Supporting information for

2-Azabenzonorbornanes from 7-Azabenzonorbornanols by a Nitrogen-Directed Neophyl-Type Radical Rearrangement

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General Details

All reactions requiring anhydrous conditions were conducted in flame dried apparatus under an atmosphere of argon. Syringes and needles for the transfer of reagents were dried at 140 °C and allowed to cool in a desiccator over P₂O₅ before use. THF was distilled from benzophenone ketyl, toluene and CH₂Cl₂ from CaH₂. Reactions were monitored by TLC using commercially available (Merck or Camlab) plates, pre-coated with a 0.25 mm layer of silica containing a fluorescent indicator. Visualization of reaction components was achieved with 254 nm light, and with vanillin or KMnO₄ dips. Organic layers were dried using MgSO₄ unless stated otherwise. Column chromatography was carried out on Kieselgel 60 (40-63 µm). Petroleum ether 30-40 refers to the fraction of petroleum boiling at between 30°C and 40°C. Petroleum ether 40-60 refers to the fraction of petroleum boiling at between 40°C and 60°C. IR spectra were recorded as either KBr discs or thin films, using a Perkin-Elmer 1750 FTIR spectrophotometer. Peak intensities are specified as strong (s), medium (m) or weak (w). ¹H and ¹³C NMR spectra of compounds were recorded in CDCl₃ at 25 °C unless otherwise stated, with Varian Gemini 200, Bruker DPX400, or Bruker AMX500 spectrometers. Chemical shifts are reported relative to CDCl₃ (δ_H 7.27, δ_C (central line of t) 77.0) unless stated otherwise. Coupling constants (J) are given in Hz, multiplicities are given as multiplet (m), doublet (d), triplet (t) and quartet (q). Mass spectra were obtained using a VG mass Lab. TRIO1 (GCMS) or Micromass platform APCI spectrometer or by the EPSRC National Mass Spectrometry Service Centre at the University of Swansea, 900 XLT high resolution double focusing mass spectrometer with tandem Ion Trap.

Preparation of and data for **3b**

Magnesium turnings (272 mg, 11 mmol) were added to dry THF (5 mL) under argon and stirred with 1,2-dibromoethane (60 μ L) for 10 min. A solution of *N*-Boc 3-ethylpyrrole (2.00 g, 10 mmol) in THF (15 mL) was added and the mixture brought to reflux. One quarter of a solution of *o*-bromofluorobenzene (1.79 g, 10 mmol) in THF (5 mL) was added. When initiation occurred (darkening), the rest of the solution was added dropwise. After the addition was complete the mixture was allowed to reflux for a further 90 min. It was then allowed to cool, quenched with a solution of NH_4Cl (6.0 g) in water (20 mL) and the organic layer extracted with diethyl ether (3 x 50 mL), dried and the solvent removed at reduced pressure. Chromatography (10% Et_2O : 90 % light petroleum 30-40 to 20% Et_2O : 80 % light petroleum 30-40, gradient elution) gave **3b** as a yellow oil (1.54 g, 56 %). *R*_f 0.63 (30% Et_2O : 70% light petroleum); IR (thin film): 3051m, 3025m, 2972s, 2934s, 2877s, 1713s, 1620w, 1478m, 1456s, 1392s, 1368s, 1332s, 1253s, 1169s, 1079s, 1036w, 1008w, 958w, 928m, 893m, 861s, 831s, 809s, 751s cm^{-1} ; ^1H NMR (500 MHz, 90 $^\circ\text{C}$, DMSO-d_6) 7.34-7.30 (m, 1H), 7.28-7.24 (m, 1H), 6.98-6.90 (m, 2H), 6.42 (s, 1H), 5.39 (s, 1H), 5.21 (s, 1H), 2.35-2.10 (m, 2H), 1.35 (s, 9H), 1.00 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, 90 $^\circ\text{C}$, DMSO-d_6) 160.4 (C), 155.4 (C=O), 150.2 (C), 149.4 (C), 134.1 (CH), 125.5, 125.1, 121.2, 120.7 (4 x CH), 80.2 (C), 69.6 (CH), 67.5 (CH), 28.7 (CMe_3), 23.1 (CH_2), 12.2 (CH_3); LRMS *m/z* (ES^+) 272 ($\text{M}+\text{H}^+$, 3), 257 ($\text{M}+\text{H}^+-\text{CH}_3$, 100), 248 (10), 216 (33), 198 (42), 172 (8), 155 (28); HRMS (ES^+) calcd. for $\text{C}_{17}\text{H}_{22}\text{NO}_2$ 272.1650, found 272.1656.

Preparation of and data for **3c**

Magnesium turnings (406 mg, 17 mmol) were added to dry THF (7 mL) under argon and stirred with 1,2-dibromoethane (100 μ l) for 10 min. A solution of *N*-Boc 2,4-dimethylpyrrole (3.00 g, 15 mmol) in THF (25 mL) was added and the mixture brought to reflux. One quarter of a solution of *o*-bromofluorobenzene (2.68 g, 15 mmol) in THF (7 mL) was added. When initiation occurred (darkening), the rest of the solution was added dropwise. After the addition was complete the mixture was allowed to reflux for a further 90 min. It was then allowed to cool, quenched with a solution of NH_4Cl (9 g) in water (30 mL) and the organic layer extracted with diethyl ether (3 x 50 mL), dried (MgSO_4) and the solvent removed at reduced pressure.

Chromatography (10% Et_2O : 90 % light petroleum 30-40) gave **3c** as a yellow oil (2.37 g, 52 %). R_f 0.55 (25% Et_2O : 75% light petroleum 30-40); IR (thin film): 3067m, 3050m, 3006s, 2974s, 2931s, 2869s, 1713s, 1942m, 1629m, 1478s, 1455s, 1366s, 1336s, 1292s, 1254s, 1169s, 1093s, 1073s, 1058s, 1030s, 1007m, 851s, 833s, 809s, 749s cm^{-1} ; ^1H NMR (400 MHz) 7.29 (d, $J = 7.0$ Hz, 1H), 7.15 (d, $J = 7.0$ Hz, 1H), 7.04-6.91 (m, 2H), 6.12 (s, 1H), 5.12 (s, 1H), 2.10 (s, 3H), 1.89 (s, 3H), 1.38 (s, 9H); ^{13}C NMR (100 MHz), 155.5 (C=O), 153.9 (C), 152.3 (C), 148.7 (C), 139.1 (CH), 125.0, 124.4, 120.2, 118.2 (4 x CH), 80.2 (C), 74.2 (C), 70.7 (CH), 28.2 (CMe_3), 15.2 (CH_3), 14.9 (CH_3); LRMS m/z (CI^+ , NH_3) 272 ($\text{M}+\text{H}^+$, 1%), 233 (100), 216 (17), 172 (34), 156 (3), 131 (5); HRMS (ES^+) calcd. for $\text{C}_{17}\text{H}_{22}\text{NO}_2$ 272.1650, found 272.1648.

Preparation of and data for **3d**

To a solution of *N*-Boc pyrrole (1.50 g, 9.0 mmol) in acetonitrile (60 mL) were simultaneously added solutions of 4,5-dimethoxyanthranilic acid (1.48 g, 7.5 mmol) in CH_2Cl_2 (35 mL) and isoamyl nitrite (1.76 g, 15 mmol) in acetonitrile (30 mL) at 25°C over 30 min. The mixture was brought to reflux and heated for 2 h, then allowed to cool and the solvent was removed at reduced pressure. Chromatography (30% Et_2O : 70 % light petroleum 30-40 to 50% Et_2O : 50 % light petroleum 30-40, gradient elution) gave **3d** as a yellow gum (924 mg, 41 %). R_f 0.16 (30% Et_2O : 70% light petroleum 30-40); IR (thin film): 3079m, 2971s, 2932s, 2866s, 2833s, 1704s, 1604m, 1556w, 1480s, 1410s, 1392s, 1368s, 1318s, 1291s, 1258s, 1214s, 1162s, 1089s, 1062s, 1022s, 979m, 942w, 869m, 834m, 787m cm^{-1} ; ^1H NMR (400 MHz) 7.01 (s, 2H), 6.96 (s, 2H), 5.46 (s, 1H), 5.42 (s, 1H), 3.84 (s, 6H), 1.38 (s, 9H); ^{13}C NMR (125 MHz, 90 °C, $\text{DMSO}-d_6$) 154.9 (C=O), 147.0 (2 x C), 144.0 (2 x C), 142.5 (2 x CH), 110.2 (2 x CH), 80.4 (C), 67.1 (2 x CH), 57.7 (2 x CH_3), 29.0 (CMe_3); LRMS m/z (EI^+) 303 (M^+ , 4), 265 (55), 248 (100), 221 (3), 204 (91), 189 (69), 177 (19), 145 (6), 102 (8), 58 (10); HRMS (ES^+) calcd. for $\text{C}_{17}\text{H}_{22}\text{NO}_4$ 304.1549, found 304.1546.

Preparation of and data for **3e**

To a solution of *N*-Boc pyrrole (0.967 g, 5.8 mmol) in refluxing THF (20 mL) were simultaneously added solutions of 4,5-difluoroanthranilic acid (1.00 g, 5.8 mmol) in THF (10 mL) and isoamyl nitrite (0.750 g, 6.4 mmol) in THF (10 mL) over 30 min. The mixture was allowed to reflux for 1 h after the end of the addition, then allowed to cool. Water (40 mL) was added and the organic layer extracted with Et₂O (3 x 50 mL), dried and the solvent was removed at reduced pressure. Chromatography (20% Et₂O : 80 % light petroleum 30-40) gave **3e** as a yellow solid (330 mg, 20 %). *R_f* 0.31 (25% Et₂O : 75% light petroleum 30-40); mp (from Et₂O) 69-70 °C; IR (KBr): 3039m, 3006m, 2983s, 2934m, 1697s, 1466s, 1367s, 1345s, 1269sm 1249s, 1187s, 1168s, 1127s, 1102s, 1089s, 873s, 838s, 764s cm⁻¹; ¹H NMR (500 MHz, 90 °C, DMSO-d₆), 7.40-7.33 (m, 2H), 7.04 (s, 2H), 5.43 (s, 2H), 1.34 (s, 9H); ¹³C NMR (125 MHz, 90 °C, DMSO-d₆) 154.9 (C=O), 148.2 (2 x CF), 146.4 (2 x C), 143.9 (2 x CH) 112.1 (2 x CH), 81.0 (C), 66.8 (2 x CH), 28.0 (CMe₃); ¹⁹F NMR (235 MHz) -142.8, -142.9 ; LRMS *m/z* (Cl⁺, NH₃) 280 (M+H⁺, 15), 180 (M+H-Boc⁺, 100), 164 (55), 153 (12), 125 (3), 88 (5); HRMS (Cl⁺) calcd. for C₁₅H₁₆F₂NO₂ 280.1149, found 280.1162; Anal. calcd. for C₁₅H₁₅F₂NO₂ C, 64.5; H, 5.4; N, 5.0. Found C, 64.3; H, 5.4; N, 5.0.

Preparation of and data for 4a

9-BBN (2.40 mL of 0.5 M solution in THF, 1.2 mmol) was added dropwise to a stirred solution of **3a** (250 mg, 1.0 mmol) in THF (3 mL) under argon at 25°C. The reaction was left to stir for 24 h. The flask was then cooled to 0 °C and H₂O₂ (1.25 mL of a 35% aq. solution) was added, followed by aqueous NaOH (1.7 mL of a 2 M solution). The reaction was removed from the ice bath and then stirred at 25 °C for 5h. The mixture was washed with saturated K₂CO₃ (10 mL) and extracted with Et₂O (3 x 20 mL). The combined extracts were dried (MgSO₄) and the solvent removed at reduced pressure to give an oil. Column chromatography (50% diethyl ether : light petroleum 40-60) gave the alcohol **4a** as an oil which crystallised on standing to a white solid (180 mg, 67%): R_f 0.23 (50% diethyl ether : light petroleum 40-60); mp (from Et₂O) 90-91 °C; IR (thin film): 3254 br s, 3024m, 2978s, 2928m, 2893s, 1704s, 1690s, 1456s, 1366s, 1348s, 1294m, 1251s, 1158s, 1141m, 1102s, 1088s, 1057s, 903m, 746s cm⁻¹; ¹H NMR (400 MHz) 7.27-7.23 (m, 1H), 7.19-7.17 (m, 1H), 7.14-7.06 (m, 2H), 5.11 (s, 1H), 5.01 (s, 1H), 4.04-4.00 (m, 1H), 3.20 (br s, 1H), 1.87-1.84 (m, 2H), 1.38 (s, 9H); ¹³C NMR (100 MHz) 156.5 (C=O), 146.2, 141.5 (2 x C), 127.0, 126.4, 121.3, 119.6 (4 x CH), 80.4 (C), 72.0 (CH), 68.4 (CH), 60.8 (CH), 39.4 (CH₂), 28.2 (CMe₃); LRMS m/z (CI⁺, NH₃) 279 (M+NH₄⁺, 5), 262 (M+H⁺, 70), 162 (100), 118 (25); HRMS (CI⁺) calcd. for C₁₅H₂₀NO₃ 262.1443, found 262.1440.

Preparation of and data for **4b**

9-BBN (4.50 mL of 0.5M solution in THF, 2.3 mmol) was added to alkene **3b** (308 mg, 1.1 mmol) under argon. The reaction was stirred at 25 °C for 24h. It was then cooled to 0 °C and H₂O₂ (2.5 mL of a 35% aqueous solution) was added, followed by NaOH (3.3 mL of a 2 M solution). The mixture was allowed to warm to 25 °C and stirred for 5 h. The aqueous layer was saturated with K₂CO₃ and the organic layer extracted with Et₂O (3 x 25 mL), dried and the solvent removed at reduced pressure. Chromatography (30% Et₂O : 70 % light petroleum 30-40 to 40% Et₂O : 60 % light petroleum 30-40, gradient elution) gave **4b** as a colourless gum (145 mg, 44 %). R_f 0.23 (50% Et₂O : 50% light petroleum 30-40); IR (thin film): 3418 br s, 2970s, 2930s, 2890s, 1682s, 1470s, 1392s, 1249s, 1165s, 1110s, 1055s, 1012s, 903s, 753s cm⁻¹; ¹H NMR (400 MHz) 7.27-7.17 (m, 2H), 7.14-7.08 (m, 2H), 4.95 (s, 1H), 4.93 (s, 1H), 3.38 (d, *J* = 2.0 Hz, 1H), 3.05-2.75 (br s, 1H), 2.06-2.00 (m, 1H), 1.36 (s, 9H), 1.02-0.91 (m, 1H), 0.90 (t, *J* = 7.0 Hz, 3H), 0.78-0.68 (m, 1H); ¹³C NMR (100 MHz) 156.6 (C=O), 143.3, 141.6 (2 x C) 126.7, 126.5, 121.0, 120.4 (4 x CH), 80.4 (C), 79.2 (CH), 69.4 (CH), 64.1 (CH), 52.7 (CH), 29.2 (CMe₃), 24.0 (CH₂), 12.2 (CH₃); LRMS *m/z* (TOF ES⁺) 290 (M+H⁺, 20), 275 (15), 234 (21), 216 (100), 198 (16), 190 (25), 173 (39); HRMS (ES⁺) calcd. for C₁₇H₂₄NO₃ 290.1756, found 290.1756.

Preparation of and data for **4c**

9-BBN (7.40 mL of a 0.5 M solution in THF, 3.7 mmol) was added to alkene **3c** (500 mg, 1.8 mmol) under argon at 25 °C. The mixture was stirred for 24 h, then cooled to 0 °C. H₂O₂ (3.9 mL of a 35% aq. solution) was added dropwise, followed by NaOH (5.25 mL of a 2M aq. solution). The mixture was allowed to warm to 25 °C and stirred for 5 h. The aqueous layer was saturated with K₂CO₃, and the organic layer was extracted with Et₂O (3 x 20 mL), dried and the solvent removed at reduced pressure. Chromatography (30% Et₂O : 70 % light petroleum 30-40 to 50% Et₂O : 50 % light petroleum 30-40, gradient elution) gave **4c** as a white solid (340 mg , 64 %): R_f 0.19 (50% Et₂O : 50% light petroleum 30-40); mp (from Et₂O) 86-88 °C; IR (KBr): 3414s, 2977s, 2963s, 2930m, 2884m, 1659s, 1458s, 1381s, 1253m, 1175s, 1116m, 1056m, 863s, 751s cm⁻¹; ¹H NMR (400 MHz) 7.20-7.07 (m, 4H), 4.85 (d, *J* = 4.0 Hz, 1H), 3.07 (d, *J* = 4.0 Hz, 1H), 2.41 (d, *J* = 7.0 Hz, 1H), 2.15-2.07 (m, 1H), 1.94 (s, 3H), 1.38 (s, 9H), 0.67 (d, *J* = 7.0 Hz, 3H); ¹³C NMR (100 MHz) 156.4 (C=O), 145.3, 143.1 (2 x C), 126.7, 126.4, 121.7, 119.2 (4 x CH), 83.8 (CH), 80.1 (C), 73.1 (C), 65.3 (CH), 44.6 (CH), 28.3 (CMe₃), 15.5 (CH₃), 13.1 (CH₃); LRMS *m/z* (ES⁻) 288 ((M-H)⁻, 42), 283 (15), 269 (12), 265 (12), 239 (23), 232 (100), 214 (48), 212 (35), 202 (20), 199 (13), 157 (21); HRMS (ES⁻) calcd. for C₁₇H₂₂NO₃ 288.1600, found 288.1598.

Preparation of and data for 4d

9-BBN (10.9 mL of a 0.5 M solution in THF, 5.5 mmol) was added to alkene **3d** (830 mg, 2.7 mmol) under argon at 25 °C. The mixture was stirred for 24 h, then cooled to 0 °C. H₂O₂ (5.8 mL of a 35% aq. solution) was added dropwise, followed by NaOH (7.8 mL of a 2M aq. solution). The mixture was allowed to warm to 25 °C and stirred for 5 h. The aqueous layer was saturated with K₂CO₃, and the organic layer was extracted with Et₂O (3 x 30 mL), dried and the solvent removed at reduced pressure. Chromatography (Et₂O) gave **4d** as a colourless gum (490 mg, 56%): R_f 0.44 (50% EtOAc : 50% light petroleum); IR (thin film): 3428s, 2978s, 2939s, 1690s, 1492s, 1466s, 1367s, 1307s, 1251s, 1214s, 1159s, 1095s, 1055s, 912s, 733s cm⁻¹; ¹H NMR (400 MHz) 6.87 (s, 1H), 6.80 (s, 1H), 5.01 (s, 1H), 4.91 (s, 1H), 3.92 (s, 1H), 3.83 (s, 3H) and 3.82 (s, 3H), 2.90 (br s, 1H), 1.84-1.79 (m, 2H), 1.36 (s, 9H); ¹³C NMR (100 MHz) 156.5 (C=O), 148.1, 147.5 (2 x C), 138.7, 133.5 (2 x C), 105.9, 104.5 (2 x CH), 80.4 (C), 73.2 (CH), 69.0 (CH), 61.0 (CH), 56.2 and 56.1 (2 x CH₃), 40.1 (CH₂), 28.3 (CMe₃); LRMS m/z (ES⁺) 344 (M+Na⁺, 6), 329 (M+Na-CH₃)⁺, 12), 322 (M+H⁺, 13), 289 (17), 266 (14), 248 (64), 205 (100), 177 (4); HRMS (ES⁺) calcd. for C₁₇H₂₃NO₅Na 344.1485, found 344.1474.

Preparation of and data for **4e**

9-BBN (6.40 mL of a 0.5 M solution in THF, 3.2 mmol) was added to alkene **3e** (450 mg, 1.6 mmol) under argon at 25 °C. The mixture was stirred for 24 h, then cooled to 0 °C. H₂O₂ (3.4 mL of a 35% aq. solution) was added dropwise, followed by NaOH (4.6 mL of a 2M aq. solution). The mixture was allowed to warm to 25 °C and stirred for 5 h. The aqueous layer was saturated with K₂CO₃, and the organic layer was extracted with Et₂O (3 x 20 mL), dried and the solvent removed at reduced pressure. Chromatography (50% Et₂O : 50 % light petroleum 30-40 to 100% Et₂O, gradient elution) gave **4e** as a white solid (235 mg, 49 %): R_f 0.59 (Et₂O); mp (from Et₂O) 115-116 °C; IR (KBr): 3259s, 3028m, 2985s, 2963s, 1694s, 1615m, 1482s, 1350s, 1301m, 1271m, 1254m, 1170s, 1089m, 1071m, 1041m, 803m cm⁻¹; ¹H NMR (400 MHz) 7.11 (dd, *J* = 9.0 Hz and 7.0 Hz, 1H), 7.03 (dd, *J* = 9.0 Hz and 7.0 Hz, 1H), 5.06 (s, 1H), 4.96 (s, 1H), 3.96-3.92 (m, 1H), 3.00-2.65 (br s, 1H), 1.87-1.84 (m, 2H), 1.37 (s, 9H); ¹³C NMR (100 MHz) 156.2 (C=O), 149.3 (dd, *J* = 246 Hz and 13 Hz, CF), 148.9 (dd, 245 Hz and 13 Hz, CF), 142.3 (C), 137.5 (C), 111.3 (d, *J* = 19 Hz, CH), 109.8 (d, *J* = 20 Hz, CH), 81.0 (C), 72.6 (CH), 68.5 (CH), 60.6 (CH), 39.3 (CH₂), 28.3 (CMe₃); ¹⁹F NMR (235 MHz) -139.3 (d, *J* = 19 Hz), -140.2 (d, *J* = 19 Hz); LRMS *m/z* (TOF CI⁺) 288 (M+H⁺, 52), 242 (10), 198 (100), 153 (30); HRMS (TOF CI⁺) calcd. for C₁₅H₁₈F₂NO₃ 298.1255, found 298.1246.

Preparation of and data for **4f**

9-BBN (6.80 mL of 0.5 M solution in THF, 3.4 mmol) was added dropwise to a stirred solution of alkene **3f** (500mg, 1.7 mmol) in THF (5 mL) at 0 °C. The solution was allowed to warm to room temperature and stirred overnight. The flask was then cooled to 0 °C and H₂O₂ (2.0 mL of a 35% aq. solution) was added, followed by aqueous NaOH (3.0 mL of a 2 M solution). The mixture was allowed to warm to 25 °C and stirred for 5 h. The aqueous layer was saturated with K₂CO₃, and extracted with Et₂O (3 x 30 mL). The combined extracts were dried and the solvent removed at reduced pressure to give an oil. Chromatography (40% diethyl ether : 60% light petroleum 30-40 to 60% diethyl ether : 40 % light petroleum 30-40, gradient elution) gave the alcohol **4f** as a white solid (311 mg, 59%): R_f 0.21 (50% Et₂O : 50% light petroleum 30-40); mp (from Et₂O) 177-178 °C; IR (KBr): 3512 br s, 2985m, 2919m, 1670s, 1391s, 1370m, 1165m, 1097m, 1046m, 888m, 749m cm⁻¹; ¹H NMR (400 MHz) 7.81-7.77 (m, 2H), 7.70 (s, 1H), 7.60 (s, 1H), 7.50-7.44 (m, 2H), 5.25 (s, 1H), 5.15 (s, 1H), 4.10 (s, 1H), 2.9-2.6 (br s, 1H), 2.00 (m, 2H), 1.39 (s, 9H); ¹³C NMR (100 MHz) 156.5 (C=O), 143.6, 139.1, 132.5, 132.8 (4 x C), 128.1, 128.0, 125.9, 125.7, 120.0, 117.6 (6 x CH), 80.6 (C), 73.2 (CH), 68.7 (CH), 60.2 (CH), 40.5 (CH₂), 28.1 (CMe₃); LRMS m/z (Cl⁺, NH₃) 312 (M+H⁺, 52), 273 (4), 256 (8), 238 (6), 212 (100), 194 (11), 167 (21), 90 (4); HRMS (ES⁺) calcd. for C₁₉H₂₂NO₃ 312.1599, found 312.1597.

Xanthate formation: typical procedure

Alcohol **4a** (200 mg, 0.76 mmol) was added to KH (400 mg of 30% suspension, 3.0 mmol) in THF (10 mL) at 0 °C under argon and the mixture was then stirred at 25 °C for 20 min. The mixture was cooled to 0 °C and CS₂ (228 mg, 3.0 mmol) was added and the mixture stirred for 10 min at 0 °C. Finally iodomethane (425 mg, 3.0 mmol) was added and the solution was stirred at room temperature for 20 min. The reaction was quenched with dropwise addition of water under argon until effervescence had ceased and the organic layer extracted with diethyl ether (2 x 10 mL), dried and the solvent removed at reduced pressure. Chromatography (20% diethyl ether : 80% light petroleum 40–60) gave **5a** as a yellow solid (250 mg, 95 %) R_f 0.59 (50% diethyl ether : 50% light petroleum 40–60). The xanthate was not fully characterized, but was identified by a shift in the CH–O signal in the ¹H NMR spectrum from 4.00 to 5.4 ppm and the appearance of a 3H singlet at 2.6 ppm assigned to SCH₃.

7a

Preparation of and data for 7a

A mixture of AIBN (60 mg, 0.36 mmol) and TTMSS (266 mg, 1.1 mmol), in toluene (2 mL), was added over 1 h 40 min to a preheated solution of xanthate **5a** (250 mg, 0.71 mmol) in toluene (21 mL) at reflux. The reaction was left at reflux for a further 30 min after completion of the addition, allowed to cool, and the solvent removed at reduced pressure. Chromatography (10% diethyl ether : light petroleum 40-60) gave **7a** as a colourless oil that crystallized on standing to a white solid (158 mg, 90%) ; Rf 0.54 (50% Et₂O : light petroleum 40-60); mp (from light petroleum 30-40) 64-66 °C; IR (thin film): 2977s, 2889m, 1698s, 1462m, 1392s, 1251m, 1181m, 1152s, 1093s, 838m, 755m cm⁻¹; ¹H NMR (500 MHz, DMSO-d₆, 90 °C) 7.34 (d, *J* = 7.0 Hz, 1H), 7.24 (d, *J* = 7.0 Hz, 1H), 7.21-7.11 (m, 2H), 4.94 (br s, 1H), 3.66 (s, 1H), 3.48 (dd, *J* = 9.0 Hz and 3.0 Hz, 1H), 2.64 (dd, *J* = 9.0 Hz and 2.0 Hz, 1H), 1.96 (d, *J* = 9.0 Hz, 1H), 1.79 (d, *J* = 9.0 Hz, 1H), 1.37 (s, 9H); ¹³C NMR (125 MHz, DMSO-d₆, 90 °C) 155.4 (C=O), 146.4, 145.1 (2 x C), 127.8, 126.7, 122.2, 121.0 (4 x CH), 79.4 (C), 62.2 (CH), 49.5 (CH₂), 49.1 (CH₂), 44.5 (CH), 28.2 (CMe₃); LRMS *m/z* (Cl⁺, NH₃) 263 (M+NH₄⁺, 21), 246 (M+H⁺, 25), 207 (100), 190 (4), 163 (8), 146 (M+H-Boc⁺, 96) 116 (5); HRMS (ES⁺) calcd. for C₁₅H₂₀NO₂ 246.1494, found 246.1494.

Preparation of and data for **7b**

A mixture of AIBN (46 mg, 0.28 mmol) and TTMSS (205 mg, 0.83 mmol), in toluene (2 mL), was added over 1 h 40 min to a preheated solution of xanthate **5b** (208 mg, 0.55 mmol) in toluene (16 mL) at reflux. The reaction was left at reflux for a further 30 min after completion of the addition, allowed to cool, and the solvent removed at reduced pressure. Chromatography (50% CH₂Cl₂ : 50 % light petroleum 40-60) gave **7b** as a colourless oil (110 mg, 73%) ; R_f 0.33 (20% Et₂O : 80 % light petroleum 40-60); IR (thin film): 2963s, 2929s, 2889s, 1694s, 1477s, 1455s, 1391s, 1363s, 1247m, 1174s, 1144s, 1103s, 864m cm⁻¹; ¹H NMR (500 MHz, DMSO-d₆, 90 °C) 7.33 (d, *J* = 6.5 Hz, 1H), 7.25 (d, *J* = 7.0 Hz, 1H), 7.23-7.13 (m, 2H), 4.73 (s, 1H), 3.48 (d, *J* = 7.0 Hz, 1H), 3.42 (s, 1H), 2.64 (d, *J* = 7.0 Hz, 1H), 2.34-2.28 (m, 1H), 1.37 (s, 9H), 0.97-0.86 (m, 2H), 0.85-0.78 (m, 3H); ¹³C NMR (100 MHz, 3:1 mixture of rotamers) 154.7 and 153.8 (C=O), 143.8 and 143.5 (1 x C) , 142.3 (C), 127.2 and 127.1, 126.0, 122.8 and 122.7, 121.6 and 121.2 (4 x CH), 78.5 and 78.4 (C), 64.0 and 62.6 (CH), 60.5 (CH), 49.4 and 49.3 (CH), 47.0 and 46.3 (CH₂), 28.1 and 28.0 (CMe₃), 19.3 (CH₂), 12.2 and 12.1 (CH₃); LRMS m/z (TOF CI⁺) 274 (M+H⁺, 24), 235 (97), 218 (67), 174 (100), 144 (25); HRMS (CI⁺) calcd. for C₁₇H₂₄NO₂ 274.1807, found 274.1813. 1D nOe experiment: irradiation of C(7)H at 2.30 ppm showed enhancement of the signal at 3.48 ppm, assigned as C(3)H *exo*, demonstrating that the proton attached to C7 is *syn* to nitrogen.

Preparation of and data for **7c**

A mixture of AIBN (77 mg, 0.47 mmol) and TTMSS (316 mg, 1.3 mmol), in toluene (4 mL), was added over 1 h 10 min to a preheated solution of xanthate **5c** (244 mg, 0.64 mmol) in toluene (14 mL) at reflux. The reaction was left at reflux for a further 30 min after completion of the addition, allowed to cool, and the solvent removed at reduced pressure. Chromatography (50% CH₂Cl₂ : 50% light petroleum 40-60 to 100% CH₂Cl₂) gave **7c** as a colourless oil (155 mg, 88%) ; R_f 0.40 (20% Et₂O : 80 % light petroleum 40–60); IR (thin film): 2972s, 2929s, 2876s, 1694s, 1478s, 1459s, 1394s, 1343s, 1289s, 1246s, 1178s, 1142s, 1095s, 871m cm⁻¹; ¹H NMR (400 MHz, 2:1 mixture of rotamers) 7.36-7.30 (m, 1H), 7.28-7.21 (m, 1H), 7.20-7.13 (m, 2H), 4.90 and 4.72 (2 x s, 1H), 4.03 and 3.96 (2 x s, 1H), 3.11 (s, 1H), 2.55-2.49 (m, 1H), 1.46 and 1.42 (2 x s, 9H), 0.82 and 0.76 (2 x d, *J* = 6.0 Hz, 3H), 0.66 (3H, d, *J* = 6.0 Hz, 3H); ¹³C NMR (100 MHz) 154.7 and 153.8 (C=O), 143.2 and 143.1 (1 x C), 142.0 (C), 126.7, 126.4, 125.1 and 124.9, 122.4 and 121.8, (4 x CH), 79.1 and 78.9 (C), 66.9 and 65.8 (CH), 56.0 and 55.5 (CH), 54.8 (CH), 54.6 and 54.0 (CH), 28.4 and 28.3 (*CMe*₃), 18.0 and 16.9 (CH₃), 11.9 (CH₃); LRMS *m/z* (CI⁺, NH₃) 274 (M+H⁺, 28), 235 (90), 218 (73), 174 (100), 130 (32); HRMS (CI⁺) calcd. for C₁₇H₂₄NO₂ 274.1807, found 274.1795. 1D nOe experiment: irradiation of C(7)H at 2.52 ppm showed enhancement of both signals at 4.03 and 3.96 ppm, assigned as C(3)H, demonstrating that the protons attached to C7 and C3 are *syn* to one another. Irradiation of C(3)H also gave enhancement of the C(7)H signal.

Preparation of and data for 7d

A mixture of AIBN (28 mg, 0.16 mmol) and TTMSS (124 mg, 0.50 mmol), in toluene (2 mL), was added over 1 h 40 min to a preheated solution of xanthate **5d** (137 mg, 0.33 mmol) in toluene (8 mL) at reflux. The reaction was left at reflux for a further 30 min after completion of the addition, allowed to cool, and the solvent removed at reduced pressure. Chromatography (40% diethyl ether : 60 % light petroleum 40-60) gave **7d** as a colourless oil (79 mg, 77%); R_f 0.15 (40% Et₂O : 60 % light petroleum 40-60); IR (thin film): 2976s, 2886s, 1694s, 1613s, 1492s, 1392s, 1328s, 1298s, 1251s, 1217s, 1183s, 1145s, 1119s, 1092s, 1070s, 1020m, 916m, 855s cm⁻¹; ¹H NMR (400 MHz, 3 : 2 mixture of rotamers) 6.96 and 6.83 (2 x s, 1H), 6.89 (s, 1H), 5.06 and 4.88 (2 x s, 1H), 3.85 (s, 6H), 3.55 (s, 1H), 3.50-3.43 (m, 1H), 2.75 and 2.67 (2 x d, *J* = 9.0 Hz, 1H), 1.97 and 1.92 (2 x d, *J* = 9.0 Hz, 1H), 1.84 (d, *J* = 9.0 Hz, 1H), 1.41 and 1.35 (2 x s, 9H); ¹³C NMR (100 MHz) 155.6 and 154.8 (C=O), 148.2 and 147.9, 147.8 and 147.2, 137.6 and 137.5, 136.7 and 136.5 (4 x C), 106.3 and 105.9 (CH), 105.6 and 105.4 (CH), 80.4 (C), 62.2 and 61.0 (CH), 56.2 and 56.1 (2 x CH₃), 48.9 and 48.6 (CH₂), 48.8 (CH₂), 44.6 and 44.0 (CH), 28.7 and 28.5 (CMe₃); LRMS *m/z* (Cl⁺, NH₃) 323 (M+NH₄⁺, 3), 306 (M+H⁺, 23), 250 (100), 232 (53), 206 (35), 191 (17); HRMS (Cl⁺) calcd. for C₁₇H₂₄NO₄ 306.1705, found 306.1710.

Preparation of and data for **7e**

A mixture of AIBN (33 mg, 0.20 mmol) and TTMSS (143 mg, 0.58 mmol), in toluene (2 mL), was added over 1 h 40 min to a preheated solution of xanthate **5e** (150 mg, 0.39 mmol) in toluene (9 mL) at reflux. The reaction was left at reflux for a further 30 min after completion of the addition, allowed to cool, and the solvent removed at reduced pressure. Chromatography (15% diethyl ether : 85 % light petroleum 40-60) gave **7e** as a colourless oil (70 mg, 64%); R_f 0.22 (20% Et₂O : 80 % light petroleum 40-60); IR (thin film): 2977s, 2890s, 1694s, 1614s, 1478s, 1392s, 1363s, 1276s, 1249s, 1149s, 1046s, 1008m, 867s cm⁻¹; ¹H NMR (400 MHz, 2 : 1 mixture of rotamers) 7.19-6.95 (m, 2H), 5.04 and 4.90 (2 x br s, 1H), 3.59 (s, 1H), 3.51 (dd, J = 9.0 Hz and 3.0 Hz, 1H), 2.79 and 2.70 (2 x d, J = 9.0 Hz, 1H), 2.07-1.93 (m, 1H), 1.87 (d, J = 9.0 Hz, 1H), 1.43 and 1.35 (2 x s, 9H); ¹³C NMR (100 MHz) 155.2 and 154.8 (C=O), 149.4 (dd, J = 245 Hz and 12 Hz, C-F), 148.8 (dd, J = 245 Hz and 13 Hz, C-F), 141.2, 140.2 (2 x C), 111.4 and 111.0 (2 x d, J = 20 Hz, CH), 110.7 and 109.8 (2 x d, J = 20 Hz, CH), 79.7 (C), 61.4 and 60.3 (CH), 48.8 and 48.6 (CH₂), 48.2 (CH₂), 44.3 and 44.0 (CH), 28.5 and 28.3 (CMe₃); ¹⁹F NMR (235 MHz) -140.2 (d, J = 19 Hz), -140.5 (d, J = 19 Hz), -141.3 (d, J = 19 Hz), -141.5 (d, J = 19 Hz); LRMS m/z (Cl⁺, NH₃) 299, (M+NH₄⁺, 5), 282 (M+H⁺, 15), 243 (62), 226 (22), 182 (100), 152 (24); HRMS (Cl⁺) calcd. for C₁₅H₁₈F₂NO₂ 282.1306, found 282.1305.

7f

Preparation of and data for **7f**

A mixture of AIBN (40 mg, 0.24 mmol) and TTMSS (172 mg, 0.69 mmol) in toluene (2 mL) were added over 1h 40 min to a pre-heated solution of xanthate **5f** (185 mg, 0.46 mmol) in toluene at reflux (14 mL). The reaction was left for a further 30 min at reflux after completion of the addition, allowed to cool and then the solvent removed at reduced pressure.

Chromatography (10% Et₂O : 90% light petroleum 30-40) gave **7f** as a white solid (115 mg, 84%); R_f 0.21(10% Et₂O : 90% light petroleum 30-40); mp (from light petroleum 30-40) 130-132 °C; IR (KBr): 2987s, 2960m, 2930m, 1681s, 1367s, 1284m, 1150s, 1090s, 865m cm⁻¹; ¹H NMR (500 MHz, DMSO-d₆, 90°C), 7.89-7.84 (m, 2H), 7.78 (s, 1H), 7.68 (s, 1H), 7.47-7.44 (m, 2H) 5.08 (s, 1H), 3.78 (s, 1H), 3.58 (dd, *J* = 9.0 Hz and 3.0 Hz, 1H), 2.81 (dd, *J* = 9.0 Hz and 3.0 Hz, 1H), 2.10 (d, *J* = 9.0 Hz, 1H), 1.88 (d, *J* = 9.0 Hz, 1H), 1.37 (s, 9H); ¹³C NMR (125 MHz, DMSO-d₆, 90°C) 155.2 (C=O), 144.8, 143.4, 133.8, 133.2 (4 x C), 128.9, 128.6, 126.3, 126.1, 120.3, 118.8 (6 x CH), 79.5 (C), 61.6 (CH), 50.4 (CH₂), 48.1 (CH₂), 44.2 (CH), 29.1 (CMe₃); LRMS m/z (CI⁺, NH₃) 313 (M+NH₄⁺, 10), 296 (M+H⁺, 8), 257 (100), 240 (8), 196 (M+H-Boc⁺, 63), 166 (12) 154 (3); HRMS (ES⁺) calcd. for C₁₉H₂₂NO₂ 296.1650, found 296.1648; Anal. calcd. for C₁₉H₂₁NO₂: C, 77.3 ; H, 7.2 ; N, 4.7. Found: C, 77.3 ; H, 7.3 ; N, 4.8.

4c

4f

7a

7f