hz, \(J_2 = 2.1\) Hz, 2 H), 7.20-7.22 (m, 2 H), 7.23-7.25 (m, 2 H), 7.25-7.28 (m, 5 H), 7.37-7.41 (m, 3 H), 7.47 (d, \(J = 8.2\) Hz, 2 H), 7.71 (dd, \(J_1 = 8.4\) Hz, \(J_2 = 1.9\) Hz, 3 H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 21.7, 69.6, 86.0, 123.0, 125.2, 125.3 (q, \(J_{\text{C,F}} = 3.8\) Hz), 126.5, 126.87 (q, \(J_{\text{C,F}} = 1.7\) Hz), 126.89, 128.2, 128.4, 128.5, 128.7, 129.5 (q, \(J_{\text{C,F}} = 32.4\) Hz), 129.92, 129.94, 130.0, 131.4, 134.0, 135.8, 136.2, 136.9, 145.6; FT-IR (KBr) \(\bar{\nu}\) 2237, 1770, 1759, 1375, 1322, 1246, 1172, 1126, 1072, 842, 759, 688, 577, 544 cm\(^{-1}\); HRMS (ESI\(^+\)) m/z calcd for C\(_{30}\)H\(_{23}\)F\(_3\)NO\(_2\)S\(_2\) [M+H]\(^+\) 518.1396 found 518.1399.

4-Methyl-N-((E)-oct-3-enynyl)-N-(2-((E)-styryl)phenyl)benzenesulfonamide (6v)

Prepared according to Sonogashira general procedure from 6a (0.15 g, 0.40 mmol) and 1-iodohexene; silica gel purification (ethyl acetate / petroleum ether = 1:70, then 1:50, \(R_t = 0.71\) (EtOAc/PE = 1:5); yield 52% (94 mg, yellow oil); \(^1\)H NMR (400 MHz, CDCl\(_3\))
\[ \delta 0.83 \text{ (t, } J = 8.2 \text{ Hz, 3 } \text{H}), 1.22-1.28 \text{ (m, 4 } \text{H}), 2.03 \text{ (qd, } J_1 = 7.2 \text{ Hz, } J_2 = 1.5 \text{ Hz, 2 } \text{H}), 2.23 \text{ (s, 3 } \text{H}), 5.50 \text{ (dt, } J_1 = 15.7 \text{ Hz, } J_2 = 1.5 \text{ Hz, 1 } \text{H}), 5.99 \text{ (dt, } J_1 = 15.7 \text{ Hz, } J_2 = 7.1 \text{ Hz, 1 } \text{H}), 6.89 \text{ (d, } J = 16.3 \text{ Hz, 1 } \text{H}), 7.00 \text{ (d, } J = 16.3 \text{ Hz, 1 } \text{H}), 7.13-7.18 \text{ (m, 3 } \text{H}), 7.19-7.24 \text{ (m, 2 } \text{H}), 7.26-7.28 \text{ (m, 4 } \text{H}), 7.29-7.34 \text{ (m, 1 } \text{H}), 7.65 \text{ (d, } J = 8.2 \text{ Hz, 3 } \text{H}); ^{13}\text{C NMR (100 MHz, CDCl}_3\text{) } \delta 14.0, 21.7, 22.2, 31.0, 32.9, 69.2, 81.6, 108.7, 123.4, 126.3, 126.9, 128.0, 128.3, 128.4, 128.6, 129.6, 129.9, 130.9, 134.4, 139.6, 136.6, 137.3, 144.9, 145.1; \text{ FT-IR (KBr) } \bar{\delta} 2956, 2928, 2971, 1701, 1597, 1494, 1451, 1366, 1172, 1088, 813, 760, 670, 657, 574, 543 \text{ cm}^{-1}; \text{ HRMS (ESI\textsuperscript{+}) } m/z \text{ caled for } C_{29}H_{38}NO_2S^+ \text{ [M+H]}^+ \text{ 456.1992 found 456.2008.}

\[ \text{N-((E)-4-Cyclohexylbuten-1-ynyl)-4-methyl-N-(2-((E)-styryl)phenyl)benzenesulfonamide (6w)} \]

Prepared according to Sonogashira general procedure from 6a (0.15 g, 0.40 mmol) and (2-iodovinyl)cyclohexane; silica gel purification (ethyl acetate / petroleum ether = 1:70, then 1:50, \text{Rf} = 0.74 \text{ (EtOAc/PE = 1:5); yield 64\% (123 mg, yellow oil)}; ^{1}\text{H NMR (500 MHz, CDCl}_3\text{) } \delta 0.97-1.02 \text{ (m, 2 } \text{H}), 1.06-1.12 \text{ (m, 1 } \text{H}), 1.15-1.24 \text{ (m, 3 } \text{H}), 1.60-1.67 \text{ (m, 4 } \text{H}), 1.92-2.00 \text{ (m, 1 } \text{H}), 2.22 \text{ (s, 3 } \text{H}), 5.46 \text{ (dd, } J_1 = 15.9 \text{ Hz, } J_2 = 1.3 \text{ Hz, 1 } \text{H}), 5.94 \text{ (dd, } J_1 = 15.9 \text{ Hz, } J_2 = 7.0 \text{ Hz, 1 } \text{H}), 6.89 \text{ (d, } J = 16.3 \text{ Hz, 1 } \text{H}), 7.00 \text{ (d, } J = 16.3 \text{ Hz, 1 } \text{H}), 7.13-7.18 \text{ (m, 4 } \text{H}), 7.20-7.24 \text{ (m, 3 } \text{H}), 7.27-7.28 \text{ (m, 2 } \text{H}), 7.32 \text{ (td, } J_1 = 7.1 \text{ Hz, } J_2 = 0.9 \text{ Hz, 1 } \text{H}), 7.65 \text{ (d, } J = 8.2 \text{ Hz, 3 } \text{H}); ^{13}\text{C NMR (125 MHz, CDCl}_3\text{) } \delta 21.7, 25.9, 26.1, 32.4, 41.4, 69.3, 81.8, 106.5, 123.4, 126.3, 126.9, 128.0, 128.3, 128.4, 128.6, 129.6, 129.8, 130.9, 134.2, 136.2, 136.4, 137.1, 145.1, 150.2; \text{ FT-IR (KBr) } \bar{\delta} 3840, 3819, 3650, 3030, 2925, 2852, 2231, 1706, 1597, 1494, 1450, 1363, 1172, 1088, 967, 814, 761, 691, 657, 575, 544 \text{ cm}^{-1}; \text{ HRMS (ESI\textsuperscript{+}) } m/z \text{ caled for } C_{31}H_{32}NO_2S^+ \text{ [M+H]}^+ \text{ 482.2148 found 482.2162.}

\[ (E)-N-(3-Hydroxy-3-methylbutynyl)-4-methyl-N-(2-styrylphenyl)benzenesulfonfoni

\[ \text{amide (6x)} \]

To a solution of 6a (0.99 mmol) in anhydrous THF (10 mL) under nitrogen atmosphere was injected \textit{n}-BuLi (475 \text{\mu}L, 1.19 mmol, 1.2 equiv.) at -78 °C. After stirring for 30 min., anhydrous acetone (89 \text{\mu}L, 1.2 mmol, 1.5 equiv.) was injected dropwise and the reaction mixture was stirring for 5 hours at 0 °C until complete consumption of 6a as indicated by TLC. Upon completion, the mixture was quenched with water and extracted with ethyl acetate. The combined organic layers were concentrated, dried by MgSO4, filtered and evaporated. Silica gel purification (ethyl acetate / petroleum ether = 1:50, then 1:20, \text{Rf} = 0.27 \text{ (EtOAc/PE = 1:5); yield 41\% (175 mg, yellow oil)}; ^{1}\text{H NMR (500 MHz, CDCl}_3\text{) } \delta 1.46 \text{ (s, 6 } \text{H}), 1.71 \text{ (s, 1 } \text{H}), 2.29 \text{ (s, 3 } \text{H}), 6.91 \text{ (s, 2 } \text{H}), 7.20 \text{ (dd, } J_1 = 7.9 \text{ Hz, } J_2 = 1.1 \text{ Hz, 1 } \text{H}), 7.23 \text{ (d, } J = 8 \text{ Hz, 2 } \text{H}), 7.25 \text{ (d, } J = 8.5 \text{ Hz, 4 } \text{H}), 7.29-7.33 \text{ (m, 2 } \text{H}).}
7.37 (td, J₁ = 7.6 Hz, J₂ = 1.2 Hz, 1 H), 7.68 (d, J = 8.2 Hz, 1 H), 7.70 (d, J = 8.3 Hz, 2 H); ¹³C NMR (125 MHz, CDCl₃) δ 21.7, 31.5, 65.5, 75.1, 77.1, 123.4, 126.4, 126.8, 127.8, 128.2, 128.3, 128.5, 128.7, 129.6, 129.8, 129.9, 130.9, 134.0, 136.0, 137.0, 145.4; FT-IR (KBr) δ 2980, 2931, 1597, 1480, 1451, 1370, 1187, 1170, 1132, 1089, 962, 869, 813, 760, 691, 647, 586, 543 cm⁻¹; HRMS (ESI⁺) m/z calcd for C₂₆H₂₆NO₅S⁺ [M+H]⁺ 432.1628 found 432.1635.

(E)-N-(3-Methoxy-3-methylbutynyl)-4-methyl-N-(2-styrylphenyl)benzenesulfonamide (6y)

\[
\text{Ph} \quad \text{Ts} \quad \text{OMe} \quad \text{Ph}
\]

To a solution of 6x (0.34 mmol) in anhydrous THF (5 mL) under nitrogen atmosphere was charged sodium hydride (16.3 mg, 0.41 mmol, 1.2 equiv.) at 0 °C. After stirring for 30 min at room temperature, methyl iodide (32 μL, 0.51 mmol, 1.5 equiv.) was injected. The reaction mixture was stirring for 8 hours at room temperature until complete consumption of 6y as indicated by TLC. Upon completion, the mixture was quenched with water and extracted with ethyl acetate. The combined organic layers were concentrated, dried by MgSO₄, filtered and evaporated. Silica gel purification (ethyl acetate / petroleum ether = 1:70, then 1:50, Rf = 0.56 (EtOAc/PE = 1:5); yield 59% (89 mg, yellow oil); ¹H NMR (500 MHz, CDCl₃) δ 1.36 (s, 6 H), 2.23 (s, 3 H), 3.19 (d, J = 2.3 Hz, 3 H), 6.89 (s, 2 H), 7.17-7.27 (m, 9 H), 7.33 (t, J = 7.3 Hz, 1 H), 7.64-7.67 (m, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 21.6, 28.5, 51.7, 71.0, 72.1, 78.9, 123.2, 126.3, 126.8, 128.1, 128.3, 128.4, 128.6, 129.6, 129.7, 130.0, 130.9, 134.1, 135.9, 136.1, 137.0, 145.3; FT-IR (KBr) δ 2983, 2935, 2238, 1597, 1494, 1451, 1373, 1229, 1172, 1126, 1089, 1074, 962, 836, 814, 759, 712, 691, 670, 586, 544 cm⁻¹; HRMS (ESI⁺) m/z calcd for C₂₆H₂₆NO₅S⁺ [M+H]⁺ 446.1784 found 446.1788.

4. Deuterium isotope labelling experiment

4.1

Trapping diene C with the dienophile failed, no Diels-Alder cycloaddition product was observed, with 7a recovered and partially decomposed.

4.2

Re-addition of an intermolecular Pd-H species to 11e failed.

4.3
It was found out that water was not a proton source for protonation of B or E palladium species.

4.4

1,2-Intramolecular D migration was observed.

4.5

<table>
<thead>
<tr>
<th>entry</th>
<th>D-solvent</th>
<th>result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>d8-1,4-dioxane</td>
<td>N.R.</td>
</tr>
<tr>
<td>2</td>
<td>D7-DMF</td>
<td>trace</td>
</tr>
<tr>
<td>3</td>
<td>D8-i-PrOH</td>
<td>36%</td>
</tr>
</tbody>
</table>

It was found out that d8-i-PrOH was indeed involved as a H-donor at the methylene position of indole 14a.

4.6

6a, according to the proposed mechanism, arising from reversible β-H-PdCl elimination of A, was employed for reductive Heck cycloisomerisation to see if the enynamide 6a would be an intermediate for the reductive Heck cycloisomerisation. 8a was not observed, instead, 6a decomposed to C-N cleaved 8a in the presence of Pd.

4.7

When subjecting in-situ generated 16a to the reductive cycloisomerisation condition,
14a was delivered with one deuterium lost, indicating that the missing deuterium was from D-H exchange of 16a with isopropanol, indicating syn-β-D-Pd elimination of A and re-addition to the ynamide 6 occurs reversibly.

4.8

It was found that an intermolecular D-Pd species failed to exchange H from indole 8a, which excludes the possibility of D-Pd insertion to the indole 8a and β-H-Pd elimination, revealing that there was no D-H exchange between the product 8a and the solvent.

4.9 4-Methyl-N,N′-diphenyl-N′-tosylbenzenesulfonohydrazide (20)

An intermolecular reductive Heck coupling of chloroenamide 19 with styrene failed in the absence of aromatisation as the driving force. Instead, a tosylbenzenesulfonohydrazide was formed in the presence of oxygen.

The known compound 19 was synthesized from 18 via the procedure of chlorotrimethylsilane-mediated hydrochlorination of ynamide, and used directly without further purification.

To an oven-dried, septum-capped 10 mL Schlenk tube equipped was charged the substrate crude 19 (0.2 mmol, 1.0 equiv.), PdCl₂ (3.4 mg, 10 mol %) and an additive styrene (23 μL, 0.2 mmol) in 1,4-dioxane (4 mL) under a balloon pressure of oxygen. The mixture was then stirred at 100 °C overnight until complete consumption of 19 as indicated by TLC. Upon completion, the mixture was quenched with water and extracted with CH₂Cl₂. The combined organic layers were concentrated, dried by MgSO₄, filtered and evaporated. Flash chromatography on silica gel (petroleum ether / EtOAc = 20:1, then 10:1, Rf = 0.3 (EtOAc/PE = 1:5)) gave 20 (67 mg, yellow oil) in quantitative yield; ¹H NMR (400 MHz, CDCl₃) δ 2.37 (s, 6 H), 7.08-7.11 (m, 6 H), 7.22 (d, J = 8.2 Hz, 7 H), 7.24-7.25 (m, 1 H), 7.69 (dd, J₁ = 8.3 Hz, J₂ = 1.6 Hz, 4 H); ¹³C NMR (100 MHz, CDCl₃) δ 21.6, 121.56, 121.61, 125.3, 125.4, 127.4, 129.4, 129.8, 136.2, 136.7, 136.8, 144.0; FT-IR (KBr) v 3258, 1599, 1497, 1412, 1340, 1222, 1186, 1160, 1092, 921, 813, 754, 696, 662, 563, 544 cm⁻¹; HRMS (APCI⁺) m/z calcd for C₂₆H₂₆N₂O₄S₂ 2+ [M+2H]²⁺ 494.1323 found 494.1309.

5. References:


6. $^1$H and $^{13}$C NMR spectra
\( \text{Ao} \ (Z + E) \)
crude 7a $^1$HNMR 400 MHz
**8a DEPT 135 400 MHz**

**$^1$H-$^1$H COSY 400 MHz**
8a $\text{H}^{13}\text{C}\text{HSQC 400 MHz}$
(Z / E, Z / E)-11e
7. X-ray crystal structures
3-Benzyl-6-fluoro-2-methyl-1-tosyl-1H-indole (8o)

Colourless prism crystal; m.p. 151.3 °C ; recrystallised in chloroform and petroleum ether, CCDC 1890685