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Arylation and Alkenylation of Activated Alkyl Halides using Sulfonamides

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1. General remarks

^1H NMR, ^{13}C $\{^1\text{H}\}$ NMR and ^{19}F NMR were recorded at 500/400 MHz, 126/101 MHz, 470/376 MHz on Bruker Avance 500 or 400 spectrometers. All ^1H NMR and ^{13}C chemical shifts were referenced to the residual solvent peak of CDCl_3 (^1H referenced to 7.26 ppm and ^{13}C referenced to 77.16 ppm), $(\text{CD}_3)_2\text{SO}$ (^1H referenced to 2.50 ppm and ^{13}C referenced to 39.52 ppm), methanol (^1H referenced to 3.31 ppm and ^{13}C referenced to 49.00 ppm), CD_3CN (^1H referenced to 1.94 ppm and ^{13}C referenced to 1.32 ppm), and acetone (^1H referenced to 2.05 ppm and ^{13}C referenced to 29.84 ppm). All ^{19}F chemical shifts were unadjusted from raw data. All chemical shifts are quoted in parts per million (ppm), measured from the centre of the signal except in the case of multiplets, which are quoted as a range. Coupling constants are quoted to the nearest 0.1 Hz. Splitting patterns are abbreviated as follows: singlet (s), doublet (d), triplet (t), quartet (q), quintet (quin), sextet (sxt), multiplet (m), broad singlet (br. s) and combinations thereof. Assignment of spectra was aided by DEPT 135 and 2D NMR spectroscopy (COSY, HSQC and HMBC). Assignments are provided in the following format: chemical shift (multiplicity, coupling constant, integration, description of functional group, letter referenced to molecule drawn above).

Low resolution mass spectrometry was performed on an Agilent 6100 mass spectrometer (ESI ionisation) and Hewlett Packard 5971 MSD (GC/MS with EI). High resolution mass spectrometry was performed on a Waters QTOF with ESI/APCI ionisation and a Thermo Finnigan MAT95XP (EI).

Melting points were determined using a Kofler hot-stage apparatus and are uncorrected.

Thin layer chromatography (TLC) was performed on commercially available pre-coated TLC plates (Merck Silica gel 60 F254 aluminium sheets). Visualisation was either achieved under UV light at 254 nm or with a KMnO_4 stain.

Column chromatography was conducted on silica gel (Sigma Aldrich, 40-63 μm , 60 Å) or Biotage KP-Sil or Snap Ultra cartridges on a Biotage Isolera automated columning machine.

2. Synthesis of Arylsulfonamides

General Procedure A for the synthesis of *N*-methyl arylsulfonamides

To a solution of sulfonyl chloride (1.0 eq.) in diethyl ether or ethyl acetate (0.10 M), alkylamine (2.5 eq.) was added dropwise. The reaction mixture was stirred for 16 hours at room temperature, then it was concentrated under reduced pressure. HCl (1.0 M) was added, the organic compounds were extracted with DCM. The combined organic layers were washed with H_2O and brine, dried over MgSO_4 , filtered and concentrated under reduced pressure to give the crude product, which was purified by column chromatography on silica gel.

General Procedure B for the synthesis of *N*-phenyl arylsulfonamides

To a solution of substituted aniline (1.0 eq.) in freshly distilled THF (0.10 M), pyridine (1.2 eq.) and 4-nitrobenzenesulfonyl chloride (1.2 eq.) were added at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 16 hours. The reaction was quenched with aqueous saturated NH_4Cl . The organic layers were extracted with EtOAc, washed with H_2O and brine, dried over MgSO_4 , filtered and concentrated under reduced pressure to give the crude product, which was purified by column chromatography on silica gel.

2.1 *N*-Alkyl Sulfonamide Syntheses

4-nitro-*N*-methylbenzenesulfonamide **6a**

Prepared according to **General Procedure A** from 4-nitrobenzenesulfonyl chloride (4.5 mmol, 1.00 g), methylamine (30 wt% in EtOH, 11 mmol, 1.17 mL), Et₂O (45.0 mL). Purification by column chromatography on silica gel (0–40% EtOAc in hexanes) afforded **6a** as a pale yellow solid (888 mg, 4.1 mmol, 91%), m.p. 93–95 °C.

¹H NMR (400 MHz, CDCl₃): δ 8.41 (app. d, *J* = 9.0 Hz, 2H, CH_{ar}-2), 8.09 (app. d, *J* = 9.0 Hz, 2H, CH_{ar}-3), 4.67 (q, *J* = 5.2 Hz, 1H, NH), 2.76 (d, *J* = 5.2 Hz, 3H, CH₃-5); ¹³C NMR (101 MHz, CDCl₃): δ 150.3 (C-1), 145.0 (C-4), 128.6 (C-3), 124.6 (C-2), 29.5 (C-5).

IR (neat film, cm⁻¹): 3302, 3107, 2985, 1733, 1536, 1383, 1354, 1174, 854, 739.

MS (ES⁻) found *m/z* 215 [M-H]⁻; HRMS (ES⁻) found 215.0110, C₇H₇N₂O₄S [M-H]⁻ requires 215.0121.

Data is in accordance with literature reports.^[1]

2-nitrobenzene-*N*-methyl-sulfonamide **6b**

Prepared according to **General Procedure A** from 2-nitrobenzenesulfonyl chloride (2.3 mmol, 510 mg), methylamine (30 wt% in EtOH, 5.8 mmol, 595 μL), Et₂O (23.0 mL). Purification by column chromatography on silica gel (0–40% EtOAc in hexanes) afforded **6b** as a white solid (218 mg, 1.0 mmol, 44%).

¹H NMR (400 MHz, CD₃CN): δ 8.16–8.11 (m, 1H, CH_{ar}-5), 7.90–7.85 (m, 1H, CH_{ar}-2), 7.78–7.73 (m, 2H, CH_{ar}-3, 4), 5.23 (br. s, 1H, NH), 2.79 (d, *J* = 5.3 Hz); ¹³C NMR (101 MHz, CDCl₃): δ 148.4 (C-1), 133.8 (C-4), 132.8 (C-3), 132.6 (C-6), 131.7 (C-5), 125.6 (C-2), 29.9 (C-7).

Data is in accordance with literature reports.^[2]

4-nitro-3-(trifluoromethyl)-*N*-methylbenzenesulfonamide **6c**

Prepared according to **General Procedure A** from 4-nitro-3-(trifluoromethyl)benzenesulfonyl chloride (0.92 mmol, 263 mg), methylamine (30 wt% in EtOH, 2.3 mmol, 239 μ L), Et₂O (10.0 mL). Purification by column chromatography on silica gel (0–40% EtOAc in hexanes) afforded **6c** as a dark brown solid (225 mg, 0.79 mmol, 86%), m.p. 81–84 °C.

¹H NMR (400 MHz, CDCl₃): δ 8.33 (d, J = 1.9 Hz, 1H, CH_{ar}-5), 8.25 (dd, J = 8.4, 1.9 Hz, 1H, CH_{ar}-3), 8.04 (d, J = 8.4 Hz, 1H, CH_{ar}-2), 4.65 (q, J = 5.2 Hz, 1H, NH), 2.80 (d, J = 5.2 Hz, 3H, CH₃-8); ¹³C NMR (101 MHz, CDCl₃): δ 150.2 (C-1), 143.9 (C-4), 132.2 (C-3), 127.2–127.1 (m, C-5), 126.3 (q, J = 22.6 Hz, C-6), 126.1 (C-2), 123.8 (q, J = 225.5 Hz, C-7), 29.5 (C-8); ¹⁹F NMR (376 MHz, CDCl₃): δ –60.16.

IR (neat film, cm^{–1}): 3307, 3114, 3089, 3043, 2770, 1614, 1543, 1307, 1291, 836, 639.

MS (ES[–]) found m/z 283 [M–H][–]; HRMS (ES[–]) found 283.0005, C₈H₆F₃N₂O₄S [M–H][–] requires 282.9995.

4-nitro-2-methoxy-*N*-methylbenzenesulfonamide **6d**

Prepared according to **General Procedure A** from 4-nitro-2-methoxybenzenesulfonyl chloride (1.0 mmol, 256 mg), methylamine (30 wt% in EtOH, 2.6 mmol, 269 μ L), Et₂O (10.0 mL). Purification by column chromatography on silica gel (0–40% EtOAc in hexanes) afforded **6d** as a clear yellow solid (237 mg, 0.96 mmol, 94%), m.p. 169–172 °C.

¹H NMR (400 MHz, CDCl₃): δ 8.13 (d, J = 8.5 Hz, 1H, CH_{ar}-3), 7.97 (dd, J = 8.5, 2.0 Hz, 1H, CH_{ar}-2), 7.91 (d, J = 2.0 Hz, 1H, CH_{ar}-6), 4.92 (q, J = 5.5 Hz, 1H, NH), 4.13 (s, 3H, CH₃-7), 2.67 (d, J = 5.5, 3H, CH₃-8); ¹³C NMR (101 MHz, CDCl₃): δ 156.9 (C-1), 151.7 (C-4), 132.4 (C-3), 132.0 (C-2), 115.8 (C-6), 107.5 (C-5), 57.4 (C-7), 29.6 (C-8).

IR (neat film, cm^{–1}): 3310, 3108, 2925, 2853, 1717, 1406, 1313, 1265, 1164, 1025, 802, 611.

MS (ES^-) found m/z 245 $[\text{M}-\text{H}]^-$, 247 $[\text{M}+\text{H}]^+$; **HRMS** (ES^-) found 245.0239, $\text{C}_8\text{H}_9\text{N}_2\text{O}_5\text{S}$ $[\text{M}-\text{H}]^-$ requires 245.0227.

2.2 *N*-Aryl Sulfonamide Syntheses

4-nitro-*N*-phenylbenzenesulfonamide **6e**

Prepared according to **General Procedure A** from 4-nitrobenzenesulfonyl chloride **147a** (4.5 mmol, 1.00 mg), aniline (11 mmol, 1.03 mL), EtOAc (45.0 mL). Purification by column chromatography on silica gel (0–40% EtOAc in hexanes) afforded **6e** as a light pink solid (834 mg, 3.0 mmol, 67%), m.p. 157–159 °C.

^1H NMR (500 MHz, CDCl_3): δ 8.28 (app. d, $J = 8.5$ Hz, 2H, $\text{CH}_{\text{ar}}-2$), 7.92 (app. d, $J = 8.5$ Hz, 2H, $\text{CH}_{\text{ar}}-3$), 7.31–7.25 (m, 2H, $\text{CH}_{\text{ar}}-7$), 7.21–7.17 (m, 1H, $\text{CH}_{\text{ar}}-8$), 7.09–7.06 (m, 2H, $\text{CH}_{\text{ar}}-6$), 6.68 (br. s, 1H, NH); ^{13}C NMR (126 MHz, CDCl_3): δ 150.4 (C-1), 144.8 (C-4), 135.4 (C-5), 129.8 (C-6), 128.7 (C-3), 126.7 (C-8), 124.4 (C-2), 122.6 (C-7).

IR (neat film, cm^{-1}): 3275, 3133, 2922, 2857, 1918, 1608, 1520, 1400, 1332, 1163, 854, 739, 669, 616.

MS (ES^-) found m/z 277 $[\text{M}-\text{H}]^-$; **HRMS** (ES^-) found 277.0281, $\text{C}_{12}\text{H}_9\text{N}_2\text{O}_4\text{S}$ $[\text{M}-\text{H}]^-$ requires 277.0289.

Data is in accordance with literature reports.^[3]

4-nitro-*N*-(*p*-tolyl)benzenesulfonamide **6f**

Prepared according to **General Procedure B** from *p*-toluidine (1.0 mmol, 107 mg), pyridine (1.2 mmol, 35 μL), 4-nitrobenzenesulfonyl chloride (1.2 mmol, 265 mg), THF (10.0 mL). Purification by column chromatography on silica gel (0–40% EtOAc in hexanes) afforded **6f** as a yellow solid (214 mg, 0.73 mmol, 73%), m.p. 176–178 °C.

^1H NMR (400 MHz, CD_3CN): δ 8.26 (app. d, $J = 9.0$ Hz, 2H, $\text{CH}_{\text{ar}}-2$), 8.01 (br. s, 1H, NH), 7.91 (app. d, $J = 9.0$ Hz, 2H, $\text{CH}_{\text{ar}}-3$), 7.08 (app. d, $J = 8.4$ Hz, 2H, $\text{CH}_{\text{ar}}-6$), 6.97 (d, $J = 8.4$ Hz, 2H, $\text{CH}_{\text{ar}}-7$), 2.24 (s, 3H, CH_3-9); ^{13}C NMR (101 MHz, CD_3CN): δ 151.1 (C-4),

145.8 (C-1), 136.8 (C-8), 134.7 (C-5), 130.9 (C-6), 129.5 (C-3), 125.3 (C-2), 123.3 (C-7), 20.2 (C-9).

IR (neat film, cm^{-1}): 3269, 3106, 3039, 2920, 2866, 1607, 1528, 1509, 1348, 1313, 1302, 1162, 1090, 855, 745, 736, 683, 643, 607.

MS (ES^+) found m/z 337 $[\text{M}+2\text{Na}-\text{H}]^+$; **HRMS** (ES^+) found 337.0225, $\text{C}_{13}\text{H}_{11}\text{N}_2\text{O}_4\text{SNa}_2$ $[\text{M}+2\text{Na}-\text{H}]^+$ requires 337.0229.

Data is in accordance with literature reports.^[4]

4-nitro-*N*-mesitylbenzenesulfonamide **6g**

Prepared according to **General Procedure B** from 2,4,6-trimethylaniline (1.0 mmol, 141 μL), pyridine (1.2 mmol, 35 μL), 4-nitrobenzenesulfonyl chloride (1.2 mmol, 265 mg), THF (10.0 mL). Purification by column

chromatography on silica gel (0–40% EtOAc in hexanes) afforded **6g** as a light brown solid (220 mg, 0.69 mmol, 69%), m.p. 144–146 $^{\circ}\text{C}$.

^1H NMR (400 MHz, CD_3CN): δ 8.34 (app. d, J = 8.9 Hz, 2H, $\text{CH}_{\text{ar}-2}$), 7.94 (app. d, J = 8.9 Hz, 2H, $\text{CH}_{\text{ar}-3}$), 7.43 (br. s, 1H, NH), 6.90 (s, 2H, $\text{CH}_{\text{ar}-7}$), 2.26 (s, 3H, CH_3-10), 1.97 (s, 6H, CH_3-9); **^{13}C NMR** (101 MHz, CD_3CN): δ 151.2 (C-4), 148.2 (C-1), 139.0 (C-8), 138.8 (C-6), 130.7 (C-5), 130.3 (C-7), 129.2 (C-3), 125.5 (C-2), 20.9 (C-10), 18.9 (C-9).

IR (neat film, cm^{-1}): 3281, 3105, 2924, 2862, 1524, 1349, 1311, 1163, 1091, 854, 738, 685, 622.

MS (ES^-) found m/z 319 $[\text{M}-\text{H}]^-$; **HRMS** (ES^-) found 319.0754, $\text{C}_{15}\text{H}_{15}\text{N}_2\text{O}_4\text{S}$ $[\text{M}-\text{H}]^-$ requires 319.0758.

Data is in accordance with literature reports.^[5]

4-nitro-*N*-(4-methoxyphenyl)benzenesulfonamide **6h**

Prepared according to **General Procedure B** from *p*-anisidine (1.0 mmol, 123 mg), pyridine (1.2 mmol, 35 μ L), 4-nitrobenzenesulfonyl chloride (1.2 mmol, 265 mg), THF (10.0 mL). Purification by column chromatography on silica gel (0–40% EtOAc in hexanes) afforded **6h** as a light yellow solid (180 mg, 0.59 mmol, 58%), m.p. 174–176 $^{\circ}$ C.

^1H NMR (400 MHz, CD_3CN): δ 8.26 (app. d, J = 9.0 Hz, 2H, $\text{CH}_{\text{ar-2}}$), 7.90 (br. s, 1H, NH), 7.85 (app. d, J = 9.0 Hz, 2H, $\text{CH}_{\text{ar-3}}$), 6.98 (app. d, J = 9.1 Hz, 2H, $\text{CH}_{\text{ar-7}}$), 6.80 (app. d, J = 9.1 Hz, 2H, $\text{CH}_{\text{ar-6}}$), 3.72 (s, 3H, $\text{CH}_3\text{-9}$); ^{13}C NMR (101 MHz, CD_3CN): δ 159.2 (C-8), 152.3 (C-4), 145.7 (C-1), 129.7 (C-5), 129.5 (C-3), 126.3 (C-7), 125.3 (C-2), 115.4 (C-6), 56.1 (C-9).

IR (solid, cm^{-1}): 3275, 3131, 2965, 2846, 1607, 1524, 1506, 1347, 1305, 1286, 1243, 1170, 1158, 1087, 1030, 852, 750, 739, 680, 660.

MS (ES^-) found m/z 307 $[\text{M}-\text{H}]^-$; HRMS (ES^-) found 307.0389, $\text{C}_{13}\text{H}_{11}\text{N}_2\text{O}_5\text{S}$ $[\text{M}-\text{H}]^-$ requires 307.0394.

Data is in accordance with literature reports.^[6]

Ethyl 4-((4-nitrophenyl)sulfonamido)benzoate **6i**

Prepared according to **General Procedure B** from *p*-aminoethylbenzoate (1.0 mmol, 165 mg), pyridine (1.2 mmol, 35 μ L), 4-nitrobenzenesulfonyl chloride (1.2 mmol, 265 mg), THF (10.0 mL). Purification by column chromatography on silica gel (0–40% EtOAc in hexanes) afforded **6i** as a light salmon pink solid (112 mg, 0.32 mmol, 32%), m.p. 180–184 $^{\circ}$ C.

^1H NMR (400 MHz, $(\text{CD}_3)_2\text{CO}$): δ 8.40 (app. d, J = 8.9 Hz, 2H, $\text{CH}_{\text{ar-2}}$), 8.14 (app. d, J = 8.9 Hz, 2H, $\text{CH}_{\text{ar-3}}$), 7.92 (app. d, J = 8.8 Hz, 2H, $\text{CH}_{\text{ar-7}}$), 7.36 (app. d, J = 8.8 Hz, 2H, $\text{CH}_{\text{ar-6}}$), 4.29 (q, J = 7.2 Hz, 2H, $\text{CH}_2\text{-10}$), 2.83 (br. s, 1H, NH), 1.32 (t, J = 7.2 Hz, 3H, $\text{CH}_3\text{-11}$).

11) ; ^{13}C NMR (101 MHz, $(\text{CD}_3)_2\text{CO}$): δ 166.0 (C-9), 145.9 (C-1), 142.3 (C-4), 132.0 (C-5), 131.7 (C-7), 129.5 (C-3), 127.5 (C-8), 125.4 (C-2), 120.3 (C-6), 61.4 (C-10), 14.5 (C-11).

IR (neat film, cm^{-1}): 3228, 3107, 2983, 1712, 1691, 1607, 1531, 1368, 1349, 1132, 1280, 1165, 1109, 1090, 855, 736, 609, 605.

MS (ES^-) found m/z 349 $[\text{M}-\text{H}]^-$; HRMS (ES^-) found 349.0495, $\text{C}_{15}\text{H}_{13}\text{N}_2\text{O}_6\text{S}$ $[\text{M}-\text{H}]^-$ requires 349.0500.

4-nitro-*N*-benzylbenzenesulfonamide 6j

Prepared according to **General Procedure A** from 4-nitrobenzenesulfonyl chloride (4.5 mmol, 1.00 g), benzylamine (11 mmol, 1.23 mL), EtOAc (45.0 mL).

Purification by column chromatography on silica gel (o-40% EtOAc in hexanes) afforded **6j** as a yellow solid (1.07 g, 3.7 mmol, 81%), m.p. 111–113 °C.

^1H NMR (500 MHz, CDCl_3): δ 8.30 (app. d, $J = 8.4$ Hz, 2H, $\text{CH}_{\text{ar-2}}$), 7.98 (app. d, $J = 8.4$ Hz, 2H, $\text{CH}_{\text{ar-3}}$), 7.28–7.24 (m, 3H, $\text{CH}_{\text{ar-7,9}}$), 7.18–7.15 (m, 2H, $\text{CH}_{\text{ar-8}}$), 5.06 (t, $J = 6.1$ Hz, 1H, NH), 4.22 (d, $J = 6.1$ Hz, 2H, $\text{CH}_2\text{-5}$) ; ^{13}C NMR (126 MHz, CDCl_3): δ 150.1 (C-1), 146.2 (C-4), 135.6 (C-6), 129.0 (C-8), 128.44 (C-3), 128.41 (C-9), 128.0 (C-7), 124.4 (C-2), 47.5 (C-5).

IR (neat film, cm^{-1}): 3289, 3099, 1520, 1421, 1347, 1330, 1312, 1153, 1051, 806, 754, 747, 736, 621.

MS (ES^-) found m/z 291 $[\text{M}-\text{H}]^-$; HRMS (ES^-) found 291.0441, $\text{C}_{13}\text{H}_{11}\text{N}_2\text{O}_4\text{S}$ $[\text{M}-\text{H}]^-$ requires 291.0445.

Data is in accordance with literature reports.^[7]

2.3 Phenylethenesulfonamide Syntheses

(*E*)-4-Nitrophenylethenesulfonamide **13a**^[8]

In a 100 mL Schenk flask under nitrogen atmosphere, **S1** tert-butyl (((diphenylphosphoryl)methyl)sulfonyl)carbamate (1.0 eq., 1.0 mmol, 395 mg) was dissolved in dry DMF (25.0 mL) and cooled to 0°C. To a well-stirred solution of the reagent NaH (55% in mineral oil, 2.6 eq., 2.6 mmol, 111 mg) was added. The reaction was allowed to warm to r.t. and stirred for 30 minutes. Cooled down to 0 °C, 4-nitrobenzaldehyde (1.2 eq., 1.2 mmol, 185 mg) was then added in ten portions and the reaction mixture (dark purple) was stirred vigorously overnight at room temperature. Distilled water (50.0 mL), EtOAc (40.0 mL) and 2% aq. HCl (10.0 mL) were added to the mixture and the layers were separated. The aqueous layer was extracted with EtOAc (4 × 20 mL). The organic solution was washed with distilled water (2 × 30 mL), brine (2 × 30 mL), and dried over sodium sulfate, filtered and concentrated under reduced pressure to give the crude product (590 mg dark brown oil). The crude mixture was purified by column chromatography (10–60% EtOAc in hexanes). The Boc protected **S2** compound was obtained as a yellow solid (220 mg, 0.69 mmol, 69% yield).

¹H NMR (400 MHz, (CD₃)₂CO): δ 9.99 (br. s, 1H, NH), 8.33 (d, *J* = 8.9 Hz, 2H, CH_{ar-2}), 8.07 (d, *J* = 8.9 Hz, 2H, CH_{ar-3}), 7.73 (d, *J* = 15.6 Hz, 1H, CH-5), 7.53 (d, *J* = 15.6 Hz, 1H, CH-6), 1.44 (s, 9H, CH₃-9); ¹³C NMR (101 MHz, (CD₃)₂CO): δ 149.9 (C-1), 149.1 (C-4), 140.3 (C-5), 138.9 (C-6), 129.7 (C-2), 124.1 (C-3), 82.5 (C-8), 27.2 (C-9). HRMS (APCI) C₁₃H₁₅N₂O₆S[−] ([M-H][−]) requires 327.0656; found 327.0657.

Boc-protected sulfonamide (**S2**, 2.1 mmol, 689 mg) was dissolved in DMSO (6.0 mL) and stirred for 8 hours at 80°C. The reaction mixture was cooled to room temperature,

poured into distilled water (40.0 mL) and extracted with EtOAc (4 × 20 mL). The organic solution was concentrated under reduced pressure to give the crude product (650 mg). The crude mixture was purified by column chromatography (20–80% EtOAc in hexanes) to afford **13a** as a yellow solid (345 mg, 1.5 mmol, 72% yield).

¹H NMR (400 MHz, (CD₃)₂CO): δ 8.30 (d, *J* = 8.8 Hz, 2H, CH_{ar}-2), 7.97 (d, *J* = 8.8 Hz, 2H, CH_{ar}-3), 7.52 (d, *J* = 15.6 Hz, 1H, CH-5), 7.43 (d, *J* = 15.6 Hz, 1H, CH-6), 6.51 (br. s, 2H, NH₂); **¹³C NMR** (101 MHz, (CD₃)₂CO): δ 140.9 (C-1), 135.8 (C-5), 134.8 (C-4 and C-6), 130.1 (C-3), 124.9 (C-2). **HRMS** (APCI⁺) found 229.0274, C₈H₉N₂O₄S [M+H]⁺ requires 229.0278.

(*E*)-*N*-Methyl-(4-nitrophenyl)ethenesulfonamide **13b**^[9]

In a 100 mL Schenk flask under nitrogen atmosphere, **S1** tert-butyl (((diphenylphosphoryl)methyl)sulfonyl)carbamate (1.0 eq., 1.3 mmol, 494 mg) was dissolved in dry DMF (35.0 mL) and cooled to 0 °C. To a well-stirred solution of the reagent NaH (55% in mineral oil, 2.6 eq., 3.2 mmol, 139 mg) was added in five portions. The reaction was allowed to warm to r.t. and stirred for 30 minutes. Cooled down to 0 °C, 4-nitrobenzaldehyde (1.2 eq., 1.5 mmol, 231 mg) was then added in three portions and the reaction mixture (dark purple) was stirred vigorously overnight (16 hours) at r.t. Cooled to 0 °C, MeI (5.0 eq., 6.3 mmol, 0.390 mL) was added, stirred at 40 °C for 4 hours. Ice and EtOAc (50.0 mL) were added to the reaction and the layers were separated. The aqueous layer was extracted with EtOAc (4 × 50 mL). The organic solution was washed with 2% aq. HCl (50.0 mL), distilled water (2 × 100 mL), brine (2 × 100 mL), and dried over sodium sulfate, filtered and concentrated under reduced pressure to give the crude product (610 mg dark brown oil). The crude mixture was purified by column chromatography (10–35% EtOAc in hexanes). The compound **S3** was obtained as an orange solid (259 mg, 0.757 mmol, 61% yield).

^1H NMR (400 MHz, $(\text{CD}_3)_2\text{CO}$): δ 8.32 (d, J = 8.7 Hz, 2H, $\text{CH}_{\text{ar-2}}$), 8.03 (d, J = 8.7 Hz, 2H, $\text{CH}_{\text{ar-3}}$), 7.72 (d, J = 15.5 Hz, 1H, CH-5), 7.55 (d, J = 15.5 Hz, 1H, CH-6), 3.22 (s, 3H, $\text{CH}_3\text{-7}$), 1.44 (s, 9H, $\text{CH}_3\text{-10}$); ^{13}C NMR (101 MHz, $(\text{CD}_3)_2\text{CO}$, ppm): δ 152.1 (C-8), 149.9 (C-1), 141.0 (C-4), 139.7 (C-5), 130.6 (C-2), 130.2 (C-6), 125.0 (C-3), 84.6 (C-9), 33.1 (C-7), 28.1 (C-10). HRMS (APCI $^+$) found 343.0952, $\text{C}_{14}\text{H}_{19}\text{N}_2\text{O}_6\text{S}$ $[\text{M}+\text{H}]^+$ requires 343.0958.

The Boc-sulfonamide (**S3**, 0.75 mmol, 256 mg) was dissolved in DMSO (3.75 mL) and heated to 120 °C for 8 hours. The reaction mixture was cooled to r.t., poured into distilled water (35.0 mL) and extracted with EtOAc (3 $\times$ 30 mL). The organic solution was concentrated under reduced pressure to give the crude product (240 mg). The crude mixture was purified by column chromatography (10–80% EtOAc in hexanes). The title compound **13b** was obtained as an orange solid (153 mg, 0.632 mmol, 84% yield).

^1H NMR (400 MHz, $(\text{CD}_3)_2\text{CO}$): δ 8.30 (d, J = 8.8 Hz, 2H, $\text{CH}_{\text{ar-2}}$), 8.00 (d, J = 8.8 Hz, 2H, $\text{CH}_{\text{ar-3}}$), 7.52 (d, J = 15.6 Hz, 1H, CH-5), 7.29 (d, J = 15.6 Hz, 1H, CH-6), 6.24 (br. s, 1H, NH), 2.72 (s, 3H, $\text{CH}_3\text{-7}$); ^{13}C NMR (101 MHz, $(\text{CD}_3)_2\text{CO}$): δ 149.6 (C-1), 140.6 (C-4), 138.5 (C-5), 130.8 (C-6), 130.2 (C-2), 124.9 (C-3), 28.8 (C-7). HRMS (APCI $^+$) found 242.0367, $\text{C}_9\text{H}_{10}\text{N}_2\text{O}_4\text{S}$ $[\text{M}]^+$ requires 242.0361.

3. Sulfonamide Coupling Reactions with Smiles Rearrangement

General Procedure E

In a microwave vial dried in the oven, sulfonamide (1.0 eq.), potassium carbonate (3.0 eq.) were weighted. A stirrer bar was added, the vial was sealed and the air was evacuated then the vial was filled with nitrogen. Dry DMF (0.10 M for sulfonamide),

substituted ethyl 2-chloroacetate (2.0 eq.) was added to a stirred mixture and the vial was put in a pre-warmed 70 °C oil bath to stir for 16 hours. The reaction was cooled, the vial was opened, ethyl acetate and water were added and the layers were separated. The aqueous layer was extracted with ethyl acetate. The combined organic layers were then washed three times with a 10% aqueous LiCl solution, brine, and dried over magnesium sulfate, filtered and concentrated under reduced pressure to give the crude product. The crude mixture was purified by column chromatography on silica gel.

General Procedure F

To a solution of an *N*-aryl sulfonamide (1.0 eq.), K_2CO_3 (3.0 eq.), DMF (0.10 M for sulfonamide) within a metal-capped, oven-dried microwave vial, ethyl 2-chloroacetate (2.0 eq.) was added. The vial was put in a pre-warmed 70 °C oil bath to stir for 16 hours. The reaction was cooled, the vial was opened, ethyl acetate and water were added and the layers were separated. The aqueous layer was extracted with ethyl acetate. The combined organic layers were then washed three times with a 10% aqueous LiCl solution, brine, and dried over magnesium sulfate, filtered and concentrated under reduced pressure to give the crude product. The crude mixture was purified by column chromatography on silica gel.

3.1 Compound Data for Smiles products

Ethyl 2-(methylamino)-2-(4-nitrophenyl)-2-phenylacetate **8a**

Prepared according to **General Procedure E** from 4-nitro-*N*-methylbenzenesulfonamide **6a** (0.10 mmol, 21.6 mg), K_2CO_3 (0.30 mmol, 41.5 mg), ethyl α -chlorophenylacetate **7a** (0.20 mmol, 52 μ L), DMF (1.00 mL). Purification by column chromatography on silica gel (0–40% EtOAc in hexanes)

afforded **8a** as a light yellow solid (87.0 mg, 0.28 mmol, 92%); m.p. 53–55 °C.

1H NMR (400 MHz, $CDCl_3$): δ 8.16 (app. d, J = 9.0 Hz, 2H, CH_{ar-2}), 7.73 (app. d, J = 9.0 Hz, 2H, CH_{ar-3}), 7.39–7.27 (m, 5H, $CH_{ar-10, 11, 12}$), 4.32–4.21 (m, 2H, CH_2-7), 2.34 (br. s, 1H, NH), 2.10 (s, 3H, CH_3-13), 1.15 (t, J = 7.2 Hz, 3H, CH_3-8); ^{13}C NMR (101 MHz, $CDCl_3$): δ 172.6 (C-6), 148.6 (C-4), 147.1 (C-1), 140.7 (C-9), 129.7 (C-3), 128.5 (C-10), 128.0 (C-12), 127.9 (C-11), 123.1 (C-2), 73.2 (C-5), 62.1 (C-7), 30.9 (C-13), 14.1 (C-8).

IR (neat film, cm^{-1}): 3349, 3063, 2981, 2804, 1821, 1728, 1510, 1320, 1223, 1211, 1158, 1026, 853, 734, 701, 633.

MS (ES^+) found m/z 315 $[M+H]^+$; HRMS (ES^+) found 315.1336, $C_{17}H_{19}N_2O_4$ $[M+H]^+$ requires 315.1326.

Ethyl 2-amino-2-(4-nitrophenyl)-2-phenylacetate **8b**

Prepared according to **General Procedure E** from 4-nitrobenzenesulfonamide (0.30 mmol, 66.5 mg), K_2CO_3 (0.90 mmol, 124 mg), ethyl α -chlorophenylacetate **7a** (0.60 mmol, 103 μ L), DMF (3.00 mL). Purification by column chromatography on silica gel (0–40% EtOAc in hexanes)

afforded **8b** as a clear colourless oil (13.5 mg, 0.045 mmol, 15%).

1H NMR (400 MHz, $CDCl_3$): δ 8.09 (app. d, J = 9.0 Hz, 2H, CH_{ar-2}), 7.74 (app. d, J = 9.0 Hz, 2H, CH_{ar-3}), 7.29–7.24 (m, 3H, $CH_{ar-10, 12}$), 7.23–7.19 (m, 2H, CH_{ar-11}), 4.25–4.18 (m, 2H, CH_2-7), 2.30 (br. s, 2H, NH_2), 1.17 (t, J = 7.2 Hz, 3H, CH_3-8); ^{13}C NMR (101 MHz,

CDCl₃): δ 173.8 (C-6), 150.8 (C-1), 147.3 (C-4), 143.5 (C-9), 129.2 (C-3), 128.7 (C-10), 128.2 (C-12), 127.2 (C-11), 123.2 (C-2), 68.4 (C-5), 62.6 (C-7), 14.1 (C-8).

IR (neat film, cm⁻¹): 3106, 2923, 2853, 2360, 2343, 1737, 1530, 1368, 1348, 1307, 1193, 1146, 1080, 1014, 854, 750, 734, 696, 683, 612.

MS (ES⁺) found m/z 301 [M+H]⁺; HRMS (ES⁺) found 323.0998, C₁₆H₁₆N₂O₄ [M+Na]⁺ requires 323.1002.

1-(Methylamino)-1-(4-nitrophenyl)-1-phenylpropan-2-one **8c**

Prepared according to **General Procedure E** from 4-nitro-*N*-methylbenzenesulfonamide **6a** (0.10 mmol, 21.6 mg), K₂CO₃ (0.30 mmol, 41.5 mg), 1-chloro-1-phenylpropan-2-one (0.20 mmol, 30 μ L), DMF (1.00 mL). Purification by column chromatography on silica gel (0–40% EtOAc in hexanes) afforded **8c** as a yellow oil (10.2 mg, 0.036 mmol, 36%).

¹H NMR (400 MHz, CDCl₃): δ 8.19 (app. d, J = 9.0 Hz, 2H, CH_{ar}-2), 7.64 (app. d, J = 9.0 Hz, 2H, CH_{ar}-3), 7.39–7.30 (m, 5H, CH_{ar}-9,10,11), 2.15 (s, 3H, CH₃-7), 2.11 (s, 3H, CH₃-12); ¹³C NMR (101 MHz, CDCl₃): δ 205.8 (C-6), 147.6 (C-1), 147.1 (C-4), 139.4 (C-8), 130.2 (C-3), 128.9 (C-10), 128.3 (C-9), 128.2 (C-11), 123.4 (C-2), 77.7 (C-5), 30.3 (C-12), 26.3 (C-7).

IR (neat film, cm⁻¹): 3353, 3063, 2944, 2804, 1709, 1593, 1517, 1490, 1448, 1346, 1172, 1141, 1110, 850, 764, 747, 701, 668, 613.

MS (ES⁺) found m/z 301 [M+Na]⁺; HRMS (ES⁺) found 285.1220, C₁₆H₁₇N₂O₃ [M+H]⁺ requires 285.1234.

Ethyl 2-(methylamino)-2-(2-nitrophenyl)-2-phenylacetate **8d**

Prepared according to **General Procedure E** from 2-nitro-*N*-methylbenzenesulfonamide **6b** (0.10 mmol, 21.6 mg), K₂CO₃ (0.30 mmol, 41.5 mg), ethyl α -chlorophenylacetate **7a** (0.20 mmol, 34 μ L), DMF (1.00 mL). Purification by column chromatography on silica gel (0–40% EtOAc in hexanes)

afforded **8d** as a yellow solid (15.5 mg, 0.049 mmol, 49%), m.p. 103–105 °C.

¹H NMR (400 MHz, CDCl₃): δ 7.92 (app. d, *J* = 8.0 Hz, 1H, CH_{ar}-2), 7.62–7.58 (m, 2H, CH_{ar}-13), 7.53–7.48 (m, 1H, CH_{ar}-3), 7.47–7.43 (m, 1H, CH_{ar}-5), 7.36–7.29 (m, 4H, CH_{ar}-4, 12, 14), 4.19–4.02 (m, 2H, CH₂-9), 2.72 (br. s, 1H, NH), 2.19 (s, 3H, CH₃-15), 1.13 (t, *J* = 7.2 Hz, 3H, CH₃-10); ¹³C NMR (101 MHz, CDCl₃): δ 171.1 (C-8), 150.0 (C-1), 138.9 (C-11), 135.8 (C-6), 132.8 (C-4), 131.8 (C-3), 129.0 (C-13), 128.4 (C-5), 128.2 (C-12), 128.1 (C-14), 125.4 (C-2), 72.2 (C-7), 61.9 (C-9), 30.9 (C-15), 13.9 (C-10).

IR (neat film, cm⁻¹): 3324, 3075, 2951, 2806, 1819, 1724, 1524, 1445, 1350, 1236, 1206, 1176, 1163, 1100, 1022, 968, 851, 799, 772, 744, 738, 709, 699, 692, 635.

MS (ES⁺) found *m/z* 315 [M+H]⁺; HRMS (ES⁺) found 315.1339, C₁₇H₁₉N₂O₄ [M+H]⁺ requires 315.1347.

Ethyl 2-(methlamino)-2-(4-nitro-3-(trifluoromethyl)phenyl)-2-phenylacetate **8e**

Prepared according to **General Procedure E** from 4-nitro-3-(trifluoromethyl)-*N*-methylbenzenesulfonamide **6c** (0.11 mmol, 31.6 mg), K₂CO₃ (0.33 mmol, 45.6 mg), ethyl α-chlorophenylacetate **7a** (0.22 mmol, 38 μL), DMF (1.00 mL). Purification by column chromatography on silica gel (0–40% EtOAc in hexanes) afforded **150g** as a clear yellow oil (17.9 mg, 0.047 mmol, 42%).

¹H NMR (400 MHz, CDCl₃): δ 8.14 (app. d, *J* = 1.8 Hz, 1H, CH_{ar}-5), 7.97 (app. dd, *J* = 8.6, 1.8 Hz, 1H, CH_{ar}-3), 7.82 (app. d, *J* = 8.6 Hz, 1H, CH_{ar}-2), 7.38–7.28 (m, 5H, CH_{ar}-13, 14, 15), 4.34–4.23 (m, 2H, CH₂-10), 2.46 (br. s, 1H, NH), 2.18 (s, 3H, CH₃-16), 1.24 (t, *J* = 7.1 Hz, 3H, CH₃-11); ¹³C NMR (101 MHz, CDCl₃): δ 172.1 (C-9), 146.9 (C-4), 140.5 (C-12), 138.5 (C-1), 133.7 (C-3), 128.8 (C-13), 128.5 (C-5), 128.3 (C-15), 127.7 (q, *J* = 206.5 Hz, C-7), 127.4 (C-14), 124.7 (C-2), 123.3 (q, *J* = 33.8, C-6), 73.0 (C-8), 62.4 (C-10), 30.9 (C-16), 14.2 (C-11); ¹⁹F NMR (376 MHz, CDCl₃): δ –59.83.

IR (neat film, cm⁻¹): 3356, 3066, 2983, 2929, 2807, 2362, 1729, 1539, 1360, 1311, 1215, 1179, 1141, 1048, 1027, 858, 758, 701, 657.

MS (ES^+) found m/z 383 $[\text{M}+\text{H}]^+$; **HRMS** (ES^+) found 383.1205, $\text{C}_{18}\text{H}_{18}\text{F}_3\text{N}_2\text{O}_4$ $[\text{M}+\text{H}]^+$ requires 383.1213.

Ethyl 2-(2-methoxy-4-nitrophenyl)-2-(methylamino)-2-phenylacetate **8f**

Prepared according to **General Procedure E** from 4-nitro-2-methoxy-*N*-methylbenzenesulfonamide **6d** (0.11 mmol, 26.4 mg), K_2CO_3 (0.32 mmol, 44.2 mg), ethyl α -chlorophenylacetate **152a** (0.21 mmol, 36 μL), DMF (1.00 mL).

Purification by column chromatography on silica gel (0–40% EtOAc in hexanes) afforded **8f** as a clear yellow oil (17.7 mg, 0.059 mmol, 56%).

^1H NMR (400 MHz, CDCl_3): δ 7.79 (app. dd, $J = 8.6, 2.2$ Hz, 1H, $\text{CH}_{\text{ar-2}}$), 7.73–7.68 (m, 3H, $\text{CH}_{\text{ar-6, 14}}$), 7.47 (app. d, $J = 8.6$ Hz, 1H, $\text{CH}_{\text{ar-3}}$), 7.38–7.32 (m, 2H, $\text{CH}_{\text{ar-13}}$), 7.32–7.27 (m, 1H, $\text{CH}_{\text{ar-15}}$), 4.23–4.12 (m, 2H, $\text{CH}_2\text{-10}$), 3.91 (s, 3H, $\text{CH}_3\text{-7}$), 2.12 (s, 3H, $\text{CH}_3\text{-16}$), 1.17 (t, 3H, $J = 7.2$ Hz, $\text{CH}_3\text{-11}$); ^{13}C NMR (101 MHz, CDCl_3): δ 172.2 (C-9), 157.2 (C-5), 148.1 (C-1), 138.7 (C-4), 137.6 (C-12), 129.5 (C-3), 129.0 (C-14), 128.1 (C-13), 127.9 (C-15), 115.6 (C-2), 106.1 (C-6), 69.9 (C-8), 61.4 (C-10), 56.1 (C-7), 30.6 (C-16), 14.3 (C-11).

IR (neat film, cm^{-1}): 3379, 3331, 3090, 3059, 2979, 2943, 2853, 2803, 1733, 1590, 1520, 1485, 1344, 1251, 1179, 1094, 1028, 867, 767, 739, 700.

MS (ES^+) found m/z 345 $[\text{M}+\text{H}]^+$; **HRMS** (ES^+) found 345.1445, $\text{C}_{18}\text{H}_{21}\text{N}_2\text{O}_5$ $[\text{M}+\text{H}]^+$ requires 345.1431

Ethyl 2-(4-nitrophenyl)-2-phenyl-2-(phenylamino) acetate **8g**

Prepared according to **General Procedure E** from 4-nitro-*N*-phenylbenzenesulfonamide **6e** (0.10 mmol, 27.8 mg), K_2CO_3 (0.30 mmol, 41.5 mg), ethyl α -chlorophenylacetate **7a** (0.20 mmol, 34 μL), DMF (1.00 mL). Purification by column chromatography on silica gel (0–40% EtOAc in hexanes)

afforded **8g** as a yellow oil (32.3 mg, 0.086 mmol, 86%).

¹H NMR (400 MHz, CDCl₃): δ 8.15 (app. d, *J* = 8.4 Hz, 2H, CH_{ar}-2), 7.84 (app. d, *J* = 8.4 Hz, 2H, CH_{ar}-3), 7.49–7.46 (m, 2H, CH_{ar}-11), 7.38–7.28 (m, 3H, CH_{ar}-10, 12), 7.03 (app. dd, *J* = 8.6, 7.5 Hz, 2H, CH_{ar}-15), 6.71 (app. tt, *J* = 7.5, 1.1 Hz, 1H, CH_{ar}-16), 6.44 (app. dd, *J* = 8.6, 1.1 Hz, 2H, CH_{ar}-14), 5.33 (s, 1H, NH), 4.26–4.12 (m, 2H, CH₂-7), 1.03 (t, *J* = 7.1 Hz, 3H, CH₃-8); **¹³C NMR** (101 MHz, CDCl₃): δ 172.1 (C-6), 147.4 (C-4), 147.2 (C-1), 145.0 (C-13), 140.5 (C-9), 129.9 (C-3), 129.0 (C-10), 128.9 (C-15), 128.5 (C-12), 127.5 (C-11), 123.2 (C-2), 119.1 (C-16), 115.7 (C-14), 71.7 (C-5), 62.7 (C-7), 13.8 (C-8).

IR (neat film, cm⁻¹): 3392, 3054, 2981, 1731, 1602, 1518, 1498, 1347, 1257, 1224, 1196, 1023, 1015, 854, 750, 736, 720, 694.

MS (ES⁺) found *m/z* 399 [M+Na]⁺; **HRMS** (ES⁺) found 399.1315, C₂₂H₂₀N₂O₄Na [M+Na]⁺ requires 399.1305.

Ethyl 2-(4-nitrophenyl)-2-phenyl-2-(p-tolylamino)acetate **8h**

Prepared according to **General Procedure E** from 4-nitro-*N*-(*p*-tolyl)benzenesulfonamide **6f** (0.10 mmol, 29.2 mg), K₂CO₃ (0.30 mmol, 41.5 mg), ethyl α-chlorophenylacetate **7a** (0.20 mmol, 34 μL), DMF (1.00 mL). Purification by column chromatography on silica gel (0–40% EtOAc in hexanes) afforded **8h** as a yellow oil (36 mg, 0.092 mmol, 92%).

¹H NMR (400 MHz, CDCl₃): δ 8.14 (app. d, *J* = 9.0 Hz, 2H, CH_{ar}-2), 7.84 (app. d, *J* = 9.0 Hz, 2H, CH_{ar}-3), 7.49–7.46 (m, 2H, CH_{ar}-11), 7.37–7.28 (m, 3H, CH_{ar}-10, 12), 6.84 (app. d, *J* = 8.3 Hz, 2H, CH_{ar}-15), 6.35 (app. d, *J* = 8.3 Hz, 2H, CH_{ar}-14), 5.21 (s, 1H, NH), 4.25–4.13 (m, 2H, CH₂-7), 2.17 (s, 3H, CH₃-17), 1.05 (t, *J* = 7.2 Hz, 3H, CH₃-8); **¹³C NMR** (101 MHz, CDCl₃): δ 172.2 (C-6), 147.6 (C-1), 147.1 (C-4), 142.5 (C-16), 140.7 (C-13), 129.9 (C-3), 129.5 (C-15), 128.8 (C-10), 128.4 (C-12), 128.3 (C-9), 127.5 (C-11), 123.2 (C-2), 115.8 (C-14), 71.7 (C-5), 62.7 (C-7), 20.5 (C-17), 13.9 (C-8).

IR (neat film, cm⁻¹): 3390, 2980, 2920, 2865, 2359, 1731, 1515, 1348, 1301, 1254, 1226, 1195, 1024, 1015, 855, 812, 736, 703.

MS (ES^+) found m/z 413 $[\text{M}+\text{Na}]^+$; **HRMS** (ES^+) found 413.1469, $\text{C}_{23}\text{H}_{22}\text{N}_2\text{O}_4\text{Na}$ $[\text{M}+\text{Na}]^+$ requires 413.1472.

Ethyl 2-(mesitylamino)-2-(4-nitrophenyl)-2-phenylacetate **8i**

Prepared according to **General Procedure E** from 4-nitro-*N*-mesitylbenzenesulfonamide **6g** (0.10 mmol, 32.0 mg), K_2CO_3 (0.30 mmol, 41.5 mg), ethyl α -chlorophenylacetate **7a** (0.20 mmol, 34 μL), DMF (1.00 mL). Purification by column chromatography on silica gel (0–40% EtOAc in hexanes) afforded **8i** as a light red solid (9.7 mg, 0.023 mmol, 23%), m.p. 155–157 $^\circ\text{C}$.

^1H NMR (400 MHz, CDCl_3): δ 8.27 (app. d, $J = 8.9$ Hz, 2H, $\text{CH}_{\text{ar-2}}$), 7.85 (app. d, $J = 8.9$ Hz, 2H, $\text{CH}_{\text{ar-3}}$), 7.21–7.15 (m, 3H, $\text{CH}_{\text{ar-10, 12}}$), 7.11–7.07 (m, 2H, $\text{CH}_{\text{ar-11}}$), 6.72 (br. s, 1H, $\text{CH}_{\text{ar-15}}$), 6.55 (br. s, 1H, $\text{CH}_{\text{ar-15}}$), 5.74 (s, 1H, NH), 4.19 (m, 2H, CH-7), 2.15 (s, 3H, CH-17), 2.13 (s, 3H, $\text{CH}_3\text{-17}$), 1.79 (s, 3H, $\text{CH}_3\text{-18}$), 1.22 (t, $J = 7.1$ Hz, 3H, $\text{CH}_3\text{-8}$); ^{13}C NMR (101 MHz, CDCl_3): δ 170.6 (C-6), 150.1 (C-4), 145.7 (C-1), 140.7 (C-9), 139.6 (C-16), 138.8 (C-13), 131.9 (C-14), 131.3 (C-14), 130.2 (C-10), 129.94 (C-3), 129.86 (C-12), 129.7 (C-15), 129.3 (C-15), 128.2 (C-11), 123.8 (C-2), 68.5 (C-5), 62.0 (C-7), 21.0 (C-17), 20.0 (C-18), 19.1 (C-17), 14.1 (C-8).

IR (neat film, cm^{-1}): 3105, 3066, 2982, 2926, 2867, 1743, 1530, 1378, 1311, 1203, 1165, 1090, 1020, 853, 738, 699, 689, 625.

MS (ES^+) found m/z 441 $[\text{M}+\text{Na}]^+$; **HRMS** (ES^+) found 441.1783, $\text{C}_{25}\text{H}_{26}\text{N}_2\text{O}_4\text{Na}$ $[\text{M}+\text{Na}]^+$ requires 441.1785.

Ethyl 2-((4-methoxyphenyl)amino)-2-(4-nitrophenyl)-2-phenylacetate **8j**

Prepared according to **General Procedure E** from 4-nitro-*N*-(4-methoxyphenyl)benzenesulfonamide **6h** (0.10 mmol, 30.8 mg), K_2CO_3 (0.30 mmol, 41.5 mg), ethyl α -chlorophenylacetate **7a** (0.20 mmol, 34 μL), DMF (1.00 mL). Purification by column chromatography on silica

gel (0–40% EtOAc in hexanes) afforded **8j** as a clear yellow oil (38.7 mg, 0.095 mmol, 95%).

¹H NMR (400 MHz, CDCl₃): δ 8.14 (app. d, *J* = 9.2 Hz, 2H, CH_{ar}-2), 7.83 (app. d, *J* = 9.2 Hz, 2H, CH_{ar}-3), 7.48–7.44 (m, 2H, CH_{ar}-11), 7.36–7.27 (m, 3H, CH_{ar}-10, 12), 6.61 (app. d, *J* = 8.4 Hz, 2H, CH_{ar}-15), 6.39 (app. d, *J* = 8.4 Hz, 2H, CH_{ar}-14), 5.04 (br. s, 1H, NH), 4.25–4.11 (m, 2H, CH₂-7), 3.67 (s, 3H, CH₃-17), 1.04 (t, *J* = 7.2 Hz, 3H, CH₃-8); ¹³C NMR (101 MHz, CDCl₃): δ 172.3 (C-6), 153.1 (C-16), 147.9 (C-1), 147.1 (C-4), 140.9 (C-9), 138.8 (C-13), 129.8 (C-3), 128.8 (C-10), 128.4 (C-12), 127.4 (C-11), 123.2 (C-2), 117.3 (C-14), 114.4 (C-15), 72.1 (C-5), 62.6 (C-7), 55.6 (C-17), 13.9 (C-8).

IR (neat film, cm⁻¹): 3378, 3062, 2979, 2933, 2833, 1731, 1510, 1347, 1237, 1195, 1179, 1026, 1015, 854, 823, 763, 735, 701.

MS (ES⁺) found *m/z* 429 [M+Na]⁺; HRMS (ES⁺) found 407.1593, C₂₃H₂₃N₂O₅ [M+H]⁺ requires 407.1601.

Ethyl 2-((4-chlorophenyl)amino)-2-(4-nitrophenyl)-2-phenylacetate **8k**

Prepared according to **General Procedure E** from 4-nitro-*N*-(4-chlorophenyl)benzenesulfonamide **6i** (0.10 mmol, 31.3 mg), K₂CO₃ (0.30 mmol, 41.5 mg), ethyl α-chlorophenylacetate **7a** (0.20 mmol, 34 μL), DMF (1.00 mL). Purification by column chromatography on silica gel (0–40% EtOAc in hexanes) afforded **8k** as a vibrant yellow solid (32.3 mg, 0.076 mmol, 76%), m.p. 48–51 °C.

¹H NMR (500 MHz, CDCl₃): δ 8.08 (app. d, *J* = 9.0 Hz, 2H, CH_{ar}-2), 7.72 (app. d, *J* = 9.0 Hz, 2H, CH_{ar}-3), 7.38–7.35 (m, 2H, CH_{ar}-10), 7.29–7.25 (m, 2H, CH_{ar}-11), 7.25–7.21 (m, 1H, CH_{ar}-12), 6.89 (app. dt, *J* = 8.8, 3.4 Hz, 2H, CH_{ar}-15), 6.27 (app. dt, *J* = 8.8, 3.4 Hz, 2H, CH_{ar}-14), 5.35 (s, 1H, NH), 4.18–4.08 (m, 2H, CH₂-7), 0.99 (t, *J* = 7.2 Hz, 3H, CH₃-8); ¹³C NMR (126 MHz, CDCl₃): δ 171.9 (C-6), 147.3 (C-1), 146.7 (C-4), 143.4 (C-13), 139.7 (C-9), 129.9 (C-3), 128.9 (C-11), 128.8 (C-15), 128.6 (C-16), 127.7 (C-10), 123.9 (C-12), 123.3 (C-2), 116.8 (C-14), 71.6 (C-5), 63.0 (C-7), 13.9 (C-8).

IR (neat film, cm^{-1}): 3389, 2981, 1732, 1595, 1525, 1498, 1447, 1347, 1314, 1294, 1255, 1226, 1015, 819, 735, 702.

MS (ES^+) found m/z 449 $[\text{M}+\text{K}]^+$; **HRMS** (ES^+) found 449.0665, $\text{C}_{22}\text{H}_{19}\text{ClN}_2\text{O}_4\text{K}$ $[\text{M}+\text{K}]^+$ requires 449.0655.

Ethyl 4-((2-ethoxy-1-(4-nitrophenyl)-2-oxo-1-phenylethyl)amino)benzoate **8l**

Prepared according to **General Procedure E** from ethyl 4-((4-nitrophenyl)sulfonamido)benzoate **6j** (0.10 mmol, 35.0 mg), K_2CO_3 (0.30 mmol, 41.5 mg), ethyl α -chlorophenylacetate **7a** (0.20 mmol, 34 μL), DMF (1.00 mL). Purification by column chromatography on silica gel (0–40% EtOAc in hexanes) afforded **8l** as a light yellow oil (11.3 mg, 0.025 mmol, 25%).

^1H NMR (400 MHz, CDCl_3): δ 8.17 (app. d, $J = 9.0$ Hz, 2H, $\text{CH}_{\text{ar}}\text{-2}$), 7.79 (app. d, $J = 9.0$ Hz, 2H, $\text{CH}_{\text{ar}}\text{-3}$), 7.72 (app. d, $J = 8.8$ Hz, 2H, $\text{CH}_{\text{ar}}\text{-14}$), 7.47–7.41 (m, 2H, $\text{CH}_{\text{ar}}\text{-11}$), 7.39–7.32 (m, 3H, $\text{CH}_{\text{ar}}\text{-10, 12}$), 6.40 (app. d, $J = 8.8$ Hz, 2H, $\text{CH}_{\text{ar}}\text{-15}$), 5.91 (br. s, 1H, NH), 4.29–4.18 (m, 4H, $\text{CH}_2\text{-7, 18}$), 1.31 (t, $J = 7.1$ Hz, 3H, $\text{CH}_3\text{-19}$), 1.08 (t, $J = 7.2$ Hz, 3H, $\text{CH}_3\text{-8}$); **^{13}C NMR** (101 MHz, CDCl_3): δ 171.8 (C-6), 166.6 (C-17), 148.6 (C-16), 147.4 (C-4), 146.1 (C-1), 138.8 (C-9), 131.0 (C-14), 130.0 (C-3), 129.0 (C-10), 128.8 (C-12), 127.9 (C-11), 123.4 (C-2), 120.6 (C-13), 114.6 (C-15), 71.2 (C-5), 63.3 (C-18), 60.5 (C-7), 14.6 (C-19), 13.8 (C-8).

IR (neat film, cm^{-1}): 3379, 2981, 2930, 2856, 1733, 1703, 1601, 1519, 1348, 1266, 1229, 1178, 1108, 771, 701.

MS (ES^-) found m/z 447 $[\text{M}-\text{H}]^-$; **HRMS** (ES^-) found 447.1565, $\text{C}_{25}\text{H}_{23}\text{N}_2\text{O}_6$ $[\text{M}-\text{H}]^-$ requires 447.1562.

Ethyl 2-(benzylamino)-2-(4-nitrophenyl)-2-phenylacetate **8m**

Prepared according to **General Procedure E** from 4-nitro-*N*-benzylbenzenesulfonamide **6m** (0.10 mmol, 29.2 mg), K₂CO₃ (0.30 mmol, 41.5 mg),

ethyl α -chlorophenylacetate **7a** (0.20 mmol, 34 μ L), DMF (1.00 mL). Purification by column chromatography on silica gel (0–40% EtOAc in hexanes) afforded **8m** as a clear, colourless oil (86.7 mg, 0.22 mmol, 74%).

¹H NMR (400 MHz, CDCl₃): δ 8.07 (app. d, J = 9.1 Hz, 2H, CH_{ar}-2), 7.74 (app. d, J = 9.1 Hz, 2H, CH_{ar}-3), 7.39–7.35 (m, 2H, CH_{ar}-10), 7.29–7.21 (m, 6H, CH_{ar}-11, 15, 16), 7.20–7.15 (m, 2H, CH_{ar}-12, 17), 4.26–4.15 (m, 2H, CH₂-7), 3.37 (s, 2H, CH-13), 2.56 (br. s, 1H, NH), 1.16 (t, J = 7.1 Hz, 3H, CH₃-8); ¹³C NMR (101 MHz, CDCl₃): δ 172.5 (C-6), 149.0 (C-4), 147.1 (C-1), 141.0 (C-9), 139.8 (C-14), 129.5 (C-3), 128.7 (C-15), 128.6 (C-16), 128.2 (C-11), 128.1 (C-12), 127.7 (C-10), 127.4 (C-17), 123.2 (C-2), 72.7 (C-5), 62.2 (C-7), 48.6 (C-13), 14.2 (C-8).

IR (neat film, cm⁻¹): 3334, 3062, 2980, 2853, 1728, 1518, 1346, 1220, 1993, 1026, 1015, 853, 733, 699.

MS (ES⁺) found m/z 391 [M+H]⁺; HRMS (ES⁺) found 391.1652, C₂₃H₂₃N₂O₄ [M+H]⁺ requires 391.1647.

Ethyl 2-(benzylamino)-2-(4-nitrophenyl)propanoate **8n**

Prepared according to **General Procedure E** from 4-nitro-*N*-benzylbenzenesulfonamide **6o** (0.10 mmol, 29.2 mg), K₂CO₃ (0.30 mmol, 41.5 mg), ethyl 2-chloropropionate (0.20 mmol, 25 μ L), DMF (1.00 mL). Purification by column chromatography on silica gel (0–40% EtOAc in hexanes) afforded **8n** as a light yellow solid (18.7 mg, 0.057 mmol,

57%), m.p. 73–75 °C.

¹H NMR (400 MHz, CDCl₃): δ 8.20 (app. d, J = 9.0 Hz, 2H, CH_{ar}-2), 7.73 (app. d, J = 9.0 Hz, 2H, CH_{ar}-3), 7.39–7.32 (m, 4H, CH_{ar}-12, 13), 7.30–7.26 (m, 1H, CH_{ar}-14), 4.25 (d, J = 7.2 Hz, 2H, CH₂-7), 3.70 (d, J = 12.2 Hz, 1H, CH-10), 3.62 (d, J = 12.2 Hz, 1H, CH-10), 2.30 (br. s, 1H, NH), 1.74 (s, 3H, CH₃-9), 1.27 (t, J = 7.2 Hz, 3H, CH₃-8); ¹³C NMR (101 MHz,

CDCl_3): δ 174.2 (C-6), 150.9 (C-4), 147.3 (C-1), 140.0 (C-11), 128.7 (C-12), 128.3 (C-13), 127.4 (C-14), 127.2 (C-3), 123.7 (C-2), 65.8 (C-5), 61.8 (C-7), 48.4 (C-10), 25.0 (C-9), 14.3 (C-8).

IR (neat film, cm^{-1}): 3106, 1535, 1382, 1361, 1347, 1173, 854, 718, 703, 678.

MS (ES^+) found m/z 329 $[\text{M}+\text{H}]^+$; HRMS (ES^+) found 329.1496, $\text{C}_{18}\text{H}_{21}\text{N}_2\text{O}_4$ $[\text{M}+\text{H}]^+$ requires 329.1486.

Ethyl 2-(methlamino)-2-(4-nitrophenyl)propanoate **8o**

Prepared according to **General Procedure E** from 4-nitro-*N*-methylbenzenesulfonamide **6a** (0.10 mmol, 21.6 mg), K_2CO_3 (0.30 mmol, 41.5 mg), ethyl 2-chloropropionate (0.20 mmol, 25 μL), DMF (1.00 mL). Purification by column chromatography on silica gel (0–40% EtOAc in hexanes) afforded **8o** as a yellow oil (18.1 mg, 0.0718 mmol, 72%).

^1H NMR (400 MHz, CDCl_3): δ 8.19 (app. d, $J = 9.1$ Hz, 2H, $\text{CH}_{\text{ar-2}}$), 7.64 (app. d, $J = 9.1$ Hz, 2H, $\text{CH}_{\text{ar-3}}$), 4.22 (q, $J = 7.1$ Hz, 2H, CH_2 -7), 2.32 (s, 3H, CH_3 -10), 2.05 (br. s, 1H, NH), 1.64 (s, 3H, CH_3 -9), 1.24 (t, $J = 7.1$ Hz, 3H, CH_3 -8); ^{13}C NMR (101 MHz, CDCl_3): δ 174.2 (C-6), 150.8 (C-4), 147.3 (C-1), 127.2 (C-3), 123.7 (C-2), 66.0 (C-5), 61.8 (C-7), 30.5 (C-10), 23.9 (C-9), 14.3 (C-8).

IR (neat film, cm^{-1}): 3352, 2982, 2942, 2854, 2803, 1727, 1605, 1520, 1491, 1449, 1347, 1234, 1149, 1109, 1098, 1014, 855, 757, 741, 700.

MS (ES^+) found m/z 253 $[\text{M}+\text{H}]^+$; HRMS (ES^+) found 253.1176, $\text{C}_{12}\text{H}_{17}\text{N}_2\text{O}_4$ $[\text{M}+\text{H}]^+$ requires 253.1183.

Diethyl 2-(methlamino)-2-(4-nitrophenyl)-malonate **8p**

Diethyl 2-chloromalonate (4.0 eq., 3.0 mmol, 491 μL) was added to a solution of 4-nitro-*N*-methylbenzenesulfonamide **6a** (1.0 eq., 0.76 mmol, 165 mg), K_2CO_3 (3.0 eq., 2.3 mmol, 318 mg), DMF (8.00 mL) within a

metal-capped, oven-dried microwave vial. The reaction was stirred at room temperature for 16 h, after completion EtOAc was added to the mixture and washed with 10% LiCl_(aq.). The organic layers were extracted using EtOAc, washed with H₂O and sat. NaCl_(aq.), dried using MgSO₄, filtered, and concentrated *in vacuo* to give the crude product. Purification by column chromatography on silica gel (0–40% EtOAc in hexanes) afforded **8p** as a clear colourless oil (124 mg, 0.40 mmol, 53%).

¹H NMR (400 MHz, CDCl₃): δ 8.21 (app. d, *J* = 9.1 Hz, 2H, CH_{ar}-2), 7.89 (app. d, *J* = 9.1 Hz, 2H, CH_{ar}-3), 4.31–4.19 (m, 4H, CH₂-7), 2.58 (br. s, 1H, NH), 2.27 (s, 3H, CH₃-9), 1.26 (t, *J* = 7.0 Hz, 6H, CH₃-8); ¹³C NMR (101 MHz, CDCl₃): δ 168.5 (C-6), 147.9 (C-4), 142.4 (C-1), 130.2 (C-3), 123.1 (C-2), 73.7 (C-5), 62.5 (C-7), 30.3 (C-9), 14.2 (C-8).

IR (neat film, cm⁻¹): 3370, 2983, 2905, 2809, 1732, 1521, 1350, 1298, 1242, 1206, 1152, 1096, 1030, 1016, 856, 737.

MS (ES⁺) found *m/z* 311 [M+H]⁺, 333 [M+Na]⁺; HRMS (ES⁺) found 311.1230, C₁₄H₁₉N₂O₆ [M+H]⁺ requires 311.1238.

Ethyl 2-(benzylamino)-2-phenyl-2-(pyrimidin-2-yl)acetate **8q**

Prepared according to **General Procedure E** from *N*-benzylpyrimidine-2-sulfonamide (0.10 mmol, 24.9 mg), K₂CO₃ (0.30 mmol, 41.5 mg), ethyl α-chlorophenylacetate **152a** (0.20 mmol, 34 μL), DMF (1.00 mL). Purification by column chromatography on silica gel (0–40% EtOAc in hexanes) afforded **8q** as a light yellow solid (18.9 mg, 0.054 mmol, 54%),

62–64 °C.

¹H NMR (500 MHz, CDCl₃): δ 8.72 (app. d, *J* = 4.9 Hz, 2H, CH_{ar}-2), 7.79 (app. d, *J* = 7.4 Hz, 2H, CH_{ar}-9), 7.39–7.35 (m, 4H, CH_{ar}-14, 15), 7.33–7.29 (m, 3H, CH_{ar}-10, 16), 7.24 (app. t, *J* = 7.3 Hz, 1H, CH_{ar}-11), 7.16 (app. t, *J* = 4.9 Hz, 1H, CH_{ar}-1), 4.27–4.20 (m, 2H, CH₂-6), 3.71 (d, *J* = 12.9 Hz, 1H, CH₂-12), 3.56 (d, *J* = 12.9 Hz, 1H, CH₂-12), 3.31 (br. s, 1H, NH), 1.18 (t, *J* = 7.1 Hz, 3H, CH₃-7); ¹³C NMR (126 MHz, CDCl₃): δ 172.1 (C-5), 170.0 (C-3), 157.0 (C-2), 140.5 (C-13), 138.5 (C-8), 129.4 (C-9), 128.7 (C-16), 128.5 (C-10), 128.3 (C-15), 127.9 (C-14), 127.0 (C-11), 119.4 (C-1), 75.0 (C-4), 61.6 (C-6), 48.1 (C-12), 14.2 (C-7).

IR (neat film, cm^{-1}): 3349, 3031, 2979, 2364, 1737, 1562, 1453, 1403, 1217, 1028, 755, 699, 634.

MS (ES^+) found m/z 349 $[\text{M}+\text{H}]^+$; HRMS (APCI^+) found 348.1707, $\text{C}_{21}\text{H}_{22}\text{N}_3\text{O}_2$ $[\text{M}+\text{H}]^+$ requires 348.1698.

Ethyl (Z)-2-(4-nitrophenyl)-2-(phenylimino)acetate **11a**

Prepared according to **General Procedure F** from 4-nitro-*N*-phenylbenzenesulfonamide **6g** (0.36 mmol, 100 mg), K_2CO_3 (1.1 mmol, 152 mg), ethyl 2-chloroacetate **7b** (0.72 mmol, 77 μL), DMF (1.00 mL). Purification by column chromatography on silica gel (0–40% EtOAc in hexanes) afforded **11a** as a vibrant yellow solid (121 mg,

0.41 mmol, 56%), m.p. 71–74 $^\circ\text{C}$. Imine stereochemistry assigned as Z by comparison with literature data for E-**11a**.^[10]

^1H NMR (400 MHz, CDCl_3): δ 8.32 (app. d, $J = 8.9$ Hz, 2H, $\text{CH}_{\text{ar}}\text{-2}$), 8.08 (app. d, $J = 8.9$ Hz, 2H, $\text{CH}_{\text{ar}}\text{-3}$), 7.36 (app. dd, $J = 8.4, 7.5$ Hz, 2H, $\text{CH}_{\text{ar}}\text{-11}$), 7.19 (app. tt, $J = 7.5, 1.3$ Hz, 1H, $\text{CH}_{\text{ar}}\text{-12}$), 6.97 (app. dd, $J = 8.4, 1.3$ Hz, 2H, $\text{CH}_{\text{ar}}\text{-10}$), 4.16 (q, $J = 7.1$ Hz, 2H, $\text{CH}_2\text{-7}$), 1.00 (t, $J = 7.1$ Hz, 3H, $\text{CH}_3\text{-8}$); ^{13}C NMR (101 MHz, CDCl_3): δ 164.2 (C-6), 158.1 (C-5), 149.67 (C-4), 149.59 (C-1), 139.4 (C-9), 129.13 (C-3), 129.09 (C-11), 125.8 (C-12), 124.0 (C-2), 119.5 (C-10), 62.1 (C-7), 13.8 (C-8).

IR (neat film, cm^{-1}): 3067, 2989, 2922, 2855, 1725, 1617, 1601, 1595, 1579, 1521, 1483, 1464, 1349, 1307, 1301, 1174, 1009, 794, 691.

MS (ES^+) found m/z 321 $[\text{M}+\text{Na}]^+$; HRMS (ES^+) found 321.0846, $\text{C}_{16}\text{H}_{14}\text{N}_2\text{O}_4\text{Na}$ $[\text{M}+\text{Na}]^+$ requires 321.0847.

Ethyl (Z)-2-(4-nitrophenyl)-2-(p-tolylimino)acetate **11b**

Prepared according to **General Procedure F** from 4-nitro-*N*-(*p*-tolyl)benzenesulfonamide **6h** (0.10 mmol, 29.2 mg), K₂CO₃ (0.30 mmol, 41.5 mg), ethyl 2-chloroacetate **7b** (0.20 mmol, 22 μ L), DMF (1.00 mL). Purification by column chromatography on silica gel (0–40% EtOAc in hexanes) afforded **11b** as a clear brown oil (21.6 mg, 0.069 mmol, 69%).

¹H NMR (400 MHz, CDCl₃): δ 8.31 (app. d, J = 9.0 Hz, 2H, CH_{ar}-2), 8.06 (app. d, J = 9.0 Hz, 2H, CH_{ar}-3), 7.16 (app. d, J = 8.1 Hz, 2H, CH_{ar}-11), 6.89 (app. d, J = 8.1 Hz, 2H, CH_{ar}-10), 4.19 (q, J = 7.1 Hz, 2H, CH₂-7), 2.35 (s, 3H, CH-13), 1.06 (t, J = 7.1 Hz, 3H, CH₃-8); ¹³C NMR (101 MHz, CDCl₃): δ 164.6 (C-6), 157.6 (C-5), 149.6 (C-4), 147.0 (C-12), 139.7 (C-1), 135.8 (C-9), 129.7 (C-11), 129.0 (C-3), 124.0 (C-2), 119.7 (C-10), 62.1 (C-7), 21.1 (C-13), 13.9 (C-8).

IR (neat film, cm⁻¹): 3082, 3024, 2982, 2923, 2860, 1728, 1521, 1502, 1343, 1320, 1303, 1224, 1188, 1170, 1022, 1012, 863, 850, 818, 698.

MS (ES⁺) found m/z 335 [M+Na]⁺; HRMS (ES⁺) found 335.0998, C₁₇H₁₆N₂O₄Na [M+Na]⁺ requires 335.1002.

Ethyl (Z)-2-(mesitylimino)-2-(4-nitrophenyl)acetate **11c**

Prepared according to **General Procedure F** from 4-nitro-*N*-mesitylbenzenesulfonamide **6i** (0.10 mmol, 32.0 mg), K₂CO₃ (0.30 mmol, 41.5 mg), ethyl 2-chloroacetate **7b** (0.20 mmol, 22 μ L), DMF (1.00 mL). Purification by column chromatography on silica gel (0–40% EtOAc in hexanes) afforded **11c** as a red-orange solid (25.4 mg, 0.075 mmol, 75%), m.p. 68–69 °C.

¹H NMR (400 MHz, CDCl₃): δ 8.33 (app. d, J = 9.0 Hz, 2H, CH_{ar}-2), 8.11 (app. d, J = 9.0 Hz, 2H, CH_{ar}-3), 6.82 (s, 2H, CH_{ar}-11), 4.10 (q, J = 7.1 Hz, 2H, CH₂-7), 2.26 (s, 3H, CH₃-14), 2.04 (s, 6H, CH₃-13), 0.95 (t, J = 7.1 Hz, 3H, CH₃-8); ¹³C NMR (101 MHz, CDCl₃): δ

164.1 (C-6), 159.5 (C-5), 149.8 (C-4), 145.3 (C-9), 139.0 (C-1), 133.7 (C-12), 128.9 (C-3), 128.4 (C-11), 125.7 (C-10), 124.0 (C-2), 61.9 (C-7), 20.9 (C-14), 18.0 (C-13), 13.7 (C-8).

IR (neat film, cm^{-1}): 2980, 2917, 2857, 1732, 1601, 1523, 1341, 1304, 1216, 1193, 1143, 1021, 1012, 853, 701.

MS (ES^+) found m/z 363 $[\text{M}+\text{Na}]^+$; **HRMS** (ES^+) found 363.1312, $\text{C}_{19}\text{H}_{20}\text{N}_2\text{O}_4\text{Na}$ $[\text{M}+\text{Na}]^+$ requires 363.1315.

Ethyl (Z)-2-((4-methoxyphenyl)imino)-2-(4-nitrophenyl)acetate **11d**

Prepared according to **General Procedure F** from 4-nitro-*N*-(4-methoxyphenyl)benzenesulfonamide **6j** (0.10 mmol, 30.8 mg), K_2CO_3 (0.30 mmol, 41.5 mg), ethyl 2-chloroacetate **7b** (0.20 mmol, 22 μL), DMF (1.00 mL). Purification by column chromatography on silica gel (0–40% EtOAc in hexanes)

afforded **11d** as a vibrant orange oil (16.8 mg, 0.051 mmol, 51%).

^1H NMR (400 MHz, CDCl_3): δ 8.30 (app. d, $J = 9.0$ Hz, 2H, $\text{CH}_{\text{ar-2}}$), 8.05 (app. d, $J = 9.0$ Hz, 2H, $\text{CH}_{\text{ar-3}}$), 7.00 (app. d, $J = 8.9$ Hz, 2H, $\text{CH}_{\text{ar-11}}$), 6.90 (app. d, $J = 8.9$ Hz, 2H, $\text{CH}_{\text{ar-10}}$), 4.23 (q, $J = 7.2$ Hz, 2H, $\text{CH}_2\text{-7}$), 3.82 (s, 3H, $\text{CH}_3\text{-13}$), 1.11 (t, $J = 7.2$ Hz, 3H, $\text{CH}_3\text{-8}$); **^{13}C NMR** (101 MHz, CDCl_3): δ 165.0 (C-6), 158.2 (C-12), 156.8 (C-5), 149.5 (C-4), 142.5 (C-9), 139.8 (C-1), 128.9 (C-3), 124.0 (C-2), 121.6 (C-11), 114.4 (C-10), 62.1 (C-7), 55.6 (C-13), 14.0 (C-8).

IR (neat film, cm^{-1}): 3108, 3077, 2981, 2937, 2838, 1728, 1600, 1521, 1503, 1345, 1295, 1246, 1226, 1189, 1163, 1022, 1012, 851, 830, 700.

MS (ES^+) found m/z 351 $[\text{M}+\text{Na}]^+$; **HRMS** (ES^+) found 351.0944, $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}_5\text{Na}$ $[\text{M}+\text{Na}]^+$ requires 351.0951.

Ethyl (Z)-2-((4-chlorophenyl)imino)-2-(4-nitrophenyl)acetate **11e**

Prepared according to **General Procedure F** from 4-nitro-*N*-(4-chlorophenyl)benzenesulfonamide **6k** (0.10 mmol, 31.3 mg), K₂CO₃ (0.30 mmol, 41.5 mg), ethyl 2-chloroacetate **7b** (0.20 mmol, 22 μ L), DMF (1.00 mL). Purification by column chromatography on silica gel (0–40% EtOAc in hexanes) afforded **11e** as a yellow oil (16.7 mg, 0.050 mmol, 50%).

¹H NMR (400 MHz, CDCl₃): δ 8.25 (app. d, J = 8.8 Hz, 2H, CH_{ar}-2), 7.99 (app. d, J = 8.8 Hz, 2H, CH_{ar}-3), 7.25 (app. d, J = 8.4 Hz, 2H, CH_{ar}-11), 6.85 (app. d, J = 8.4 Hz, 2H, CH_{ar}-10), 4.13 (q, J = 7.1 Hz, 2H, CH₂-7), 1.00 (t, J = 7.1 Hz, 3H, CH₃-8); ¹³C NMR (101 MHz, CDCl₃): δ 164.0 (C-6), 158.6 (C-5), 149.8 (C-4), 148.0 (C-9), 139.1 (C-1), 131.4 (C-12), 129.22 (C-3), 129.18 (C-10), 124.0 (C-2), 121.0 (C-11), 62.4 (C-7), 13.9 (C-8).

IR (neat film, cm⁻¹): 3320, 3112, 3087, 2987, 2962, 2940, 2857, 1714, 1522, 1479, 1347, 1309, 1229, 1186, 1168, 1090, 1021, 1012, 851, 836, 752, 704, 696, 664.

MS (ES⁺) found m/z 333 [M+H]⁺; HRMS (ES⁺) found 333.0637, C₁₆H₁₄ClN₂O₄ [M+H]⁺ requires 333.0637.

Ethyl (Z)-4-((2-ethoxy-1-(4-nitrophenyl)-2-oxoethylidene)imino)benzoate **11f**

Prepared according to **General Procedure F** from ethyl 4-((4-nitrophenyl)sulfonamido)benzoate **6l** (0.10 mmol, 35.0 mg), K₂CO₃ (0.30 mmol, 41.5 mg), ethyl 2-chloroacetate **7b** (0.20 mmol, 22 μ L), DMF (1.00 mL). Purification by column chromatography on silica gel (0–40% EtOAc in hexanes) afforded **11f** as a yellow solid (13.5 mg, 0.037 mmol, 37%), m.p. 76–79 °C.

¹H NMR (400 MHz, CDCl₃): δ 8.33 (app. d, J = 9.0 Hz, 2H, CH_{ar}-2), 8.09 (app. d, J = 9.0 Hz, 2H, CH_{ar}-3), 8.06 (app. d, J = 8.6 Hz, 2H, CH_{ar}-10), 6.99 (app. d, J = 8.6 Hz, 2H, CH_{ar}-11), 4.38 (q, J = 7.2 Hz, 2H, CH₂-14), 4.15 (q, J = 7.1 Hz, 2H, CH₂-7), 1.40 (t, J = 7.2 Hz, 3H, CH₃-15), 1.01 (t, J = 7.1 Hz, 3H, CH₃-8); ¹³C NMR (101 MHz, CDCl₃): δ 166.3 (C-

13), 163.5 (C-6), 158.7 (C-5), 153.5 (C-9), 149.9 (C-4), 138.9 (C-1), 130.8 (C-10), 129.3 (C-3), 127.7 (C-12), 124.1 (C-2), 119.2 (C-11), 62.4 (C-7), 61.2 (C-14), 14.5 (C-15), 13.9 (C-8).

IR (neat film, cm^{-1}): 2981, 2936, 2355, 1713, 1601, 1524, 1347, 1272, 1226, 1190, 1166, 1101, 1021, 1013, 858, 697.

MS (ES^+) found m/z 393 $[\text{M}+\text{Na}]^+$; HRMS (ES^+) found 393.1056, $\text{C}_{19}\text{H}_{18}\text{N}_2\text{O}_6\text{Na}$ $[\text{M}+\text{Na}]^+$ requires 393.1057.

Ethyl (E)-2-amino-4-(4-nitrophenyl)-2-phenylbut-3-enoate **14a**

Prepared following General Procedure E using 2-(4-nitrophenyl)ethylene-1-sulfonamide **13a** (0.20 mmol, 45.6 mg), K_2CO_3 (0.60 mmol, 83.0 mg), ethyl α -chlorophenylacetate (0.40 mmol, 69 μL), DMF (2.0 mL), after purification by column chromatography on

silica gel (10–80% EtOAc in hexane) to give **14a** as a yellow oil (23.0 mg, 0.070 mmol, 35% yield).

^1H NMR (400 MHz, $(\text{CD}_3)_2\text{CO}$): δ 8.22 (d, J = 8.8 Hz, 2H, $\text{CH}_{\text{ar-2}}$), 7.77 (d, J = 8.8 Hz, 2H, $\text{CH}_{\text{ar-3}}$), 7.53 (d, 2H, J = 7.5 Hz, $\text{CH}_{\text{ar-12}}$), 7.37 (t, J = 7.5 Hz, 2H, $\text{CH}_{\text{ar-13}}$), 7.29 (m, 1H, $\text{CH}_{\text{ar-14}}$), 7.15 (d, J = 15.5 Hz, 1H, CH-5), 7.03 (d, J = 15.5 Hz, 1H, CH-6), 4.23 (qd, J = 7.2 Hz, 2.2 Hz, 2H, $\text{CH}_2\text{-9}$), 2.49 (br. s, 1H, NH), 1.23 (t, J = 7.2 Hz, 3H, $\text{CH}_3\text{-10}$). ^{13}C NMR (101 MHz, $(\text{CD}_3)_2\text{CO}$): δ 174.8 (C-8), 147.9 (C-1), 144.7 (C-4), 144.4 (C-11), 138.5 (C-6), 129.3 (C-13), 128.4 (C-5), 128.4 (C-14), 128.2 (C-2), 127.0 (C-12), 124.7 (C-3), 66.4 (C-7), 62.28 (C-9), 14.4 (C-10). HRMS (APCI $^+$) found 327.1323, $\text{C}_{18}\text{H}_{19}\text{N}_2\text{O}_4$ $[\text{M}+\text{H}]^+$ requires 327.1339.

Ethyl (E)-2-methylamino-4-(4-nitrophenyl)-2-phenylbut-3-enoate **14b**

Prepared following General Procedure E using *N*-methyl-2-(4-nitrophenyl)ethylene-1-sulfonamide **13b** (0.20 mmol, 48.4 mg), K_2CO_3 (0.60 mmol, 83.0 mg), ethyl α -chlorophenylacetate (0.40 mmol, 69

μL), DMF (2.00 mL), after purification by column chromatography on silica gel (10–80% EtOAc in hexane) to give **14b** as a yellow oil (40.1 mg, 0.12 mmol, 59% yield).

^1H NMR (400 MHz, $(\text{CD}_3)_2\text{CO}$): δ 8.21 (d, J = 8.8 Hz, 2H, $\text{CH}_{\text{ar-2}}$), 7.77 (d, J = 8.8 Hz, 2H, $\text{CH}_{\text{ar-3}}$), 7.48 (m, 2H, , $\text{CH}_{\text{ar-12}}$), 7.37 (t, J = 7.5 Hz, 2H, $\text{CH}_{\text{ar-13}}$), 7.29 (m, 1H, $\text{CH}_{\text{ar-14}}$), 7.06 (d, J = 15.5 Hz, 1H, CH-5), 6.95 (d, J = 15.5 Hz, 1H, CH-6), 4.25 (qd, J = 7.2 Hz, 2.2 Hz, 2H, $\text{CH}_2\text{-9}$), 2.66 (bs, 1H, NH), 2.27 (s, 3H, $\text{CH}_3\text{-15}$), 1.22 (t, J = 7.2 Hz, 3H, $\text{CH}_3\text{-10}$). ^{13}C NMR (101 MHz, $(\text{CD}_3)_2\text{CO}$): δ 172.9 (C-8), 147.0 (C-1), 143.8 (C-4), 141.6 (C-11), 135.1 (C-6), 128.5 (C-5), 128.4 (C-13), 127.5 (C-14), 127.4 (C-2), 126.7 (C-12), 123.8 (C-3), 70.7 (C-7), 61.1 (C-9), 42.3 (C-15), 13.6 (C-10). HRMS (APCI $^+$) found 341.1488, $\text{C}_{19}\text{H}_{21}\text{N}_2\text{O}_4$ $[\text{M}+\text{H}]^+$ requires 341.1496.

4. Reduction of Imine to Arylglycine Derivative

Ethyl 2-(4-aminophenyl)-2-(phenylamino)acetate **12a**

Method adapted from Mangas-Sánchez *et al.*^[11] $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (1.5 eq., 0.17 mmol, 40.4 mg) was added to a solution of ethyl 2-(4-nitrophenyl)-2-(phenylimino)acetate **11a** (1.0 eq., 0.11 mmol, 33.8 mg) in EtOH (1.00 mL). The solution was cooled to 0 °C and NaBH_4 (4.0 eq., 0.44 mmol, 16.6 mg) added. After

15 mins the reaction was allowed to warm to room temperature and stirred for 16 h. The mixture was filtered over Celite®, the solvents removed under reduced pressure. Purification by column chromatography on silica gel (0–40% EtOAc in hexanes) afforded **12a** as a light yellow oil (21.4 mg, 0.079 mmol, 72%).

^1H NMR (500 MHz, CDCl_3): δ 7.26 (app. d, J = 8.4 Hz, 2H, $\text{CH}_{\text{ar-2}}$), 7.12 (app. dd, J = 8.5, 7.5 Hz, 2H, $\text{CH}_{\text{ar-11}}$), 6.69 (app. tt, J = 7.5, 1.2 Hz, 1H, $\text{CH}_{\text{ar-12}}$), 6.65 (app. d, J = 8.4 Hz, 2H, $\text{CH}_{\text{ar-3}}$), 6.57 (app. dd, J = 8.5, 1.2 Hz, 2H, $\text{CH}_{\text{ar-10}}$), 4.95 (s, 1H, CH-5), 4.83 (br. s, 1H, NH), 4.26–4.19 (m, 1H, $\text{CH}_2\text{-7}$), 4.16–4.10 (m, 1H, $\text{CH}_2\text{-7}$), 3.68 (br. s, 2H, NH_2), 1.22 (t, J = 7.1 Hz, 3H, $\text{CH}_3\text{-8}$); ^{13}C NMR (126 MHz, CDCl_3): δ 172.5 (C-6), 146.5 (C-1), 146.3 (C-9), 129.3 (C-10), 128.4 (C-2), 127.5 (C-4), 118.0 (C-12), 115.4 (C-3), 113.5 (C-11), 61.7 (C-7), 60.4 (C-5), 14.2 (C-8).

Data is in accordance with previous literature reports.^[12]

5. NMR Spectra

6c

376 MHz, CDCl₃

6d

400 MHz, CDCl₃

101 MHz, CDCl₃

6i

400 MHz, (CD)₃CO 101 MHz, (CD)₃CO

8a

8b

8c

400 MHz, CDCl₃

101 MHz, CDCl₃

8d

400 MHz, CDCl₃

101 MHz, CDCl₃

8e

376 MHz, CDCl₃

8f

8g

400 MHz, CDCl₃

101 MHz, CDCl₃

8h

8i

400 MHz, CDCl₃ 101 MHz, CDCl₃

8j

8k

400 MHz, CDCl₃ 101 MHz, CDCl₃

8m

400 MHz, CDCl₃

101 MHz, CDCl₃

8n

400 MHz, CDCl₃

101 MHz, CDCl₃

80

400 MHz, CDCl₃

101 MHz, CDCl₃

8p

8q

500 MHz, CDCl₃

126 MHz, CDCl₃

11a

400 MHz, CDCl₃

101 MHz, CDCl₃

11b

11c

11d

400 MHz, CDCl₃

101 MHz, CDCl₃

11e

11f

400 MHz, CDCl₃

101 MHz, CDCl₃

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