Nitrogenous Educts Through Oxidative Amidation of Phenols: The Bimolecular Reaction

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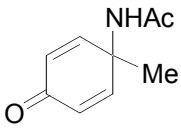
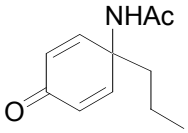
SUPPORTING INFORMATION

A. Experimental protocols. Unless otherwise indicated, proton and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively, in $CDCl_3$ solutions. Chemical shifts are reported in ppm on the δ scale. Multiplicities are described as s (singlet), d (doublet), dd, ddd, etc. (doublet of doublets, doublet of doublets of doublets, etc.), t (triplet), q (quartet) m (multiplet), and further qualified as app (apparent) b (broad) c (complex). Coupling constants, J, are reported in Hz. Low- and high-resolution mass spectra (m/e) were measured in the chemical ionization mode (CI, isobutane as the reagent gas).

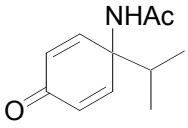
B. General procedure for oxidative amidation of phenols. A solution of $PhI(OAc)_2$ ("DIB", 232.0 mg, 0.7 mmol, 1.2 equiv.) in $(CF_3)_2CHOH$ ("HFIP", 0.5 mL) was added dropwise over 30 sec to a vigorously stirred solution of a phenol (0.6 mmol, 1 equiv.) in MeCN (2.0 mL) and HFIP (1.5 mL) kept at 15 °C (bath temperature). The mixture was stirred for 20 min, then it was concentrated. Silica gel chromatography of the residue, first with 1:1 AcOEt / Hexanes (removal of gross contaminants), and then with 5 - 10 % MeOH in CH_2Cl_2, provided the pure product.



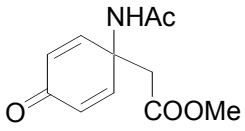
Compound 11a: Yield = 56%. **^{1}H**: 6.82 (d, 2H, *J* = 10.2 Hz), 6.31 (br s, 1H), 6.19 (d, 2H, *J* = 10.2 Hz), 1.91 (s, 3H), 1.43 (s, 3H). **^{13}C**: 185.5, 170.3, 152.5, 127.6, 52.5, 26.1, 23.1. HRMS: calc for $C_9H_{12}O_2N_1$ (MH^+): 166.0868; found: 166.0871.



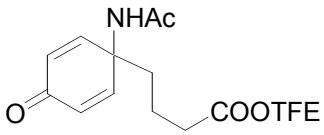
Compound 11b: Yield = 54%. **^{1}H**: 6.77 (d, 2H, *J* = 10.2 Hz), 6.67 (br s, 1H), 6.24 (d, 2H, *J* = 10.2 Hz), 1.96 (s, 3H), 1.69 (m, 2H), 1.22 (m, 2H), 0.84 (t, 3H, *J* = 7.2 Hz). **^{13}C**: 185.8, 170.0, 151.3, 128.6, 55.9, 40.4, 23.2, 16.4, 13.9. **HRMS**: calc. for $C_{11}H_{16}O_2N_1$ (MH^+): 194.1181; found: 194.1182



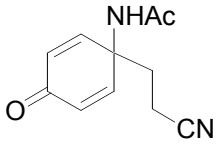
Compound 11c: Yield = 62%. **^{1}H**: 6.81 (d, 2H, *J* = 10.2 Hz), 6.31 (br s, 1H), 6.26 (d, 2H, *J* = 10.2 Hz), 2.21 (h, 1H, *J* = 7.0 Hz), 1.91 (s, 3H), 0,89 (d, 6H, *J* = 7.0 Hz). **^{13}C**: 185.8, 170.1, 149.8, 129.3, 58.9, 34.7, 23.3, 16.9. **HRMS**: calc for $C_{11}H_{16}O_2N_1$ (MH^+): 194.1181; found: 194.1181.



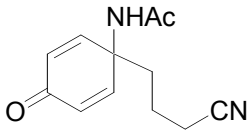
Compound 11d: Yield = 58%. **^{1}H**: 6.95 (d, 2H, *J* = 10.2 Hz), 6.80 (br s, 1H), 6.29 (d, 2H, *J* = 10.2 Hz), 3.72 (s, 3H), 2.76 (s, 2H), 1.97 (s, 3H). **^{13}C**: 184.7, 170.2, 170.1, 148.4, 128.8, 53.2, 52.3, 42.2, 23.5.



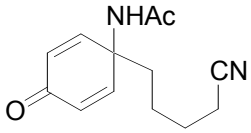
Compound 11e: Yield = 57%.**^{1}H**: 6.84 (d, 2H, *J* = 10.2 Hz), 6.43 (br s, 1H), 6.28 (d, 2H, *J* = 10.2 Hz), 4.47 (q, 2H, *J* = 8.3 Hz), 2.41 (t, 2H, J = 6.8 Hz),1.94 (s, 3H), 1.83 (m, 2H), 1.62 (m, 2H). **^{13}C**: 185.4, 171.4, 170.0, 150.0, 129.2, 60.5(q), 55.6, 37.2, 32.7, 23.4, 18.4.



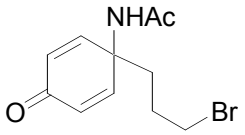
Compound 11f: Yield = 67%. **^{1}H**: 6.89 (d, 2H, *J* = 10.2 Hz), 6.70 (br s, 1H), 6.31 (d, 2H, *J* = 10.2 Hz), 2.26 (br, 4H), 1.91 (s, 3H). **^{13}C**:184.7, 170.5, 148.0, 130.0, 118.7, 55.0, 32.4, 23.4, 11.9.



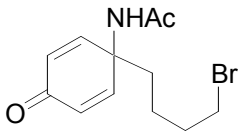
Compound 11g: Yield = 71%. **^{1}H**: 6.91 (br s, 1H), 6.82 (d, 2H, *J* = 10.2 Hz), 6.26 (d, 2H, *J* = 10.2 Hz), 2.31(t, 2H, *J* = 6.8 Hz), 1.97 (m, 2H), 1.89 (s, 3H), 1.52 (m, 2H). **^{13}C**: 185.3, 170.2, 149.9, 129.1, 118.8, 55.3,36.1, 23.2, 19.2, 16.8.



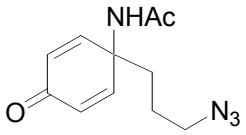
Compound 11h: Yield = 71%. **^{1}H**: 6.86 (d, 2H, *J* = 10.2 Hz), 6.60 (br s, 1H), 6.26 (d, 2H, *J* = 10.2 Hz), 2.31 (t, 2H, *J* = 7.2 Hz), 1.92 (s, 3H), 1.87 (m, 2H),1.60 (q, 2H, *J* = 7.2 Hz), 1.35 (m, 2H). **^{13}C**: 185.4, 170.1, 150.2, 129.0, 119.2, 55.7, 36.9, 25.0, 23.4, 22.4, 16.8.



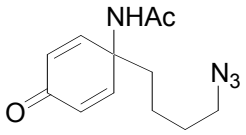
Compound 11j: Yield = 65%. **^{1}H** 6.81 (d, 2H, *J* = 10.2 Hz), 6.37 (br s, 1H), 6.30 (d, 2H, *J* = 10.2 Hz), 3.35 (t, 2H, *J* = 6.0 Hz), 2.01 (m, 2H), 1.96 (s, 3H), 1.73 (m, 2H). **^{13}C** 185.3, 170.0, 149.9, 129.4, 55.5, 36.4, 32.8, 26.3, 23.5.



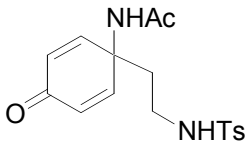
Compound 11k: Yield = 72%. **^{1}H**: 6.84 (d, 2H, *J* = 10.2 Hz), 6.68 (br s, 1H), 6.26 (d, 2H, *J* = 10.2 Hz), 3.32 (t, 2H, *J* = 6.8 Hz), 1.91 (s, 3H), 1.80 (m, 4H), 1.37 (m, 2H). **^{13}C**: 185.6, 170.1, 150.6, 128.9, 55.8, 37.0, 32.9, 32.1, 23.3, 21.7.



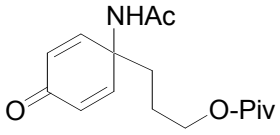
Compound 11l: Yield = 42%. **^{1}H**: 6.82 (d, 2H, *J* = 10.2 Hz), 6.29 (d, 2H, *J* = 10.2 Hz), 5.89. (br s, 1H), 3.31 (t, 2H, *J* = 6.4 Hz), 1.98 (m, 2H, overlapping a s, 3H), 1.47 (m, 2H). **^{13}C**: 185.4, 170.1, 150.0, 129.2, 55.6, 50.9, 34.9, 23.4, 22.9.



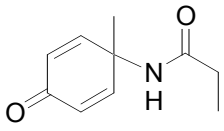
Compound 11m: Yield = 49%. **^{1}H**: 6.79 (d, 2H, *J* = 10.2 Hz), 6.25 (br s, 1H), 6.24 (d, 2H, *J* = 10.2 Hz), 3.20 (t, 2H, *J* = 7.0 Hz), 1.91 (s, 3H), 1.78 (m, 2H), 1.47 (quintuplet, 2H, *J* = 7.0 Hz), 1.25 (m, 2H). **^{13}C**: 185.6, 170.2, 150.7, 128.8, 55.8, 50.8, 37.4, 28.4, 23.2, 20.4.



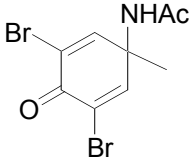
Compound 11n: Yield = 53%. **^{1}H**: 7.62 (d, 2H, *J* = 7.9 Hz), 7.24 (d, 2H, *J* = 7.9 Hz), 6.98 (br s, 1H), 6.84 (d, 2H, *J* = 9.8 Hz), 6.21 (d, 2H, *J* = 9.8 Hz), 5.83 (br s, 1H), 2.83 (br m, 2H), 2.38 (s, 3H), 2.03 (br m, 2H), 1.91 (s, 3H). **^{13}C**: 185.6, 170.8, 150.4, 143.8, 136.1, 129.8, 128.9, 126.9, 54.8, 38.2, 37.7, 23.3, 21.5.



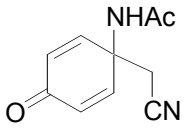
Compound 11o: Yield = 67%. **^{1}H**: 6.80 (d, 2H, *J* = 10.2 Hz), 6.30 (d, 2H, *J* = 10.2 Hz), 6.21 (br s, 1H), 3.99 (t, 2H, *J* = 6.0 Hz), 1.95 (s, 3H), 1.88 (m, 2H), 1.53 (m, 2H), 1.16 (s, 9H). **^{13}C**: 185.4, 178.4,. 169.9, 150.1, 129.1, 63.3, 55.5, 38.6, 34.2, 27.0, 23.3, 22.6. **HRMS**: calc. for $C_{16}H_{24}O_4N_1$ (MH^+): 294.1705; found 294.1705



Compound 18: Yield = 52%. **^{1}H**: 6.86 (d, 2H, *J* = 10.2 Hz), 6.37 (br s, 1H), 6.21 (d, 2H, *J* = 10.2 Hz), 2.18 (q, 1H, *J* = 7.5 Hz), 1.45 (s, 9H), 1.08 (t, 3H, *J* = 7.5 Hz). **^{13}C**: 185.3, 173.6, 152.3, 127.6, 52.3, 29.3, 26.2, 9.3.

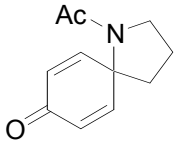


Compound 20: Yield = 24%. **^{1}H** (MeOH-d_4): 7.43 (s, 2H), 1.94 (s, 3H), 1.43 (s, 3H). **^{13}C** (MeOH-d_4): 172.4, 171.6, 153.9, 119.8, 56.5,23.6, 21.1.

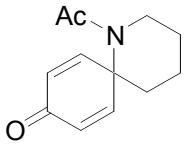


Compound 22: Yield = 31%. **^{1}H** (acetone-d_6): 7.06 (d, 2H, J = 10.2 Hz), 6.29 (d, 2H, J = 10.2 Hz), 3.15 (s, 2H), 1.91 (s, 3H). **^{13}C** (acetone-d_6): 184.8, 171.5, 147.6, 130.3, 116.5, 54.0, 27.0, 23.3.

C. Procedure for the cylization of compounds 11j and 11k. A solution of **11j** or **11k** (0.2 mmol) in dry THF (2.0 mL) was treated with solid NaH (1.1 eq.) and stirred at room temperature and under Ar. After 10 (**11j**) / 60 (**11k**) minutes, TLC showed complete conversion. The mixture was quenched with 2 drops of a saturated aqueous solution of NH_4Cl and concentrated, and the aqueous residue was extracted with $CHCl_3$ (3 x 2 mL). The combined extracts were filtered and concentrated to give essentially pure product **27** and **28** as slightly yellow oils.



Compound 27: 1:1 ratio of amide rotamers. Yield = 91%. **^{1}H**: 6.89 (d, 1H, J = 10.2 Hz) & 6.76 (d, 1H, J = 10.2 Hz), 6.30 (d, 1H, J = 10.2 Hz) & 6.23 (d, 1H, J = 10.2 Hz), 3.81 (app t, 1H, J = 6.6 Hz) & 3.72 (app t, 1H, J = 6.6 Hz), 2.23 (app t, 1H, J = 6.6 Hz) & 1.08 (c m, 3 H), 2.07 (s, 1.5H) & 1.89 (s, 1.5H).



Compound 28: Yield = 91%. **^{1}H**: 7.01 (d, 2H, J = 10.2 Hz), 6.19 (d, 2H, J = 10.2 Hz), 3.58 (app t, 2H, J = 5.7 Hz), 2.08 (s, 3H), 1.80 (m, 2H), 1.63 (m, 4H). **^{13}C**: 185.3, 171.8, 152.0, 125.9, 56.8, 38.2, 23.9, 23.2 (two overlapping signals), 19.5.