A Catalytic, Three-Component Assembly Reaction for the Synthesis of Pyrrolidines

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Supporting Information

General Information. All reactions were carried out under an atmosphere of argon or nitrogen in flame-dried glassware with magnetic stirring. THF, Et₂O, CH₂Cl₂ and toluene were purified by passage through a bed of activated alumina.¹ DME was distilled from sodium. Reagents were purified prior to use unless otherwise stated following the guidelines of Perrin and Armarego.² Purification of reaction products was carried out by flash chromatography using EM Reagent silica gel 60 (230-400 mesh). Analytical thin layer chromatography was performed on EM Reagent 0.25 mm silica gel 60-F plates. Visualization was accomplished with UV light and anisaldehyde, ceric ammonium nitrate stain, or phosphomolybdic acid followed by heating. Melting points were obtained on a Melt-temp 3 instrument and are uncorrected. Infrared spectra were recorded on a Perkin Elmer 1600 series FT-IR spectrometer. ¹H-NMR spectra were recorded on a Varian Inova 500 (500 MHz) or Mercury 400 (400 MHz) spectrometer and are reported in ppm using solvent as an internal standard (CDCl₃ at 7.26 ppm). Data are reported as (ap = apparent, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad; coupling constant(s) in Hz; integration. Proton-decoupled ¹³C-NMR spectra were recorded on a Varian Inova 500 (125 MHz) or Mercury 400 (100 MHz) spectrometer and are reported in ppm using solvent as an internal standard (CDCl₃ at 77.0 ppm). Mass spectra data were obtained on either a Thermo-Finnigan MAT900 high resolution mass spectrometer, a VG 70-250SE HRMS or

(1) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518-1520.

(2) Perrin, D. D. and Armarego, W. L. *Purification of Laboratory Chemicals*; 3rd ed., Pergamon Press, Oxford. 1988.

Thermo-Finnigan LCQ Advantage HPLC-MS in the Northwestern University Analytical Services Laboratory. Single crystal X-ray data were collected using a Bruker SMART-1000 diffractometer equipped with a CCD detector and processed using SAINT-NT from Bruker.

Ethyl diazoacetate (EDA, **2a**), *t*-butyl diazoacetate (**2b**), and dimethyl acetylene dicarboxylate (DMAD, **3a**) were purchased from Aldrich Chemical Company and used without purification. Copper(I) trifluoromethanesulfonate was prepared by a modified method of Kochi and coworkers.³ Imines were prepared by combining the corresponding aldehyde (freshly distilled), appropriately substituted aniline, and either activated 4Å molecular sieves or anhydrous magnesium sulfate in dichloromethane.⁴ The reactions were stirred for 16 h, then filtered and concentrated in vacuo. If necessary, the resulting imines were re-crystallized from a suitable organic solvent mixture to afford imines that were >95% pure by ¹H NMR analysis.

General Experimental Procedure for the Copper(I)-Catalyzed Reaction:

To a solution of imine (1.5 mmol) and dipolarophile (0.5 mmol) in CH₂Cl₂ (5.0 mL) heated at reflux was added a solution of a diazo ester (1.5 mmol) in CH₂Cl₂ via syringe pump over 3 h. After complete addition, the reaction was heated for an additional hour, cooled and then filtered through silica gel using CH₂Cl₂ (50 mL). The solvent was removed and diastereoselectivities were assigned by analysis of ¹H NMR (500 MHz) spectra and correlated with GC/MS integrations. The reaction mixture was purified by flash column chromatograph (ether/hexanes mixtures as eluent), usually by dry loading the sample, to afford the desired cycloaddition product.

(3) Salomon, R. G.; Kochi, J. K. *J. Am. Chem. Soc.* **1973**, 95, 1889-1897.

(4) (a) Antilla, J. C.; Wulff, W. D. *J. Am. Chem. Soc.* **1999**, 121, 5099-5100. (b) Derdau, V.; Snieckus, V. *J. Org. Chem.* **2001**, 66, 1992-1998. (c) Casarrubios, L.; Perez, J. A.; Brookhart, M.; Templeton, J. L. *J. Org. Chem.* **1996**, 61, 8358-8359.

Analytical data for **4a**: R_f = 0.3 (50% Et₂O/hexanes); IR (film) 3054, 2987, 1740, 1422, 1265, 896, 740, 705 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.41-7.14 (m, 7H), 7.10-6.95 (m, 3H), 6.71 (m, 1H), 6.55 (m, 2H), 6.03 (d, J = 7.6 Hz, 1H), 5.77 (d, J = 7.6 Hz, 1H), 4.14 (m, 3H), 3.80 (m, 3H), 3.65 (m, 3H), 1.09 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 169.8, 164.1, 150.9, 144.1, 143.6, 138.1, 130.1, 129.2, 129.1, 128.6, 127.5, 118.5, 114.1, 72.1, 69.8, 61.8, 53.5, 53.3, 14.4. LRMS (electrospray): 432, 410, 232, 213, 149, 130; Mass calcd for C₂₃H₂₃NO₆ [M]⁺, 409.43. Found 410.

Analytical data for **5**: R_f = 0.3 (50% Et₂O/hexanes); mp = 158-159 °C; IR (film) 2985, 2954, 2848, 1738, 1599, 1497, 1437, 1348, 1275, 1242, 1193, 1096, 1028, 817 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.35-7.22 (m, 5H), 7.05 (m, 1H), 6.50 (m, 2H), 6.01 (d, J = 6.2 Hz, 1H), 5.25 (d, J = 6.2 Hz, 1H), 4.24-4.16 (2H, m), 3.84 (s, 3H), 3.64 (s, 3H), 1.16 (m, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 169.9, 162.2, 162.4, 143.8, 142.9, 137.6, 129.7, 129.5, 128.0, 115.3, 71.3, 69.9, 62.2, 52.8, 52.6, 14.3; LRMS (electrospray): 466, 444, 365, 357, 337, 232, 149; Mass calcd for C₂₃H₂₂NO₆Cl [M]⁺, 443.88. Found 444.

Analytical data for **6**: R_f = 0.3 (50% Et₂O/hexanes); mp = 138-141 °C; IR (film) 3054, 2987, 1738, 1513, 1421, 1266, 896, 738, 705 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.41-7.25 (m, 5H), 6.80 (d, J = 9.0 Hz, 1H), 6.72 (m, 3H), 6.57 (d, J = 9.1 Hz, 2H), 6.03 (d, J = 7.0 Hz, 1H), 5.77 (d, J = 7.3 Hz, 1H), 4.24-4.16 (m, 2H), 3.89 (s, 3H), 3.78 (m, 2H), 3.68 (s, 3H), 3.62 (s, 3H), 1.17 (t, J = 6.9 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 170.1, 164.0, 152.8, 138.1, 137.8, 130.8, 129.0, 128.3, 127.5, 116.5, 115.3, 115.3, 114.9, 71.5, 70.3, 61.9, 55.8, 53.0, 52.9, 14.3; LRMS (electrospray): 462, 440, 124; Mass calcd for C₂₄H₂₅NO₇ [M+H]⁺, 439.36. Found 440.

Analytical data for **4b**: R_f = 0.38 (50% Et₂O/hexanes); mp = 131-133 °C; IR (film) 2978, 2931, 1732, 1664, 1602, 1503, 1454, 1436, 1348, 1260, 1152, 1104, 1030 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.40-7.21 (m, 5H), 7.10 (m, 2H), 6.75 (m, 1H), 6.55 (m, 2H), 5.99 (d, J = 5.4 Hz, 1H), 5.73 (d, J = 5.4 Hz, 1H), 3.88 (s, 3H), 3.65 (s, 3H), 1.29 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 178.0, 169.0, 144.0, 144.0, 138.5, 129.1, 128.9, 127.1, 127.1, 118.6, 114.1, 71.5, 53.0, 52.6, 28.0. LRMS (electrospray): 460, 438, 382, 360, 279, 149; Mass calcd for C₂₅H₂₈NO₆ [M+H]⁺, 437.48. Found 438.

Analytical data for **8**: R_f = 0.42 (50% Et₂O/hexanes); IR (film) 3054, 2987, 1739, 1601, 1504, 1438, 1422, 1349, 11265, 1197, 1105, 1025, 896, 737, 705 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.28-7.09 (m, 5H), 6.78 (m, 1H), 6.61 (m, 2H), 6.02 (d, J = 6.5 Hz, 1H), 5.79 (d, J = 6.5 Hz, 1H), 4.29-4.12 (m, 2H), 3.86 (s, 3H), 3.67 (s, 3H), 2.31 (s, 3H), 1.12 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 170.0, 163.5, 162.7, 144.2, 143.7, 138.3, 1135.1, 130.9, 129.8, 129.2, 127.4, 118.4, 114.1, 71.0, 69.9, 62.0, 52.8, 52.6, 21.5, 14.3. LRMS (electrospray): 446, 424, 387, 213, 149; Mass calcd for C₂₄H₂₅NO₆ [M]⁺, 423.46. Found 424.

Analytical data for **10**: R_f = 0.4 (50% Et₂O/hexanes); mp = 117-119 °C; IR (film) 3050, 3000, 1736, 1664, 1601, 1503, 1436, 1348, 1271, 1245, 1191, 1104, 1010 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.42 (m, 2H), 7.21 (m, 2H), 7.11 (m, 2H), 6.23 (m, 1H), 6.52 (m, 2H), 6.00 (d, J = 6.8 Hz, 1H), 5.75 (d, J = 6.8 Hz, 1H), 4.19-4.04 (m, 2H), 3.83 (m, 3H), 3.64 (m, 3H), 1.09 (m, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 170.0, 163.0, 162.3, 142.8, 142.6, 137.2, 132.0, 131.9, 129.1, 129.0, 122.3, 118.6, 113.9, 70.2, 69.7, 61.8, 52.7, 52.4, 14.0. LRMS (electrospray): 510, 489, 488, 413, 374, 365, 337, 292, 251, 213, 199, 171, 149, 141; Mass calcd for C₂₃H₂₃NO₆Br [M]⁺, 488.33. Found 489.

Analytical data for **11**: R_f = 0.45 (50% Et₂O/hexanes); mp = 112-115 °C; IR (film) 2985, 2954, 1738, 1664, 1601, 1503, 1437, 1349, 1273, 1245, 1193, 1104, 1014, 751, 692 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.28-7.20 (m, 3H), 7.05 (m 2H), 6.75 (m, 1H), 6.50 (m, 2H), 5.95 (d, J = 6.7 Hz, 1H), 5.75 (d, J = 6.7 Hz, 1H), 4.20-4.03 (m, 2H), 3.82 (s, 3H), 3.61 (s, 3H), 1.08 (m, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 169.8, 163.0, 162.7, 143.7, 143.5, 137.0, 134.2, 132.1, 129.1, 129.3, 118.8, 114.2, 70.4, 70.0, 62.1, 53.0, 52.7, 14.3. LRMS (electrospray): 466, 444, 391, 232, 213, 149; Mass calcd for C₂₃H₂₂NO₆Cl [M]⁺, 443.88. Found 444.

Analytical data for **12**: R_f = 0.31 (50% Et₂O/hexanes); mp = 112-113 °C; IR (film) 2954, 1741, 1664, 1601, 1503, 1437, 1349, 1274, 1249, 1192, 1104, 1026, 751, 691 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.40 (m, 1H), 7.30-7.09 (m, 5H), 6.75 (t, J = 5.8 Hz, 1H), 6.59 (m, 3H), 5.78 (d, J = 5.8 Hz, 1H), 4.25-4.11 (m, 2H), 3.91 (m, 3H), 3.68 (m, 3H), 1.13 (m, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 170.1, 163.5, 162.9, 143.9, 143.2, 135.8, 133.8, 131.7, 129.8, 129.4, 128.9, 128.0, 118.8, 113.9, 69.6, 66.8, 62.1, 52.9, 52.7, 14.3. LRMS (electrospray): 466, 444, 232, 149; Mass calcd for C₂₃H₂₂NO₆Cl [M]⁺, 443.88. Found 444.

Analytical data for **13**: R_f = 0.23 (50% Et₂O/hexanes); mp = 136-138 °C; IR (film) 2954, 2850, 1738, 1668, 1601, 1504, 1437, 1348, 1271, 1245, 1191, 1105, 1013, 750 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.16 (m, 3H), 6.77 (m, 1H), 6.69 (m, 3H), 6.67 (s, 1H), 6.16 (m, 1H), 5.69 (d, J = 7.5 Hz, 1H), 4.19-4.05 (m, 2H), 3.90 (s, 3H), 3.75 (s, 3H), 1.15 (m, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 169.5, 150.1, 144.1, 143.0, 142.1, 139.5, 132.6, 119.5, 114.7, 111.0, 110.2, 79.0, 64.1, 62.0, 53.9, 53.1, 14.5; LRMS (electrospray): 422, 400, 354, 232, 228, 149, 123; Mass calcd for C₂₁H₂₁NO₇ [M]⁺, 399.39. Found 400.

Analytical data for **14**: R_f = 0.25 (50% Et₂O/hexanes); mp = 138-140 °C; IR (film) 3055, 2987, 1740, 1437, 1438, 1422, 1265, 896, 740, 705 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.38-7.25 (m, 5H), 7.11 (m, 1H), 7.06 (m, 2H), 5.99 (d, J = 6.8 Hz, 1H), 5.74 (d, J = 6.8 Hz, 1H), 4.22-4.11 (m, 2H), 3.82 (s, 3H), 3.62 (s, 3H), 1.15 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 169.8, 163.0, 162.4, 143.9, 142.2, 137.7, 131.1, 129.4, 129.2, 128.9, 127.5, 123.6, 116.5, 115.2, 71.3, 69.9, 62.2, 52.9, 52.7, 14.4 LRMS (electrospray): 462, 440, 213, 182, 130, 128; Mass calcd for C₂₄H₂₅NO₇ [M]⁺, 439.46. Found 440.

Analytical data for **15**: R_f = 0.26 (50% Et₂O/hexanes); IR (film) 3054, 2988, 1740, 1497, 1437, 1421, 1265, 908, 735, 650 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.25-7.18 (m, 3H), 7.15 (m, 1H), 6.90 (m, 2H), 6.80 (m, 1H), 6.75 (m, 1H), 6.58 (m, 2H), 6.00 (d, J = 5.8 Hz, 1H), 5.81 (d, J = 5.8 Hz, 1H), 4.26-4.09 (m, 2H), 3.85 (s, 3H), 3.77 (s, 3H), 3.68 (s, 3H), 1.10 (m, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 169.9, 163.2, 162.4, 144.5, 144.3, 140.8, 130.9, 129.8, 129.2, 119.9, 118.5, 114.2, 114.1, 113.8, 71.2, 69.9, 61.9, 55.4, 52.8, 52.6, 14.3. LRMS (electrospray): 462, 440. 316, 212, 149, 135, 123, 121, 119; Mass calcd for C₂₄H₂₅NO₇ [M]⁺, 439.46. Found 440.

Analytical data for **16**: R_f = 0.30 (50% Et₂O/hexanes); mp = 107-108°C; IR (film) 2933, 2856, 1736, 1601, 1501, 909 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.25 (m, 2H), 6.79 (m, 1H), 6.68 (m, 2H), 5.50 (d, J = 7.4 Hz, 1H), 5.33 (d, J = 7.4 Hz, 1H), 4.10-3.95 (m, 2H), 3.90 (s, 3H), 3.81 (s, 3H), 2.00 (m, 1H), 1.80-1.45 (m, 6H), 1.25 (m, 7H); ¹³C NMR (125 MHz, CDCl₃) δ 169.1, 165.5, 162.1, 144.6, 131.5, 131.4, 71.8, 70.3, 61.7, 52.7, 52.6, 39.8, 29.4, 27.1, 26.6, 26.4, 14.2. LRMS (electrospray): 438, 417, 416, 260, 228, 186; Mass calcd for C₂₃H₂₉NO₆ [M]⁺, 415.48. Found 416.

Analytical data for **17**: R_f = 0.27 (40% Et₂O/hexanes); IR (film) 2984, 2918, 2850, 1727, 1629, 1602, 1503, 1300, 1266, 1030, 738 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.27–7.04 (m, 14H), 6.69–6.60 (m, 4H), 6.46 (m, 2H), 5.38 (d, J = 4.0 Hz, 1H), 5.30 (m, 2H), 5.25, (d, J = 9.1 Hz, 1H), 4.28–3.96 (m, 12H), 3.82 (m, 2H), 3.73 (m, 1H), 3.52 (m, 1H), 1.40–0.96 (b, m, 18H); ¹³C NMR (125 MHz, CDCl₃) δ 172.3, 170.6, 164.1, 161.8, 152.0, 148.7, 145.4, 142.9, 142.3, 129.5, 129.5, 129.3, 129.0, 128.9, 128.2, 127.5, 127.3, 126.2, 125.5, 121.3, 118.4, 118.1, 115.2, 113.5, 112.7, 69.0, 67.0, 64.4, 64.0, 62.8, 61.8, 61.5, 61.2, 55.8, 48.8, 46.6, 16.3, 14.4, 14.4, 14.2, 14.2, 14.1; LRMS (electrospray): 440, 290, 288, 182, 104 Mass calcd for C₂₅H₂₉NO₆ [M]⁺, 439.50. Found 440.

Analytical data for **18**: R_f = 0.37 (40% Et₂O/hexanes); IR (film) 2984, 2919, 2850, 1727, 1629, 1601, 1503 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.45–7.25 (b, m, 8H), 7.22–7.14 (m, 6H), 6.85–6.71 (m, 4H), 6.61–6.49 (m, 2H), 5.39 (d, J = 2.5 Hz, 1H), 5.32 (d, J = 2.5 Hz, 1H), 5.28 (m, 1H), 5.05 (m, 1H), 4.35–4.28 (m, 3H), 4.26–4.17 (m, 5H), 4.11–4.04 (m, 3H), 3.85–3.72 (m, 6H), 3.66 (m, 2H), 3.40 (m, 1H), 1.36–1.05 (m, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 178.4, 178.2, 172.0, 171.5, 162.1, 162.1, 159.1, 151.3, 130.0, 129.8, 129.6, 129.4, 129.1, 129.0, 127.6, 127.4, 126.4, 126.2, 124.2, 123.4, 121.2, 118.6, 115.3, 112.8, 65.7, 64.4, 61.6, 61.3, 58.8, 55.6, 53.8, 53.1, 48.6, 29.9, 14.4, 14.3; LRMS (electrospray): 434, 412, 391, 359, 306, 286, 260, 232, 199, 164; Mass calcd for C₂₃H₂₅NO₆ [M]⁺, 411.45. Found 412.

Analytical data for **19**: R_f = 0.25 (33% Et₂O/hexanes); IR (film) 3100, 2950, 2254, 1741, 1601, 1503, 1203, 908, 734 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.45–7.27 (m, 6H), 7.26–7.18 (m, 4H), 7.15–7.04 (m, 4H), 6.82 (m, 4H), 6.68 (m, 2H), 5.35 (d, J = 8.6 Hz, 1H), 5.18 (d, J = 6.4 Hz, 1H), 5.12 (d, J = 4.1 Hz, 1H), 4.96 (d, J = 8.4 Hz, 1H), 4.36 (m, 3H), 4.13 (m, 2H), 3.87 (m, 1H), 3.73 (m, 1H), 3.41 (m, 1H), 1.38–1.35 (m, 3H), 1.09–1.05 (m, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 169.1, 169.0, 138.0, 136.5, 129.8, 129.7, 129.6, 129.2, 129.2, 126.8, 126.4, 121.4, 119.6, 117.9,

117.3, 117.0, 116.9, 116.1, 114.8, 113.6, 94.4, 94.4, 67.1, 67.0, 63.2, 63.2, 62.7, 62.1, 42.4, 38.6, 35.0, 33.8, 14.5, 14.4 LRMS (electrospray): 346, 272, 196; Mass calcd for $C_{21}H_{19}N_3O_2$ $[M]^+$, 345.39. Found 346.

Analytical data for **20**: R_f = 0.15 (50% Et₂O/hexanes); IR (film) cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 7.28–7.24 (m, 4H), 7.11 (m, 2H), 6.77 (m, 2H), 6.65 (m, 2H), 5.41 (d, J = 4.5 Hz, 1H), 5.20 (d, J = 10.3 Hz, 1H), 4.07 (m, 2H), 3.98 (dd, J = 10.3, 4.5 Hz, 1H), 3.42 (dd, J = 4.1, 9.3 Hz, 1H), 3.05–3.00 (s, 3H), 1.12 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.2, 175.2, 171.0, 144.9, 141.8, 129.4, 129.2, 127.9, 126.3, 120.1, 117.1, 65.3, 65.0, 61.9, 54.6, 46.6, 25.5, 14.2 LRMS (electrospray): 401, 379, 305, 182, 149; Mass calcd for $C_{22}H_{22}N_2O_4$ $[M]^+$, 378.42, Found 379.

Analytical data for **21**: R_f = 0.61 (40% Et₂O/hexanes); IR (film) 2984, 2919, 2850, 1726, 1695, 1627, 1602 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 7.41–6.95 (m, 16H), 6.72 (m, 2H), 6.44 (m, 2H), 4.74 (d, J = 1H), 4.30–4.05 (m, 3H), 3.52–3.47 (dd, J = 13.1 Hz, J = 9.0 Hz, 1H), 3.24–3.21 (dd, J = 13.1 Hz, J = 9.0 Hz, 1H), 1.12 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.1, 171.2, 146.2, 144.7, 140.8, 140.5, 131.5, 131.4, 129.1, 128.9, 128.7, 128.6, 128.5, 127.1, 126.7, 126.2, 119.5, 115.1, 86.5, 82.3, 62.6, 6.4, 54.2, 14.4; Mass calcd for $C_{32}H_{29}NO_3$ $[M]^+$, 475.58. Found 476.

Analytical data for **22**: R_f = 0.35 (45% Et₂O/hexanes); IR (film) 2921, 2850, 1718, 1687, 1639, 1278, 1179, 1030 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.41–7.22 (m, 5H), 7.15–7.08 (m, 2H), 6.81–6.74 (m, 2H), 6.65 (m, 1H), 5.52 (dd, J_1 = 6.5 Hz, 6.8 Hz, 1H), 5.45 (d, J = 6.1 Hz, 1H), 4.21–3.98 (m, 3H), 3.60 (m, 1H), 1.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 173.8, 137.6, 131.5, 129.2, 129.2, 128.8, 128.6, 126.0, 92.7, 74.4, 65.7, 64.5, 61.8, 49.9, 49.6, 14.4 LRMS (electrospray): 388, 366, 288, 182, 104 Mass calcd for $C_{21}H_{19}NO_5$ $[M]^+$, 365.38. Found 366.

Analytical data for **23**: R_f = 0.31 (45% Et₂O/hexanes); IR (film) 2989, 2919, 2850, 1726, 1630, 1602, 1504 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) d 7.29-7.20 (m, 4H), 7.17-7.07 (m, 4H), 6.64-6.54 (m, 2H), 5.27 (d, J = 9.1 Hz, 1H), 4.73 (d, J = 8.6 Hz, 1 H), 3.85 (m, 1H), 3.81-3.65 (m, 4H), 2.96-2.84 (ddd, J = 13.4 Hz, 13.4 Hz, 9.2 Hz, 1H), 2.21-2.18 (dd, J_1 = 12.8 Hz, 6.1 Hz, 1H), 1.22-1.10 (m, 6 H) ; ¹³C NMR (100 MHz, CDCl₃) d 139.3, 138.3, 129.1, 128.6, 128.0, 127.3, 117.4, 114.1, 113.6, 113.1, 61.5, 56.9, 39.6, 30.4, 30.1 4.5, 14.2; LRMS (electrospray): Mass calcd for C₂₂H₂₅NO₄ [M]⁺, 367.44. Found 368

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Relative Stereochemical assignment based on NMR Data comparison of pyrrolidines **23** and **25** to known compounds **25** and **26**

The relative stereochemistry of pyrrolidine **23** was assigned by comparison (500 MHz ^1H NMR) to known pyrrolidine **24**. Pyrrolidine **24** stereochemistry was assigned by Che and coworkers by comparison to the X-ray structure of the *N*-4-methoxyphenyl analog.⁵

Scheidt	23	Che	24
5.27	d, $J = 9.1$ Hz, 1H	5.28	d, $J = 9.0$ Hz, 1 H
4.73	d, $J = 8.6$ Hz, 1H	4.73	d, $J = 9.0$ Hz, 1 H
3.85	m, 1H	3.91-3.84	m, 1H
2.95-2.86	ddd, $J = 13.4, 13.4, 9.2$ Hz, 1H	2.96-2.84	dt, $J = 17.4, 13.5$ Hz, 1H
2.17	dd, 12.8, 6.1	2.18	dd, $J = 13.2$ Hz, 6.3 Hz, 1H

Pyrrolidine **25** was synthesized by our standard catalytic conditions from *N*-benzylidene anisidine, EDA (**2a**), and *N*-phenylmaleamide, and then compared (500 MHz ^1H NMR) to known pyrrolidine **26**:

Scheidt	25	Che	26
5.43	d, $J = 4.5$ Hz, 1H	5.43	d, $J = 4.5$ Hz, 1H
5.20	d, $J = 9.3$ Hz, 1H	5.19	d, $J = 9.3$ Hz, 1H
4.13-4.18	dd, $J = 9.3, 9.3$ Hz, 1H	4.11-4.04	m, 1H
3.77	s, 3H	3.68	s, 3H
3.47	m, 2H	3.60-3.56	m, 4H

X-ray Crystallographic Data for Substituted Pyrrolidine **10**:

(5) Li, G.-Y.; Chen, J.; Yu, W.-Y.; Hong, W.; Che, C.-M. *Org. Lett.* **2003**, 5, 2153-2156.

Crystal data and structure refinement for pyrrolidine 10.

Identification code	s33n1m
Empirical formula	C ₂₃ H ₂₂ Br N O ₆
Formula weight	488.33
Temperature	153(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P2(1)/c
Unit cell dimensions	a = 10.1952(17) Å b = 12.015(2) Å c = 17.932(4) Å β = 95.28(2) °
Volume	2187.2(8) Å ³
Z, Calculated density	4, 1.483 Mg/m ³
Absorption coefficient	1.919 mm ⁻¹
F(000)	1000
Crystal size	0.240 x 0.104 x 0.090 mm
Theta range for data collection	2.01 to 28.85 °

Limiting indices $-13 \leq h \leq 13, -15 \leq k \leq 15, -23 \leq l \leq 23$
 Reflections collected / unique 19796 / 5306 [R(int) = 0.0600]
 Completeness to theta = 28.85 92.5 %
 Absorption correction Integration
 Max. and min. transmission 0.8521 and 0.7049
 Refinement method Full-matrix least-squares on F²
 Data / restraints / parameters 5306 / 0 / 283
 Goodness-of-fit on F² 0.993
 Final R indices [I > 2sigma(I)] R1 = 0.0358, wR2 = 0.0785
 R indices (all data) R1 = 0.0770, wR2 = 0.0925
 Largest diff. peak and hole 0.520 and -0.474 e-/Å⁻³

Table 2. Atomic coordinates and equivalent isotropic displacement parameters (Å² x 10³) for **10**.
 U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
Br(1)	0.65539(3)	1.03663(2)	1.151831(16)	49(1)
O(1)	0.66429(15)	0.35665(13)	0.88697(9)	37(1)
O(2)	0.86117(14)	0.27323(11)	0.91350(8)	29(1)
O(3)	0.92955(15)	0.62024(12)	0.76520(8)	29(1)
O(4)	0.96641(15)	0.44350(12)	0.80431(9)	31(1)
O(5)	0.76236(17)	0.82423(12)	0.85729(9)	38(1)
O(6)	0.63890(14)	0.70728(12)	0.78170(8)	29(1)
N(1)	0.78066(17)	0.52306(13)	0.99431(9)	21(1)
C(1)	0.6954(2)	0.61169(16)	0.96109(11)	21(1)
C(2)	0.7550(2)	0.63223(16)	0.88855(11)	21(1)

C(3)	0.8410(2)	0.55321(16)	0.87513(12)	22(1)
C(4)	0.8497(2)	0.46714(16)	0.93645(11)	22(1)
C(5)	0.7457(2)	0.46219(16)	1.05640(11)	22(1)
C(6)	0.8216(2)	0.37050(17)	1.08226(12)	28(1)
C(7)	0.7899(2)	0.31197(18)	1.14460(13)	33(1)
C(8)	0.6834(2)	0.34226(19)	1.18240(13)	34(1)
C(9)	0.6086(2)	0.43306(18)	1.15730(12)	30(1)
C(10)	0.6384(2)	0.49271(17)	1.09499(12)	25(1)
C(11)	0.6883(2)	0.71518(16)	1.00939(11)	21(1)
C(12)	0.5711(2)	0.77462(17)	1.00541(12)	28(1)
C(13)	0.5614(2)	0.87145(17)	1.04757(13)	31(1)
C(14)	0.6690(2)	0.90539(17)	1.09369(13)	29(1)
C(15)	0.7865(2)	0.84773(18)	1.09839(12)	30(1)
C(16)	0.7954(2)	0.75196(17)	1.05548(12)	26(1)
C(17)	0.7787(2)	0.35945(17)	0.90870(11)	23(1)
C(18)	0.8100(3)	0.16400(17)	0.88985(14)	37(1)
C(19)	0.8402(3)	0.0838(2)	0.95265(16)	53(1)
C(20)	0.9159(2)	0.54553(17)	0.80870(12)	24(1)
C(21)	1.0472(2)	0.4234(2)	0.74318(14)	37(1)
C(22)	0.7210(2)	0.73289(17)	0.84101(12)	25(1)
C(23)	0.6012(2)	0.79958(19)	0.73200(13)	37(1)

Table 3. Bond lengths [Å] and angles [deg] for **10**.

Br(1)-C(14)	1.902(2)
O(1)-C(17)	1.196(2)
O(2)-C(17)	1.332(2)
O(2)-C(18)	1.461(2)
O(3)-C(20)	1.206(2)
O(4)-C(20)	1.335(2)

O(4)-C(21)	1.451(3)
O(5)-C(22)	1.202(2)
O(6)-C(22)	1.327(3)
O(6)-C(23)	1.452(2)
N(1)-C(5)	1.405(3)
N(1)-C(1)	1.466(2)
N(1)-C(4)	1.469(3)
C(1)-C(2)	1.506(3)
C(1)-C(11)	1.521(3)
C(1)-H(1)	1.0000
C(2)-C(3)	1.330(3)
C(2)-C(22)	1.502(3)
C(3)-C(20)	1.476(3)
C(3)-C(4)	1.506(3)
C(4)-C(17)	1.543(3)
C(4)-H(4)	1.0000
C(5)-C(10)	1.397(3)
C(5)-C(6)	1.401(3)
C(6)-C(7)	1.384(3)
C(6)-H(6)	0.9500
C(7)-C(8)	1.381(3)
C(7)-H(7)	0.9500
C(8)-C(9)	1.382(3)
C(8)-H(8)	0.9500
C(9)-C(10)	1.384(3)
C(9)-H(9)	0.9500
C(10)-H(10)	0.9500
C(11)-C(16)	1.380(3)
C(11)-C(12)	1.388(3)
C(12)-C(13)	1.396(3)

C(12)-H(12)	0.9500
C(13)-C(14)	1.374(3)
C(13)-H(13)	0.9500
C(14)-C(15)	1.380(3)
C(15)-C(16)	1.392(3)
C(15)-H(15)	0.9500
C(16)-H(16)	0.9500
C(18)-C(19)	1.492(3)
C(18)-H(18A)	0.9900
C(18)-H(18B)	0.9900
C(19)-H(19A)	0.9800
C(19)-H(19B)	0.9800
C(19)-H(19C)	0.9800
C(21)-H(21A)	0.9800
C(21)-H(21B)	0.9800
C(21)-H(21C)	0.9800
C(23)-H(23A)	0.9800
C(23)-H(23B)	0.9800
C(23)-H(23C)	0.9800
C(17)-O(2)-C(18)	118.24(16)
C(20)-O(4)-C(21)	116.51(17)
C(22)-O(6)-C(23)	115.24(17)
C(5)-N(1)-C(1)	121.06(16)
C(5)-N(1)-C(4)	119.64(16)
C(1)-N(1)-C(4)	110.49(15)
N(1)-C(1)-C(2)	101.47(16)
N(1)-C(1)-C(11)	114.84(16)
C(2)-C(1)-C(11)	113.71(16)
N(1)-C(1)-H(1)	108.8
C(2)-C(1)-H(1)	108.8

C(11)-C(1)-H(1)	108.8
C(3)-C(2)-C(22)	126.43(19)
C(3)-C(2)-C(1)	111.39(18)
C(22)-C(2)-C(1)	122.14(17)
C(2)-C(3)-C(20)	126.15(19)
C(2)-C(3)-C(4)	110.70(19)
C(20)-C(3)-C(4)	123.12(18)
N(1)-C(4)-C(3)	101.65(15)
N(1)-C(4)-C(17)	111.74(16)
C(3)-C(4)-C(17)	110.24(17)
N(1)-C(4)-H(4)	111.0
C(3)-C(4)-H(4)	111.0
C(17)-C(4)-H(4)	111.0
C(10)-C(5)-C(6)	118.47(19)
C(10)-C(5)-N(1)	121.56(18)
C(6)-C(5)-N(1)	119.94(19)
C(7)-C(6)-C(5)	120.3(2)
C(7)-C(6)-H(6)	119.9
C(5)-C(6)-H(6)	119.9
C(8)-C(7)-C(6)	121.0(2)
C(8)-C(7)-H(7)	119.5
C(6)-C(7)-H(7)	119.5
C(7)-C(8)-C(9)	118.9(2)
C(7)-C(8)-H(8)	120.5
C(9)-C(8)-H(8)	120.5
C(8)-C(9)-C(10)	121.1(2)
C(8)-C(9)-H(9)	119.5
C(10)-C(9)-H(9)	119.5
C(9)-C(10)-C(5)	120.3(2)
C(9)-C(10)-H(10)	119.9

C(5)-C(10)-H(10)	119.9
C(16)-C(11)-C(12)	119.74(19)
C(16)-C(11)-C(1)	121.74(18)
C(12)-C(11)-C(1)	118.52(18)
C(11)-C(12)-C(13)	120.3(2)
C(11)-C(12)-H(12)	119.9
C(13)-C(12)-H(12)	119.9
C(14)-C(13)-C(12)	118.7(2)
C(14)-C(13)-H(13)	120.6
C(12)-C(13)-H(13)	120.6
C(13)-C(14)-C(15)	121.9(2)
C(13)-C(14)-Br(1)	118.76(17)
C(15)-C(14)-Br(1)	119.31(17)
C(14)-C(15)-C(16)	118.8(2)
C(14)-C(15)-H(15)	120.6
C(16)-C(15)-H(15)	120.6
C(11)-C(16)-C(15)	120.5(2)
C(11)-C(16)-H(16)	119.7
C(15)-C(16)-H(16)	119.7
O(1)-C(17)-O(2)	126.2(2)
O(1)-C(17)-C(4)	122.93(19)
O(2)-C(17)-C(4)	110.88(17)
O(2)-C(18)-C(19)	108.50(19)
O(2)-C(18)-H(18A)	110.0
C(19)-C(18)-H(18A)	110.0
O(2)-C(18)-H(18B)	110.0
C(19)-C(18)-H(18B)	110.0
H(18A)-C(18)-H(18B)	108.4
C(18)-C(19)-H(19A)	109.5
C(18)-C(19)-H(19B)	109.5

H(19A)-C(19)-H(19B)	109.5
C(18)-C(19)-H(19C)	109.5
H(19A)-C(19)-H(19C)	109.5
H(19B)-C(19)-H(19C)	109.5
O(3)-C(20)-O(4)	125.3(2)
O(3)-C(20)-C(3)	125.08(19)
O(4)-C(20)-C(3)	109.63(18)
O(4)-C(21)-H(21A)	109.5
O(4)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21B)	109.5
O(4)-C(21)-H(21C)	109.5
H(21A)-C(21)-H(21C)	109.5
H(21B)-C(21)-H(21C)	109.5
O(5)-C(22)-O(6)	126.0(2)
O(5)-C(22)-C(2)	122.7(2)
O(6)-C(22)-C(2)	111.32(18)
O(6)-C(23)-H(23A)	109.5
O(6)-C(23)-H(23B)	109.5
H(23A)-C(23)-H(23B)	109.5
O(6)-C(23)-H(23C)	109.5
H(23A)-C(23)-H(23C)	109.5
H(23B)-C(23)-H(23C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for **10**.

The anisotropic displacement factor exponent takes the form:

$$-2 \pi^2 [h^2 a^{*2} U_{11} + \dots + 2 h k a^* b^* U_{12}]$$

	U11	U22	U33	U23	U13	U12
Br(1)	61(1)	30(1)	57(1)	-18(1)	9(1)	6(1)
O(1)	26(1)	31(1)	53(1)	-9(1)	-8(1)	0(1)
O(2)	32(1)	19(1)	34(1)	-3(1)	-3(1)	2(1)
O(3)	35(1)	27(1)	26(1)	4(1)	5(1)	0(1)
O(4)	36(1)	25(1)	33(1)	-1(1)	13(1)	3(1)
O(5)	61(1)	24(1)	29(1)	2(1)	6(1)	-8(1)
O(6)	31(1)	29(1)	27(1)	9(1)	-3(1)	3(1)
N(1)	28(1)	17(1)	18(1)	0(1)	2(1)	3(1)
C(1)	23(1)	21(1)	18(1)	1(1)	0(1)	1(1)
C(2)	23(1)	21(1)	19(1)	0(1)	0(1)	-4(1)
C(3)	25(1)	20(1)	20(1)	0(1)	1(1)	-1(1)
C(4)	23(1)	20(1)	23(1)	-2(1)	1(1)	1(1)
C(5)	28(1)	19(1)	19(1)	-1(1)	-3(1)	-4(1)
C(6)	31(1)	23(1)	28(1)	1(1)	-5(1)	-1(1)
C(7)	39(1)	26(1)	32(1)	7(1)	-11(1)	-4(1)
C(8)	45(2)	33(1)	22(1)	6(1)	-4(1)	-14(1)
C(9)	38(1)	28(1)	23(1)	-3(1)	1(1)	-10(1)
C(10)	30(1)	21(1)	23(1)	-2(1)	-2(1)	-3(1)
C(11)	26(1)	20(1)	17(1)	2(1)	3(1)	0(1)
C(12)	27(1)	26(1)	31(1)	1(1)	-1(1)	-1(1)
C(13)	32(1)	23(1)	40(1)	3(1)	8(1)	5(1)
C(14)	39(1)	20(1)	29(1)	-3(1)	9(1)	-1(1)
C(15)	34(1)	28(1)	27(1)	-5(1)	1(1)	-3(1)
C(16)	25(1)	24(1)	27(1)	-2(1)	2(1)	2(1)
C(17)	29(1)	22(1)	19(1)	0(1)	2(1)	1(1)
C(18)	46(2)	19(1)	44(2)	-7(1)	-1(1)	-2(1)
C(19)	72(2)	27(1)	57(2)	10(1)	-5(2)	-8(1)

C(20)	23(1)	25(1)	25(1)	-3(1)	-2(1)	-1(1)
C(21)	41(1)	33(1)	41(2)	-6(1)	18(1)	4(1)
C(22)	29(1)	23(1)	25(1)	3(1)	9(1)	2(1)
C(23)	41(1)	38(1)	34(1)	15(1)	3(1)	11(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for **10**.

	x	y	z	U(eq)
H(1)	6044	5814	9496	25
H(4)	9435	4518	9548	26
H(6)	8952	3484	10569	33
H(7)	8422	2500	11616	39
H(8)	6619	3014	12250	40
H(9)	5356	4549	11832	36
H(10)	5855	5547	10784	30
H(12)	4971	7493	9739	34
H(13)	4818	9131	10444	37
H(15)	8601	8729	11303	35
H(16)	8758	7116	10579	31
H(18A)	8515	1389	8450	44
H(18B)	7136	1683	8769	44
H(19A)	9353	836	9672	79
H(19B)	8119	90	9364	79
H(19C)	7933	1062	9956	79
H(21A)	9974	4428	6956	56
H(21B)	10718	3446	7426	56
H(21C)	11269	4692	7501	56

H(23A)	5663	8603	7608	56
H(23B)	5334	7749	6933	56
H(23C)	6784	8258	7084	56