Supporting Information

for

Synthesis of 2-Anilinotropones via Palladium-Catalyzed Amination of 2-Triflatotropone

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Details on the synthesis and characterization of compounds in the Table (5 pages)

General Considerations. Argon was purified by passage through columns of BASF R3-11 catalyst (Chemalog) and 4 Å molecular sieves. Toluene was deoxygenated and dried over a column of activated alumina[1] 2-Triflatotropone was prepared by the method of Stille.[2] 2,6-diphenylaniline was prepared by the method of Miura.[3] 99% pure 2,6-diisopropylaniline was purchased from Carbolabs. All other chemicals were obtained from commercial sources and used as purchased without further purification.

Flash chromatography was performed on Merck grade 9385 silica gel, 230-400 mesh, 60 Å. Yields refer to isolated yields of compounds of greater than 95% purity as estimated by ^{1}H NMR analysis and elemental analysis. Nuclear magnetic resonance (NMR) spectra were recorded on either a Brucker AC 200, Brucker WM 250, Brucker Avance 300 or Brucker Avance 400. Splitting patterns are designated as follows: s, singlet; bs, broad singlet; d, doublet; dd, doublet of doublets; t, triplet; q, quartet; dt, doublet of triplets; dm, doublet of multiplets; m, multiplet. All ^{1}H NMR spectra are reported in δ units, parts per million (ppm) downfield from tetramethylsilane. All ^{13}C NMR spectra are reported in ppm relative to deuterochloroform. Infrared (IR) spectra were recorded on an ASI ReactIR 1000. Elemental analyses were performed by Atlantic Microlab Inc. of Norcross, GA.

General Procedure A - The Conversion of 2-Triflatotropone to 2-Anilinotropones with Liquid Anilines: A Schlenk tube, flame-dried in vacuo, was placed under an Ar atmosphere on a vacuum line. The tube was charged with $Pd_2(dba)_3$ (5 mg, 0.005 mmol), rac-BINAP (7 mg, 0.01 mmol), Cs_2CO_3 (456 mg, 1.4 mmol), and 2-triflatotropone (254 mg, 1.0 mmol). Toluene (2 mL) was added followed by the appropriate aniline (1.2 mmol). The Schlenk tube was sealed and heated to 80 °C for approximately 12 h. The reaction mixture was allowed to cool to rt, filtered through a pad of silica gel with the aid of ether (100 mL), and concentrated to afford the crude product. Purification was effected via flash column chromatography on silica gel.

General Procedure B - The Conversion of 2-Triflatotropone to 2-Anilinotropones with Solid Anilines: A Schlenk tube, flame-dried in vacuo, was placed under an Ar atmosphere on a vacuum line. The tube was charged with $Pd_2(dba)_3$ (5 mg, 0.005 mmol), rac-BINAP (7 mg, 0.01 mmol), Cs_2CO_3 (456 mg, 1.4 mmol), 2-triflatotropone (254 mg, 1.0 mmol), and the appropriate aniline (1.2 mmol). Toluene (2 mL) was added and the Schlenk tube was sealed and heated to 80 °C for approximately 12 h. The reaction mixture was allowed to cool to rt, filtered through a pad of silica gel with the aid of ether (100 mL), and concentrated to afford the crude product. Purification was effected via flash column chromatography on silica gel.

(Table 1, entry 1): General procedure A was used to convert 2,6-dimethylaniline (148 μl, 1.2 mmol) to the desired product in 15 hours. Purification via flash column chromatography (eluants 3:2 hexane:ether) afforded 201 mg (90 % yield) of an orange solid. Mp: 76 - 78 °C. ^1H NMR (250 MHz, $CDCl_3$): δ 8.40 (bs, 1 H); 7.32 (m, 2 H); 7.18 (m, 3 H); 7.08 (t, $J = 10.5$ Hz, 1 H); 6.73 (m, 1 H); 6.22 (d, $J = 10.5$ Hz, 1 H); 2.15 (s, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.6, 154.6, 137.3, 136.3, 136.2, 135.1, 129.9, 128.7, 127.8, 123.5, 109.6, 18.0. IR (neat on a DiComp probe, cm^{-1}): 3244, 2916, 1602, 1547, 1492, 1455, 1376, 1248, 776, 720. Anal. calcd for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22. Found: C, 79.92; H, 6.71; N, 6.05.

(Table 1, entry 2): General procedure A was used to convert 2,6-diisopropylaniline (227 μl, 1.2 mmol) to the desired product in 14 hours. Purification via flash column chromatography (eluants 2:1 hexane:ether) afforded 242 mg (86 % yield) of an orange solid. Mp: 86 - 88 °C. ^1H NMR (200 MHz, $CDCl_3$): δ 8.42 (bs, 1 H); 7.43 - 7.24 (m, 5 H); 7.06 (t, $J = 10.2$ Hz,1 H); 6.71 (m, 1 H); 6.26 (d, $J = 10.2$ Hz, 1 H); 2.90 (m, 2 H); 1.15 (d, $J = 7.0$ Hz, 6 H); 1.11 (d, $J = 7.0$ Hz, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.5, 156.4, 146.9, 137.5, 136.2, 132.5, 130.0, 128.9, 124.4, 123.6, 110.4, 28.6, 24.6, 23.4. IR (neat on a DiComp probe, cm^{-1}): 3228, 2960, 1602, 1547, 1499, 1437, 1243, 806, 720. Anal. calcd for $C_{19}H_{23}NO$: C, 81.10; H, 8.24; N, 4.98. Found: C, 81.15; H, 8.20; N, 4.94.

(Table 1, entry 3): General procedure A was used to convert 2-*t*-butylaniline (187 µl, 1.2 mmol) to the desired product in 16 hours. Purification via flash column chromatography (eluants 3:1 hexane:ether) afforded 221 mg (88 % yield) of an orange solid. Mp: 92 - 94 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.80 (bs, 1 H); 7.53 (m, 1 H); 7.35 - 7.25 (m, 4 H); 7.20 (m, 1 H); 7.10 (d, *J* = 10.2 Hz, 1 H); 6.75 (m, 2 H); 1.37 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.8, 155.2, 146.8, 137.5, 136.8, 136.2, 130.0, 128.6, 127.7, 127.3, 127.2, 123.7, 110.8, 35.1, 30.5. IR (neat on a DiComp probe, cm^{-1}): 3201, 2956, 2867, 1602, 1549, 1497, 1455, 1225, 1214, 1090, 876, 768, 714. Anal. calcd for $C_{17}H_{19}NO$: C, 80.59; H, 7.56; N, 5.53. Found: C, 80.34; H, 7.52; N, 5.51.

(Table 1, entry 4): General procedure A was used to convert 2-*t*-butyl-6-methylaniline (196 mg, 1.2 mmol) to the desired product in 15.5 hours. Purification via flash column chromatography (eluants 2:1 hexane:ether) afforded 97 mg (36 % yield) of an orange solid. Mp: 115 - 117 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.69 (bs, 1 H); 7.41 - 7.18 (m, 5 H); 7.09 (t, *J* = 10.2 Hz, 1 H); 6.73 (m, 1 H); 6.17 (d, *J* = 10.2 Hz, 1 H); 2.06 (s, 3 H); 1.32 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.7, 155.2, 148.4, 137.6, 135.1, 130.0, 129.5, 127.9, 125.4, 123.6, 111.0, 35.5, 31.1, 18.6. Anal. calcd for $C_{18}H_{21}NO$: C, 80.86; H, 7.92; N, 5.24. Found: C, 80.61; H, 7.93; N, 5.14.

(Table 1, entry 5): General procedure B was used to convert 2,6-diphenylaniline (294 mg, 1.2 mmol) to the desired product in 16.5 hours. Purification via flash column chromatography (eluants 2:1 hexane:ether) afforded 127 mg (37 % yield) of a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.40 (bs, 1 H); 7.44 - 7.5 (m, 3 H); 7.32 (m, 3 H); 7.27 - 7.18 (m, 7 H); 7.10 (dd, *J* = 8.6, 11.5 Hz, 1 H); 7.04 (t, *J* = , 1 H); 6.83 (t, *J* = 10.1 Hz, 1 H); 6.52 (t, *J* = 9.2 Hz, 1 H); 6.35

(d, *J* = 10.3 Hz, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.1, 153.3, 140.1, 138.8, 136.8, 135.3, 132.5, 130.4, 130.0, 128.4, 128.3, 127.7, 127.5, 123.5, 111.2. Anal. calcd for $C_{25}H_{19}NO$: C, 85.93; H, 5.48; N, 4.01. Found: C, 85.58; H, 5.65; N, 3.89.

(Table 1, entry 6): General procedure B was used to convert 2,6-dichloroaniline (194 mg, 1.2 mmol) to the desired product in 14.5 hours. Purification via flash column chromatography (eluants 2:1 hexane:ether) afforded 200 mg (75 % yield) of an orange solid. Mp: 63 - 65 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.48 (bs, 1 H); 7.47 (d, *J* = 8.0 Hz, 2 H); 7.37 (m, 2 H); 7.26 (t, *J* = 8.0 Hz, 1 H); 7.13 (t, *J* = 10.2 Hz, 1 H); 6.83 (m, 1 H); 6.29 (d, *J* = 10.2 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.1, 152.4, 137.5, 135.7, 134.0, 133.5, 131.7, 129.0, 128.7, 125.3, 111.3. IR (neat on a DiComp probe, cm^{-1}): 3232, 1549, 1493, 1470, 1436, 1380, 1229, 903, 780, 716. Anal. calcd for $C_{13}H_9NOCl_2$: C, 58.67; H, 3.41; N, 5.26. Found: C, 58.78; H, 3.46; N, 5.22.

(Table 1, entry 7): General procedure B on half the scale with the modification of 12 mg (0.0125 mmol) Pd_2dba_3 and 16 mg (0.025 mmol) rac-BINAP was used to convert 2,6-dibromoaniline (151 mg, 0.60 mmol) to the desired product in 15 hours. Purification via flash column chromatography (eluants 2:1 hexane:ether) afforded 122 mg (69 % yield) of an orange solid. Mp: 73 - 75 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.49 (bs, 1 H); 7.68 (d, *J* = 8.0 Hz, 2 H); 7.35 (m,2 H); 7.12 (m, 2 H); 6.83 (m, 1 H); 6.27 (d, *J* = 10.2 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.1, 152.5, 137.6, 136.3, 135.4, 133.0, 131.9, 129.9, 125.3, 124.4, 111.3. Anal. calcd for $C_{13}H_9NOBr_2$: C, 43.98; H, 2.56; N, 3.95. Found: C, 43.88; H, 2.61; N, 3.88.

(Table 1, entry 8): General procedure B was used to convert 2,3,4,5,6-pentafluoroaniline (220 mg, 1.2 mmol) to the desired product in 15.5 hours. Purification via flash column chromatography (eluants 2:1 hexane:ether) afforded 256 mg (84 % yield) of a green solid. The compound was isolated as a hydrate. Mp: 156-158 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ

8.19 (bs, 1 H); 7.38 (dd, *J* = 8.2, 11.8 Hz, 1 H); 7.32 (d, *J* = 11.0 Hz, 1 H); 7.15 (t, *J* = 10.2 Hz, 1 H); 6.87 (t, *J* = 9.0 Hz, 1 H); 6.49 (dt, *J* = 2.6, 10.0 Hz, 1 H); 2.14 (s, 2 H, coordinated H_2O). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.2, 151.6, 143.0 (dm, *J* = 250 Hz), 139.7 (dm, *J* = 253 Hz), 138.1 (dm, *J* = 253 Hz), 137.7, 135.2, 132.5, 126.4, 113.7 (dt, *J* = 3.8, 14.2 Hz), 111.6. ^{19}F NMR (376 MHz, $CDCl_3$): δ –144.5 (m), –157.31 (m), –161.87 (m). IR (neat on a DiComp probe, cm^{-1}): 3203, 2921, 1596, 1565, 1493, 1441, 1380, 1200, 1071, 988, 967. Anal. calcd for $C_{13}H_6NOF_5$: C, 54.36; H, 2.11; N, 4.88. Found: C, 54.31; H, 2.18; N, 4.81.

(Table 1, entry 9): General procedure A was used to convert 3,5-bis(trifluoromethyl)aniline (188 µl, 1.2 mmol) to the desired product in 15.5 hours. Purification via flash column chromatography (eluants 2:1 hexane:ether) afforded 313 mg (89 % yield) of a green solid. Compound was isolated as a hydrate. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.87 (bs, 1 H); 7.75 (s, 2 H); 7.66 (s, 1 H); 7.38 (dd, *J* = 8.5, 11.8 Hz, 1 H); 7.31 (d, *J* = 11.8 Hz, 1 H); 7.20 (m, 2 H); 6.89 (m, 1 H); 2.15 (s, 2.7 H, coordinated H_2O). ^{13}C NMR (100 MHz, $CDCl_3$): δ 117.5, 151.7, 140.8, 137.8, 135.4, 132.9 (q, *J* = 33.5 Hz), 132.3, 126.6, 122.9 (q, *J* = 271 Hz), 122.7, (d, *J* = 2.9 Hz), 117.9 (t, *J* = 3.4 Hz), 111.1. ^{19}F NMR (376 MHz, $CDCl_3$): δ –63.6 (s). Anal. calcd for $C_{15}H_9NOF_6$: C, 54.07; H, 2.72; N, 4.20. Found: C, 54.26; H, 2.74; N, 4.24.

References

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