Supporting Materials

Highly Efficient Copper-Catalyzed Nitro-Mannich Type Reaction: Cross-Dehydrogenative-Coupling (CDC) between sp^3 C-H Bond and sp^3 C-H Bond

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- 1) Experimental details and characterization data for all new compounds;
- 2) PDF file of copies of ^1H NMR and ^{13}C NMR spectra for all new compounds.

1) Experimental details and characterization data for all new compounds

General information: ^1H NMR spectra were recorded on Varian 300 and 400 MHz spectrometer in CDCl_3 solution and the chemical shifts were reported in parts per million (δ) relative to internal standard TMS (0 ppm). The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; dt, doublet of triplet; dq, doublet of quartet; ddd, doublet of doublet of doublet; dddd, doublet of doublet of doublet of doublet; m, multiplet; q, quartet. The coupling constants, J , are reported in Hertz (Hz). ^{13}C NMR spectra were obtained at 75 and 100 MHz and referenced to the internal solvent signals (central peak is 77.00 ppm). MS data were obtained by Agilent 6890N Network GC System/Agilent 5973 Mass Selective Detector. HRMS were made by McGill University. IR spectra were recorded by an ABB Bomem MB100 instrument. Melting points were recorded by Melting Point Apparatus, Gallenkamp. Flash column chromatography was performed over SORBENT silica gel 30-60 μm . Thin layer chromatography was performed using Sorbent Silica Gel 60 F₂₅₄ TLC plates and visualized with ultraviolet light. All reagents were weighed and handled in air, and backfilled under an inert atmosphere of nitrogen at room temperature. All reagents were purchased from Aldrich and Acros and used without further purification. 2-Aryl-1,2,3,4-tetrahydro-isoquinolines and 1-phenyl-pyrrolidine were prepared by the literature method^[1].

General procedure: To a mixture of CuBr (1.4 mg, 0.01 mmol) and 2-phenyl-1,2,3,4-tetrahydro-isoquinoline (42 mg, 0.2 mmol), 1 ml CH_3NO_2 was added. Then *tert*-butyl hydroperoxide (0.04 mL, 5–6M in decane) was dropped into the mixture under nitrogen at room temperature. The reaction tube was sealed and the resulting mixture was stirred at the room temperature for 6 hours. The resulting suspension was diluted with diethyl ether and filtrated through a short silicon gel in one pipette eluting with diethyl ether. Solvent was evaporated and the residue was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 5:1), and the fraction with an $R_f = 0.5$ was collected and concentrated to give the desired product 3a.

1,2,3,4-tetrahydro-1-(nitromethyl)-2-phenylisoquinoline (3a). Isolated by flash column chromatography (hexane/ethyl acetate = 5:1, R_f = 0.5). Melting point is 89.0-90.0 °C. IR (KBr): $\nu_{\max}$ 3061, 3038, 2980, 2964, 2918, 1596, 1550, 1495, 1430, 1382, 1220, 1193, 1139, 1113, 1032, 1006, 892, 775, 756, 691, 639 cm^{-1} ; ^1H NMR (400 MHz, ppm) δ 7.25-7.20(m, 2H), 7.18(dd, J = 4.4, 1.6 Hz, 1H), 7.16-7.13(m, 2H), 7.08(d, J = 7.6 Hz, 1H), 6.94(d, J = 8.0 Hz, 2H), 6.81(dd, J = 7.4, 7.4 Hz, 1H), 5.51(dd, J = 7.6, 6.8 Hz, 1H), 4.81(dd, J = 12.0, 7.6 Hz, 1H), 4.50(dd, J = 12.0, 6.8 Hz, 1H), 3.64-3.53(m, 2H), 3.04(ddd, J = 14.0, 8.6, 5.2 Hz, 1H), 2.74(dt, J = 16.4, 4.8 Hz, 1H); ^{13}C NMR (100 MHz, ppm) δ 148.17, 135.06, 132.68, 129.30, 128.99, 127.90, 126.79, 126.48, 119.22, 114.91, 78.65, 58.15, 42.02, 26.45; MS (EI) m/z (%) 268, 253, 209, 208(100), 193, 115, 104, 91, 77, 65, 51; HRMS calcd for $\text{C}_{16}\text{H}_{16}\text{N}_2\text{O}_2$: 268.1211; found: 268.1208.

1,2,3,4-tetrahydro-2-(4-methoxyphenyl)-1-(nitromethyl)isoquinoline (3b). Isolated by flash column chromatography (hexane/ethyl acetate = 5:1, R_f = 0.4). IR (neat liquid): $\nu_{\max}$ 3070, 3001, 2952, 2938, 2910, 2839, 1609, 1553, 1512, 1466, 1383, 1247, 1215, 1184, 1036, 1006, 912 cm^{-1} ; ^1H NMR (400 MHz, ppm) δ 7.24-7.17(m, 2H), 7.16-7.11(m, 2H), 6.89(d, J = 8.8 Hz, 2H), 6.79(d, J = 8.8 Hz, 2H), 5.37(dd, J = 8.4, 6.0 Hz, 1H), 4.80(dd, J = 12.0, 8.8 Hz, 1H), 4.54(dd, J = 12.0, 6.0 Hz, 1H), 3.73(s, 3H), 3.60-3.50(m, 2H), 3.00(ddd, J = 16.4, 8.8, 6.4 Hz, 1H), 2.68(dt, J = 16.4, 4.0 Hz, 1H); ^{13}C NMR (100 MHz, ppm) δ 153.74, 142.85, 135.24, 132.71, 129.28, 127.72, 126.75, 126.44, 118.70, 114.57, 78.90, 58.91, 55.60, 43.16,

25.88; MS (EI) m/z (%) 298, 267, 253, 238(100), 223, 193, 165, 115, 91, 77, 63; HRMS calcd for $C_{17}H_{18}N_2O_3$: 298.1317; found: 298.1310.

1,2,3,4-tetrahydro-2-(2-methoxyphenyl)-1-(nitromethyl)isoquinoline (3c). Isolated by flash column chromatography (hexane/ethyl acetate = 5:1, R_f = 0.5). Melting point is 103.0-104.0 °C. IR (KBr): ν_{max} 3075, 3007, 2957, 2919, 2839, 1596, 1553, 1501, 1381, 1250, 1220, 1178, 1140, 1117, 1030, 1003, 923, 843, 760, 650 cm^{-1} ; 1H NMR (300 MHz, ppm) δ 7.24-7.19(m, 2H), 7.17-7.11(m, 2H), 7.00(ddd, J = 8.1, 7.2, 1.8 Hz, 1H), 6.88-6.78(m, 3H), 5.48(dd, J = 8.7, 5.1 Hz, 1H), 4.80(dd, J = 12.0, 8.4 Hz, 1H), 4.51(dd, J = 12.0, 4.8 Hz, 1H), 3.81(s, 3H), 3.59(dddd, J = 15.0, 6.3, 2.4, 0.9 Hz, 1H), 3.46(ddd, J = 13.2, 11.4, 5.2 Hz, 1H), 2.97(ddd, J = 16.8, 11.1, 6.3 Hz, 1H), 2.70(ddd, J = 16.5, 3.9, 2.1 Hz, 1H); ^{13}C NMR (75 MHz, ppm) δ 152.88, 138.71, 135.20, 133.48, 129.40, 127.42, 126.69, 126.29, 123.96, 121.78, 120.88, 112.34, 79.10, 58.14, 55.77, 42.94, 26.87; MS (EI) m/z (%) 298, 267, 238(100), 222, 165, 128, 115, 102, 91, 77, 65, 51; HRMS calcd for $C_{17}H_{18}N_2O_3$: 298.1317; found: 298.1308.

1,2,3,4-tetrahydro-1-(1-nitroethyl)-2-phenylisoquinoline (3d). The ratio of isolated diastereoisomers is 1.7. Isolated by flash column chromatography (hexane/ethyl acetate = 5:1, R_f = 0.6). IR (neat liquid): ν_{max} 3067, 3029, 2987, 2938, 2903, 2858, 1599, 1550, 1505, 1452, 1390, 1358, 1319, 1296, 1275, 1222, 1156, 1114, 1037, 999, 950, 912 cm^{-1} ; The major

isomer: ^1H NMR (300 MHz, ppm) δ 5.21(d, J = 7.8 Hz, 1H), 5.03(dq, J = 8.4, 6.6 Hz, 1H), 3.62-3.49(m, 2H), 1.53(d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, ppm) δ 148.68, 135.47, 131.86, 129.30, 129.18, 128.23, 128.08, 126.00, 119.19, 115.27, 85.37, 62.73, 42.66, 26.43, 16.47; The minor isomer: ^1H NMR (300 MHz, ppm) δ 5.24(d, J = 7.8 Hz, 1H), 4.87(dq, J = 8.7, 6.9 Hz, 1H), 3.82(ddd, J = 13.5, 8.1, 5.7 Hz, 2H), 1.69(d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, ppm) δ 148.96, 134.63, 133.66, 129.18, 128.98, 128.58, 127.12, 126.48, 118.64, 114.33, 88.90, 61.13, 43.57, 26.80, 17.52; Other overlapped peaks: ^1H NMR (300 MHz, ppm) δ 7.28-7.18(m), 7.16-7.06(m), 7.00-6.95(m), 6.83-6.76(m), 3.09-2.99(m), 2.94-2.81(m); MS (EI) m/z (%) 282, 281, 267, 236, 208(100), 193, 165, 128, 115, 104, 91, 77, 65, 51; HRMS calcd for $\text{C}_{17}\text{H}_{18}\text{N}_2\text{O}_2$: 282.1368; found: 282.1358.

1,2,3,4-tetrahydro-2-(4-methoxyphenyl)-1-(1-nitroethyl)isoquinoline (3e). The ratio of isolated diastereoisomers is 1.7. Isolated by flash column chromatography (hexane/ethyl acetate = 5:1, R_f = 0.4). IR (neat liquid): ν_{max} 3067, 2998, 2938, 2907, 2837, 1550, 1512, 1452, 1386, 1358, 1292, 1268, 1243, 1187, 1145, 1118, 1037, 950, 912 cm^{-1} ; The major isomer: ^1H NMR (300 MHz, ppm) δ 3.72(s, 3H), 3.53-3.44(m, 2H), 1.52(d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, ppm) δ 153.58, 143.31, 135.67, 131.88, 129.14, 128.26, 127.89, 125.90, 118.74, 114.43, 85.70, 63.43, 55.54, 43.98, 26.03, 16.68; The minor isomer: ^1H NMR (300 MHz, ppm) δ 4.85(dq, J = 8.6, 6.6 Hz, 1H), 3.81-3.75(m, 2H), 3.74(s, 3H), 1.67(d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, ppm) δ 153.34, 143.71, 134.88, 133.51, 128.84, 127.85, 127.06, 126.39, 118.07, 114.56, 88.76, 62.13, 56.60, 45.02, 26.30, 17.19; Other overlapped peaks: ^1H NMR (300 MHz, ppm) δ 7.25-7.07(m), 7.01-6.98(m), 6.92-6.87(m), 6.83-6.75(m), 5.06-4.93(m),

3.02-2.92(m), 2.84-2.72(m); MS (EI) m/z (%) 312, 311, 281, 267, 253, 239(100), 238, 224, 191, 165, 135, 104, 91, 78, 77, 57; HRMS calcd for $C_{18}H_{20}N_2O_3$: 312.1474; found: 312.1468.

1,2,3,4-tetrahydro-2-(2-methoxyphenyl)-1-(1-nitroethyl)isoquinoline (3f). The ratio of isolated diastereoisomers is 1.5. Isolated by flash column chromatography (hexane/ethyl acetate = 5:1, R_f = 0.5). IR (neat liquid): $\nu_{\max}$ 3067, 3022, 2998, 2938, 2837, 1592, 1550, 1498, 1452, 1390, 1358, 1292, 1243, 1176, 1110, 1026, 947, 915 cm^{-1} ; The major isomer: ^1H NMR (300 MHz, ppm) δ 4.97(d, J = 7.8 Hz, 1H), 4.89(dq, J = 8.1, 6.6 Hz, 1H), 3.76(s, 3H), 1.46(d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, ppm) δ 153.62, 139.46, 136.13, 132.76, 129.10, 127.99, 127.53, 125.77, 124.19, 123.07, 120.99, 112.86, 86.01, 63.36, 55.94, 44.51, 27.22, 16.84; The minor isomer: ^1H NMR (300 MHz, ppm) δ 5.01(d, J = 7.8 Hz, 1H), 4.81(dq, J = 7.5, 6.6 Hz, 1H), 3.82(s, 3H), 1.65(d, J = 6.3 Hz, 3H); ^{13}C NMR (75 MHz, ppm) δ 153.34, 139.66, 135.23, 133.93, 129.05, 127.50, 126.89, 126.17, 124.08, 123.34, 120.85, 111.81, 88.68, 62.90, 55.46, 44.95, 26.89, 16.91; Other overlapped peaks: ^1H NMR (300 MHz, ppm) δ 7.26-7.17(m), 7.14-7.09(m), 7.03-6.96(m), 6.90-6.75(m), 3.67-3.58(m), 3.52-3.36(m), 2.99-2.69(m); MS (EI) m/z (%) 312, 281, 266, 251, 238(100), 222, 115, 91, 77, 65, 51; HRMS calcd for $C_{18}H_{20}N_2O_3$: 312.1474; found: 312.1465.

N-methyl-N-(2-nitroethyl)benzenamine (3g). Isolated by flash column chromatography (hexane/ethyl acetate = 5:1, R_f = 0.4). IR (neat liquid): $\nu_{\max}$ 3067, 3033, 2914, 2823, 1599,

1550, 1505, 1428, 1386, 1348, 1229, 1191, 1125, 1058, 1030, 992 cm^{-1} ; ^1H NMR (300 MHz, ppm) δ 7.28-7.22(m, 2H), 6.78(dd, J = 7.2, 7.2 Hz, 1H), 6.72(dd, J = 9.0, 0.9 Hz, 2H), 4.56(t, J = 6.3 Hz, 2H), 4.00(td, J = 6.6 Hz, 2H), 2.98(s, 3H); ^{13}C NMR (75 MHz, ppm) δ 147.65, 129.40, 117.88, 112.54, 72.58, 50.64, 38.89; MS (EI) m/z (%) 180, 132, 120(100), 104, 91, 77, 65, 51; HRMS calcd for $\text{C}_9\text{H}_{12}\text{N}_2\text{O}_2$: 180.0899; found: 180.0901.

***N*,4-dimethyl-*N*-(2-nitroethyl)benzenamine (3h).** Isolated by flash column chromatography (hexane/ethyl acetate = 5:1, R_f = 0.5). IR (neat liquid): ν_{max} 3019, 2921, 2865, 2820, 1616, 1554, 1522, 1452, 1432, 1348, 1323, 1229, 1128, 1055, 985, 961 cm^{-1} ; ^1H NMR (300 MHz, ppm) δ 7.05(d, J = 8.7 Hz, 2H), 6.64(d, J = 8.7 Hz, 2H), 4.52(t, J = 6.3 Hz, 2H), 3.93(t, J = 6.3 Hz, 2H), 2.92(s, 3H), 2.25(s, 3H); ^{13}C NMR (75 MHz, ppm) δ 145.64, 129.85, 127.27, 113.00, 72.56, 50.96, 38.96, 20.29; MS (EI) m/z (%) 194, 148, 146, 134(100), 120, 118, 91, 77, 65, 51; HRMS calcd for $\text{C}_{10}\text{H}_{14}\text{N}_2\text{O}_2$: 194.1055; found: 194.1058.

2-(nitromethyl)-1-phenylpyrrolidine (3i-1). Isolated by flash column chromatography (hexane/ethyl acetate = 5:1, R_f = 0.6). IR (neat liquid): ν_{max} 3067, 3029, 2973, 2917, 2879, 2851, 1599, 1547, 1505, 1463, 1428, 1362, 1341, 1247, 1212, 1184, 1159, 1034, 992, 964 cm^{-1} ; ^1H NMR (300 MHz, ppm) δ 7.29-7.22(m, 2H), 6.76(dd, J = 7.5, 7.5 Hz, 1H), 6.67(d, J = 7.8 Hz, 2H), 4.61(dd, J = 11.4, 3.3 Hz, 1H), 4.43-4.38(m, 1H), 4.17(dd, J = 11.1, 9.9 Hz, 1H), 3.51-3.44(m, 1H), 3.24-3.15(m, 1H), 2.16-2.04(m, 4H); ^{13}C NMR (75 MHz, ppm) δ

145.58, 129.54, 117.19, 111.84, 75.75, 57.42, 48.10, 29.33, 22.87; MS (EI) m/z (%) 206, 160, 158, 146(100), 118, 104, 91, 77, 65, 51; HRMS calcd for $C_{11}H_{14}N_2O_2$: 206.1055; found: 206.1058.

***trans*-2,5-bis(nitromethyl)-1-phenylpyrrolidine (3i-2).** Isolated by flash column chromatography (hexane/ethyl acetate = 5:1, R_f = 0.5). IR (neat liquid): $\nu_{\max}$ 3067, 3036, 2970, 2924, 2879, 1599, 1547, 1498, 1456, 1428, 1379, 1351, 1309, 1222, 1177, 1037, 996, 968 cm^{-1} ; ^1H NMR (400 MHz, ppm) δ 7.36-7.31(m, 2H), 6.92(ddt, J = 7.2, 7.2, 0.8 Hz, aH), 6.87(ddt, J = 7.2, 7.2, 0.8 Hz, bH)[a+b=1], 6.81(d, J = 7.6 Hz, cH), 6.79(d, J = 7.6 Hz, eH)[c+e=2], 4.71(dd, J = 11.6, 3.6 Hz, 1H), 4.64(dd, J = 12.0, 2.8 Hz, 1H), 4.60-4.56(m, 1H), 4.43-4.39(m, 1H), 4.30(dd, J = 11.2, 8.8 Hz, 1H), 4.11(dd, J = 11.2, 8.8 Hz, 1H), 2.35-2.05(m, 4H); ^{13}C NMR (75 MHz, ppm) δ 144.96(141.46), 130.27(129.14), 119.80(119.05), 113.66 (113.07), 77.73, 74.44, 59.54, 56.31, 28.52, 26.60; MS (EI) m/z (%) 265, 218, 207, 205(100), 172, 158, 144, 130, 118, 104, 91, 77, 65, 51; HRMS calcd for $C_{12}H_{15}N_3O_4$: 265.1062; found: 265.1056.

Reference:

[1] Kwong, F. Y.; Klapars, A.; Buchwald, S. L. *Org. Lett.* **2002**, 4, 581-584.

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3i-2