Supporting Information

Copper Catalyzed Electrophilic Amination of Functionalized Diarylzinc Reagents

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Experimental Section

Materials and Methods: General. Proton and carbon magnetic resonance spectra (¹H NMR and ¹³C NMR) were recorded with tetramethylsilane or solvent resonance as the internal standard (¹H NMR: TMS at 0.00 ppm, CDCl₃ at 7.24 ppm; ¹³C NMR: CDCl₃ at 77.0 ppm). ¹H NMR data are reported as follows: chemical shift, multiplicity (s = singlet, br s = broad singlet, d = doublet, br d = broad doublet, t = triplet, br t = broad triplet, q = quartet, m = multiplet), coupling constants (Hz), and integration. GLC analysis was performed with the following operating parameters (30 m x 0.316 mm column, pressure = 10.0 psi, flow = 1.4 mL/min, detector = FID, 250 °C) with helium gas as carrier. SFC analysis was performed with the following operating parameters (pressure = 150 bar, flow = 1.5 mL/min, detector = UV-vis). Samples were eluted with SFC grade CO₂ and 1.5% MeOH. Analytical thin layer chromatography (TLC) was performed on 0.25 mm silica gel 60 plates. Visualization was accomplished with UV light and aqueous ceric ammonium molybdate solution followed by heating. Purification of the reaction products was carried out either by acid/base extractive work-up or flash chromatography using silica gel 60 (32-63 μm). All reactions were carried out under an atmosphere of nitrogen in oven-dried glassware with magnetic stirring. All transfers involving organometallic reagents were conducted in a dry box. Yield refers to isolated yield of analytically pure material. Yields are reported for a specific experiment and as a result may differ slightly from those found in the tables, which are averages of at least two experiments. Tetrahydrofuran was dried by passage through a column of neutral alumina under nitrogen prior to use.¹ 4-(Benzyloxy)morpholine and *O*-benzoyl-*N,N*-dibenzylhydroxylamine were prepared as described previously.² 4-Iodobenzonitrile, 4-iodobenzoic acid ethyl ester, and 2-iodopyridine were prepared from the corresponding aryl bromides

according to the method of Buchwald.³ All other reagents were obtained from commercial sources and used without further purification.

General Procedure (A) for the copper catalyzed amination of functionalized diarylzinc reagents.

An oven-dried round bottom flask equipped with magnetic stir bar was charged with the aryl iodide (0.55 mmol), anhydrous tetrahydrofuran (3.0 mL), and the solution was cooled to -35 °C. A tetrahydrofuran solution of isopropyl magnesium bromide (0.60 mL, 1.0 M) was slowly added along the edges of the flask and the reaction mixture was stirred at -35 °C for 1 hour. A tetrahydrofuran solution of zinc(II) chloride (1.0 mL, 0.28 M) was slowly added along the edges of the flask and the reaction mixture was stirred at -35 °C for 10 minutes. A second oven-dried round bottom flask equipped with magnetic stir bar was charged with the *N,N*-dialkyl *O*-benzoyl hydroxylamine derivative (0.25 mmol), copper(I) trifluoromethanesulfonate benzene complex ([CuOTf]₂·C₆H₆, 0.0031 mmol), and anhydrous tetrahydrofuran (2.0 mL). The contents of the first flask were added to this second flask and the reaction mixture was stirred at room temperature for 1 hour. The reaction mixture was diluted with diethyl ether (10 mL), the organic layer was washed with a saturated sodium bicarbonate solution (2 x 10 mL), and the aqueous layer was extracted with dichloromethane (2 x 10 mL). The organic layers were combined and the solvent was removed under reduced pressure. The resulting residue was taken up in diethyl ether (10 mL) and washed with a 1M hydrochloric acid solution (2 x 10 mL), the aqueous layer was basified with a 10% sodium hydroxide solution and extracted with dichloromethane (2 x 10 mL). The organic extracts were combined, dried over sodium sulfate, and the solvent was removed under reduced pressure, affording the desired product of ≥95 % purity as judged by ¹H NMR spectroscopy and GLC or SFC analysis (see Appendix).

4-(Morpholin-4-yl)-benzonitrile (Table 1, entry 1). The title compound was prepared according to General Procedure A using 4-iodobenzonitrile (0.1258 g, 0.55 mmol), 4-(benzoyloxy)morpholine (0.0520 g, 0.25 mmol), and copper(I) trifluoromethanesulfonate benzene complex ([CuOTf]₂·C₆H₆, 0.0016 g, 0.0031 mmol) to yield 4-(morpholin-4-yl)-benzonitrile (0.0370 g, 0.20 mmol, 79% yield) as a white solid. The ¹H NMR spectrum was consistent with that reported in the literature.⁴

4-(Morpholin-4-yl)-benzoic acid ethyl ester (Table 1, entry 2). The title compound was prepared according to General Procedure A using 4-iodobenzoic acid ethyl ester (0.1520 g, 0.55 mmol), 4-(benzoyloxy)morpholine (0.0518 g, 0.25 mmol), and copper(I) trifluoromethanesulfonate benzene complex ([CuOTf]₂·C₆H₆, 0.0017 g, 0.0031 mmol) to yield 4-(morpholin-4-yl)-benzoic acid ethyl ester (0.0443 g, 0.19 mmol, 75% yield) as a white solid. The ¹H NMR spectrum was consistent with that reported in the literature.⁵

4-(4-Chlorophenyl)-morpholine (Table 1, entry 3). The title compound was prepared according to General Procedure A using 1-chloro-4-iodo-benzene (0.1312 g, 0.55 mmol), 4-(benzoyloxy)morpholine (0.0520 g, 0.25 mmol), and copper(I) trifluoromethanesulfonate benzene complex ([CuOTf]₂·C₆H₆, 0.0016 g, 0.0031 mmol) to yield 4-(4-chlorophenyl)-morpholine (0.0477 g, 0.24 mmol, 97% yield) as a white solid. The ¹H NMR spectrum was consistent with that reported in the literature.⁶

4-(4-Fluorophenyl)-morpholine (Table 1, entry 4). The title compound was prepared according to General Procedure A using 1-fluoro-4-iodo-benzene (0.1224 g, 0.55 mmol), 4-(benzoyloxy)morpholine (0.0518 g, 0.25 mmol), and copper(I) trifluoromethanesulfonate benzene complex ([CuOTf]₂·C₆H₆, 0.0016 g, 0.0031 mmol) to yield 4-(4-fluorophenyl)-morpholine (0.0327 g, 0.18 mmol, 72% yield) as a pale yellow oil. Analytical data for the title compound: ¹H NMR (400 MHz, CDCl₃) δ 7.00 – 6.96 (m, 2H), 6.88 – 6.85 (m, 2H), 3.87 – 3.85 (m, 4H), 3.09 – 3.07 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 117.6, 117.5, 115.7, 115.5, 66.9, 50.4.

4-(3-Trifluoromethylphenyl)-morpholine (Table 1, entry 5). The title compound was prepared according to General Procedure A using 1-iodo-3-trifluoromethyl-benzene (0.1496 g, 0.55 mmol), 4-(benzyloxymethyl)morpholine (0.0519 g, 0.25 mmol), and copper(I) trifluoromethanesulfonate benzene complex ($[\text{CuOTf}]_2 \cdot \text{C}_6\text{H}_6$, 0.0017 g, 0.0031 mmol) to yield 4-(3-trifluoromethyl-phenyl)-morpholine (0.0416 g, 0.18 mmol, 72% yield) as a pale yellow oil. Analytical data for the title compound: ^1H NMR (400 MHz, CDCl_3) δ 7.37 – 7.35 (m, 1H), 7.12 – 7.05 (m, 3H), 3.88 – 3.86 (m, 4H), 3.21 – 3.19 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 151.5, 129.6, 125.7, 123.0, 118.4, 116.2, 111.9, 66.7, 48.9.

General Procedure (B) for the copper catalyzed amination of functionalized diarylzinc reagents.

An oven-dried round bottom flask equipped with magnetic stir bar was charged with the aryl iodide (0.55 mmol), anhydrous tetrahydrofuran (3.0 mL), and the solution cooled to $-35\text{ }^{\circ}\text{C}$. A tetrahydrofuran solution of isopropyl magnesium bromide (0.60 mL, 1.0 M) was slowly added along the edges of the flask and the reaction mixture was stirred at $-35\text{ }^{\circ}\text{C}$ for 1 hour. A tetrahydrofuran solution of zinc(II) chloride (1.0 mL, 0.28 M) was slowly added along the edges of the flask and the reaction mixture was stirred at $-35\text{ }^{\circ}\text{C}$ for 10 minutes. A second oven-dried round bottom flask equipped with magnetic stir bar was charged with the *N,N*-dialkyl *O*-benzoyl hydroxylamine derivative (0.25 mmol), copper(I) trifluoromethanesulfonate benzene complex ($[\text{CuOTf}]_2 \cdot \text{C}_6\text{H}_6$, 0.0031 mmol), and anhydrous tetrahydrofuran (2.0 mL). The contents of the first flask were added to this second flask and the reaction mixture was stirred at room temperature for 1 hour. The reaction mixture was diluted with diethyl ether (10 mL) and the organic layer was washed with a saturated sodium bicarbonate solution (2 x 10 mL), dried over magnesium sulfate, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography, eluting with the indicated solvent system, to afford the desired product of $\geq 95\%$ purity as judged by ^1H NMR spectroscopy and GLC or SFC analysis (see Appendix).

4-(4-acetoxyphenyl)-morpholine (Table 1, entry 6). The title compound was prepared according to General Procedure **B** using 1-acetoxy-4-iodobenzene (0.144 g, 0.55 mmol), 4-(benzoyloxy)morpholine (0.0518 g, 0.25 mmol), and copper(I) trifluoromethanesulfonate benzene complex ($[\text{CuOTf}]_2 \cdot \text{C}_6\text{H}_6$, 0.0016 g, 0.0031 mmol) to yield 4-(4-acetoxyphenyl)-morpholine (0.0408 g, 0.18 mmol, 74% yield) as a white solid after flash chromatography with 30% ethyl acetate:hexanes. Analytical data for the title compound: **IR** (Nujol, cm^{-1}) 2924, 2854, 1761, 1514, 1460, 1377, 1201, 1120, 922, 834, 719; **^1H NMR** (400 MHz, CDCl_3) δ 7.00 – 6.98 (m, 2H), 6.90 – 6.88 (m, 2H), 3.86 – 3.84 (m, 4H), 3.13 – 3.11 (m, 4H), 2.27 (s, 3H); **^{13}C NMR** (100 MHz, CDCl_3) δ 169.8, 149.3, 144.0, 122.0, 116.6, 66.9, 49.8, 21.0. **Anal.** Calcd for $\text{C}_{12}\text{H}_{15}\text{NO}_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.12; H, 6.91; N, 6.15.

Trifluoromethanesulfonic acid 4-(morpholin-4-yl)-phenyl ester (Table 1, entry 7). The title compound was prepared according to General Procedure **B** using trifluoromethanesulfonic acid 4-iodophenyl ester (0.1936 g, 0.55 mmol) 4-(benzoyloxy)morpholine (0.0518 g, 0.25 mmol), and copper(I) trifluoromethanesulfonate benzene complex ($[\text{CuOTf}]_2 \cdot \text{C}_6\text{H}_6$, 0.0016 g, 0.0031 mmol) to yield trifluoromethanesulfonic acid 4-(morpholin-4-yl)-phenyl ester (0.0737 g, 0.24 mmol, 95% yield) as a clear oil after flash chromatography with 30% ethyl acetate:hexanes. The ^1H NMR spectrum was consistent with that reported in the literature.⁷

4-(Pyridin-2-yl)-morpholine (Table 1, entry 12). The title compound was prepared according to General Procedure **B** using 2-iodo-pyridine (0.1127 g, 0.55 mmol) 4-(benzoyloxy)morpholine (0.0518 g, 0.25 mmol), and copper(I) trifluoromethanesulfonate benzene complex ($[\text{CuOTf}]_2 \cdot \text{C}_6\text{H}_6$, 0.0015 g,

0.0031 mmol) to yield 4-(pyridin-2-yl)-morpholine (0.0190 g, 0.12 mmol, 46% yield) as a pale yellow oil after flash chromatography with 40% ethyl acetate:hexanes. The ^1H NMR spectrum was consistent with that reported in the literature.⁸

***N*-(4-Chloro-phenyl)-dibenzylamine (Table 1, entry 16).** The title compound was prepared according to General Procedure **B** using 1-chloro-4-iodo-benzene (0.1312 g, 0.55 mmol), *O*-benzoyl-*N,N*-dibenzylhydroxylamine (0.0792 g, 0.25 mmol), and copper(I) trifluoromethanesulfonate benzene complex ($[\text{CuOTf}]_2 \cdot \text{C}_6\text{H}_6$, 0.0016 g, 0.0031 mmol) to yield *N*-(4-chloro-phenyl)-dibenzylamine (0.0709 g, 0.23 mmol, 92% yield) as a white solid after flash chromatography with 1% ethyl acetate:hexanes. The ^1H NMR spectrum was consistent with that reported in the literature.⁹

4-Dibenzylamino-benzoic acid ethyl ester (Table 1, entry 15). The title compound was prepared according to General Procedure **B** using 4-iodobenzoic acid ethyl ester (0.1518 g, 0.55 mmol), *O*-benzoyl-*N,N*-dibenzylhydroxylamine (0.0793 g, 0.25 mmol), and copper(I) trifluoromethanesulfonate benzene complex ($[\text{CuOTf}]_2 \cdot \text{C}_6\text{H}_6$, 0.0016 g, 0.0031 mmol) to yield 4-dibenzylamino-benzoic acid ethyl ester (0.0855 g, 0.25 mmol, 100% yield) as a white solid after flash chromatography with 5% ethyl acetate:hexanes. Analytical data for the title compound: ^1H NMR (400 MHz, CDCl_3) δ 7.87 – 7.84 (m, 2H), 7.35 – 7.20 (m, 10H), 6.72 – 6.70 (m, 2H), 4.71 (s, 4H), 4.30 (q, 2H, $J = 7.1$), 1.33 (t, 3H, $J = 7.1$); ^{13}C NMR (100 MHz, CDCl_3) δ 166.7, 152.4, 137.4, 131.4, 128.8, 127.2, 126.4, 118.3, 111.2, 60.1, 54.0, 14.4.

4-Dibenzylamino-benzonitrile (Table 1, entry 14). The title compound was prepared according to General Procedure **B** using 4-iodobenzonitrile (0.1259 g, 0.55 mmol), *O*-benzoyl-*N,N*-

dibenzylhydroxylamine (0.0793 g, 0.25 mmol), and copper(I) trifluoromethanesulfonate benzene complex ($[\text{CuOTf}]_2 \cdot \text{C}_6\text{H}_6$, 0.0016 g, 0.0031 mmol) to yield 4-dibenzylamino-benzonitrile (0.0712 g, 0.24 mmol, 96% yield) as a white solid after flash chromatography with 15% ethyl acetate:hexanes. Analytical data for the title compound: $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.42 – 7.18 (m, 12H), 6.72 – 6.70 (m, 2H), 4.71 (s, 4H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 151.9, 136.8, 133.6, 128.9, 127.4, 126.4, 120.3, 112.2, 98.7, 54.2.

General Procedure (C) for the copper catalyzed amination of functionalized diarylzinc reagents.

An oven-dried round bottom flask equipped with magnetic stir bar was charged with the aryl iodide (0.55 mmol), anhydrous tetrahydrofuran (3.0 mL), and the solution cooled to -35°C . A tetrahydrofuran solution of phenyl magnesium bromide (0.60 mL, 1.0 M) was slowly added along the edges of the flask and the reaction mixture was stirred at -35°C for 10 minutes. A tetrahydrofuran solution of zinc(II) chloride (1.0 mL, 0.28 M) was slowly added along the edges of the flask and the reaction mixture was stirred at -35°C for 10 minutes. A second oven-dried round bottom flask equipped with magnetic stir bar was charged with the *N,N*-dialkyl *O*-benzoyl hydroxylamine derivative (0.25 mmol), copper(I) trifluoromethanesulfonate benzene complex ($[\text{CuOTf}]_2 \cdot \text{C}_6\text{H}_6$, 0.0031 mmol), and anhydrous tetrahydrofuran (2.0 mL). The contents of the first flask were added to this second flask and the reaction mixture was stirred at room temperature for 1 hour. The reaction mixture was diluted with diethyl ether (10 mL) and the organic layer was washed with a saturated sodium bicarbonate solution (2 x 10 mL), dried over magnesium sulfate, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography, eluting with the indicated solvent system, to afford the desired product of $\geq 95\%$ purity as judged by $^1\text{H NMR}$ spectroscopy and GLC or SFC analysis (see Appendix).

4-(2-Nitrophenyl)-morpholine (Table 1, entry 10). The title compound was prepared according to General Procedure C using 1-iodo-2-nitrobenzene (0.1369 g, 0.55 mmol), 4-(benzoyloxy)morpholine (0.0518 g, 0.25 mmol), and copper(I) trifluoromethanesulfonate benzene complex ($[\text{CuOTf}]_2 \cdot \text{C}_6\text{H}_6$, 0.0016 g, 0.0031 mmol) to yield 4-(2-nitro-phenyl)-morpholine (0.0515 g, 0.25 mmol, 100% yield) as a yellow, viscous oil after flash chromatography with 15% ethyl acetate:hexanes. The $^1\text{H NMR}$ spectrum was consistent with that reported in the literature.¹⁰

4-(2,4-Dinitrophenyl)-morpholine (Table 1, entry 11). The title compound was prepared according to General Procedure C using 1-iodo-2,4-dinitrobenzene (0.1617 g, 0.55 mmol), 4-(benzoyloxy)morpholine (0.0518 g, 0.25 mmol), and copper(I) trifluoromethanesulfonate benzene complex ($[\text{CuOTf}]_2 \cdot \text{C}_6\text{H}_6$, 0.0016 g, 0.0031 mmol) to yield 4-(2,4-dinitro-phenyl)-morpholine (0.0372 g, 0.15 mmol, 59% yield) as a yellow solid after flash chromatography with 30% ethyl acetate:hexanes. The ^1H NMR spectrum was consistent with that reported in the literature.¹¹

N-(2-nitrophenyl)-dibenzylamine (Table 1, entry 18). The title compound was prepared according to General Procedure C using 1-iodo-2-nitrobenzene (0.1369 g, 0.55 mmol), *O*-benzoyl-*N,N*-dibenzylhydroxylamine (0.0792 g, 0.25 mmol), and copper(I) trifluoromethanesulfonate benzene complex ($[\text{CuOTf}]_2 \cdot \text{C}_6\text{H}_6$, 0.0016 g, 0.0031 mmol) to yield *N*-(2-nitro-phenyl)-dibenzylamine (0.0764 g, 0.24 mmol, 96% yield) as a yellow, viscous oil after flash chromatography with 15% ethyl acetate:hexanes. Analytical data for the title compound: ^1H NMR (400 MHz, CDCl_3) δ 7.74 – 7.71 (m, 1H), 7.34 – 7.21 (m, 11H), 7.08 – 7.06 (m, 1H), 6.99 – 6.97 (m, 1H), 4.20 (s, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 145.1, 144.6, 137.5, 133.1, 128.9, 128.8, 127.8, 126.1, 123.9, 122.0, 57.1.

General Procedure (D) for the copper catalyzed amination of functionalized diarylzinc reagents.

An oven-dried round bottom flask equipped with magnetic stir bar was charged with the aryl iodide (0.55 mmol) and anhydrous tetrahydrofuran (3.0 mL). A tetrahydrofuran solution of isopropyl magnesium bromide (0.60 mL, 1.0 M) was slowly added and the reaction mixture was stirred at room temperature for 1 hour. A tetrahydrofuran solution of zinc(II) chloride (1.0 mL, 0.28 M) was slowly added and the reaction mixture was stirred at room temperature for 10 minutes. A second oven-dried round bottom flask equipped with magnetic stir bar was charged with the *N,N*-dialkyl *O*-benzoyl hydroxylamine derivative (0.25 mmol), copper(I) trifluoromethanesulfonate benzene complex ($[\text{CuOTf}]_2 \cdot \text{C}_6\text{H}_6$, 0.0031 mmol), and anhydrous tetrahydrofuran (2.0 mL). The contents of the first

flask were added to this second flask and the reaction mixture was stirred at room temperature for 1 hour. The reaction mixture was diluted with diethyl ether (10 mL) and the organic layer was washed with a saturated sodium bicarbonate solution (2 x 10 mL), dried over magnesium sulfate, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography, eluting with the indicated solvent system, to afford the desired product of ≥ 95 % purity as judged by ^1H NMR spectroscopy and GLC or SFC analysis (see Appendix).

2-(4-Morpholin-4-yl-phenyl)-2-methyl-1,3-dioxolane (Table 1, entry 9). The title compound was prepared according to General Procedure **D** using 2-(4-iodophenyl)-2-methyl-1,3-dioxolane (0.1594 g, 0.55 mmol), 4-(benzoyloxy)morpholine (0.0518 g, 0.25 mmol), and copper(I) trifluoromethanesulfonate benzene complex ($[\text{CuOTf}]_2 \cdot \text{C}_6\text{H}_6$, 0.0016 g, 0.0031 mmol) to yield 2-(4-morpholin-4-yl-phenyl)-2-methyl-1,3-dioxolane (0.0512 g, 0.21 mmol, 82% yield) as a white solid after flash chromatography with 30% ethyl acetate:hexanes. Analytical data for the title compound: **IR** (Nujol, cm^{-1}) 2923, 2854, 1610, 1514, 1460, 1377, 1265, 1225, 1200, 1192, 1126, 1041, 926, 877, 818, 723; **^1H NMR** (400 MHz, CDCl_3) δ 7.39 – 7.37 (m, 2H), 6.89 – 6.87 (m, 2H), 4.04 – 4.00 (m, 2H), 3.87 – 3.85 (m, 4H), 3.80 – 3.76 (m, 2H), 3.18 – 3.15 (m, 4H), 1.64 (s, 3H); **^{13}C NMR** (100 MHz, CDCl_3) δ 150.8, 134.6, 126.2, 115.1, 108.8, 66.9, 64.4, 49.2, 27.5. **Anal.** Calcd for $\text{C}_{14}\text{H}_{19}\text{NO}_3$: C, 67.45; H, 7.68; N, 5.62. Found: C, 67.33; H, 7.77; N, 5.61.

N-(4-Methoxyphenyl)-dibenzylamine (Table 1, entry 17). The title compound was prepared according to General Procedure **D** using 4-iodoanisole (0.1287 g, 0.55 mmol), *O*-benzoyl-*N,N*-dibenzylhydroxylamine (0.0792 g, 0.25 mmol), and copper(I) trifluoromethanesulfonate benzene complex ($[\text{CuOTf}]_2 \cdot \text{C}_6\text{H}_6$, 0.0016 g, 0.0031 mmol) to yield *N*-(4-methoxyphenyl)-dibenzylamine (0.0681 g, 0.22 mmol, 90% yield) as a white solid after flash chromatography with 5% ethyl acetate:hexanes. The ^1H NMR spectrum was consistent with that reported in the literature.⁹

General Procedure (E) for the copper catalyzed amination of functionalized diarylzinc reagents.

An oven-dried round bottom flask equipped with magnetic stir bar was charged with the aryl iodide (0.55 mmol) and anhydrous tetrahydrofuran (3.0 mL). A tetrahydrofuran solution of isopropyl magnesium bromide (0.60 mL, 1.0 M) was slowly added and the reaction mixture was stirred at room temperature for 1 hour. A tetrahydrofuran solution of zinc(II) chloride (1.0 mL, 0.28 M) was slowly added and the reaction mixture was stirred at room temperature for 10 minutes. A second oven-dried round bottom flask equipped with magnetic stir bar was charged with the *N,N*-dialkyl *O*-benzoyl hydroxylamine derivative (0.25 mmol), copper(I) trifluoromethanesulfonate benzene complex ($[\text{CuOTf}]_2 \cdot \text{C}_6\text{H}_6$, 0.0031 mmol), and anhydrous tetrahydrofuran (2.0 mL). The contents of the first flask were added to this second flask and the reaction mixture was stirred at room temperature for 1 hour. The reaction mixture was diluted with diethyl ether (10 mL), the organic layer was washed with a saturated sodium bicarbonate solution (2 x 10 mL), and the aqueous layer was extracted with dichloromethane (2 x 10 mL). The organic layers were combined and the solvent was removed under reduced pressure. The resulting residue was taken up in diethyl ether (10 mL) and washed with a 1M hydrochloric acid solution (2 x 10 mL), the aqueous layer was basified with a 10% sodium hydroxide solution and extracted with dichloromethane (2 x 10 mL). The organic extracts were combined, dried over sodium sulfate, and the solvent was removed under reduced pressure, affording the desired product of ≥ 95 % purity as judged by ^1H NMR spectroscopy and GLC or SFC analysis (see Appendix).

4-(Naphthalen-1-yl)morpholine (Table 1, entry 13). The title compound was prepared according to General Procedure E using 1-iodo-naphthalene (0.1398 g, 0.55 mmol), 4-(benzoyloxy)morpholine (0.0518 g, 0.25 mmol), and copper(I) trifluoromethanesulfonate benzene complex ($[\text{CuOTf}]_2 \cdot \text{C}_6\text{H}_6$, 0.0016 g, 0.0031 mmol) to yield 4-(naphthalen-1-yl)morpholine (0.0481 g, 0.23 mmol, 90% yield) as a white solid. The ^1H NMR spectrum was consistent with that reported in the literature.¹²

4-(4-Methoxyphenyl)-morpholine (Table 1, entry 8). The title compound was prepared according to General Procedure E using 4-iodoanisole (0.1287 g, 0.55 mmol), 4-(benzyloxymethyl)morpholine (0.0518 g, 0.25 mmol), and copper(I) trifluoromethanesulfonate benzene complex ($[\text{CuOTf}]_2 \cdot \text{C}_6\text{H}_6$, 0.0016 g, 0.0031 mmol) to yield 4-(4-methoxyphenyl)-morpholine (0.0403 g, 0.21 mmol, 83% yield) as a white solid. The ^1H NMR spectrum was consistent with that reported in the literature.⁵

References

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Appendix A - ¹H NMR Spectra

Table 1, entry 1

Table 1, entry 3

Table 1, entry 4

Table 1, entry 5

Table 1, entry 7

Current Data Parameters
NAME AMB11101
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20040829
Time 13.53
INSTRUM spect
PROBHD 5 mm HR 13C/31
PULPROG zgpg30
TD 32768
SOLVENT CDCl3
AQ 5.995204 Hz
RG 143.7
FIDRES 0.162959 Hz
AQ 2.7329011 sec
RG 143.7
DE 63.400 usec
TE 300.0 K
PC 1.0000000 sec
===== CHANNEL f1 =====
NUC1 1H
P1 10.10 usec
PL1 -3.00 dB
SFO1 399.802988 MHz
F2 - Processing parameters
SI 32768
SF 399.800004 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 23.00 cm
CY 12.50 cm
FIP 13.474 ppm
F1 5387.05 Hz
F2 11.521 ppm
F3 561.05 Hz
PRGCM 0 65198.00 Hz/cm
HZCM 260 65104.00 Hz/cm

AMS-III-101

Table 1, entry 8

Table 1, entry 10

Table 1, entry 11

Table 1, entry 12

Current Data Parameters
 NAME AMB1152
 EXPNO 1
 PROCNO 1
 F2 - Acquisition Parameters
 Date_ 20040819
 Time 12.04
 INSTRUM spect
 PULPROG zgpg30
 PROBHD 5 mm HR 130/31
 FIDRES 0.3200 Hz
 T0 32768
 SOLVENT CDCl3
 NS 16
 DS 2
 SWH 5985.204 Hz
 FIDRES 0.156359 Hz
 AQ 2.735518 sec
 RG 328
 DM 63.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.0000000 sec
 ***** CHANNEL f1 *****
 NUC1 1H
 P1 10.10 usec
 PL1 -3.00 dB
 SF01 399.8021960 MHz
 F2 - Processing parameters
 SI 32768
 SF 399.8020001 MHz
 MD 0
 SSF 0
 LB 0.00 Hz
 GB 0
 PC 1.00
 1D NMR plot parameters
 CX 23.00 cm
 CY 12.50 cm
 F1 13.478 mm
 F2 50.825 mm
 F3 11.419 mm
 F4 -605.88 Hz
 PH0M 0.85198 mm/cm
 HZCM 280.86104 Hz/cm

Table 1, entry 14

Current Data Parameters
NAME AMB11148
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20040923
Time 22:24
INSTRUM spect
PROBHD 5 mm HR 13C/31
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 5995.264 Hz
FIDRES 0.18959 Hz
AQ 2.7339011 sec
RG 320
GB 32.400 sec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
***** CHANNEL f1 *****
NUC1 13
P1 10.00 usec
PL1 -3.00 dB
SFO1 399.8033980 MHz
F2 - Processing parameters
SI 32768
SF 399.8033115 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
SFO 399.8033115 MHz
AQ 2.7339011 sec
CY 12.80 cm
F1P 13.465 ppm
F1 5384.49 Hz
F2P -1.528 ppm
F2 -610.72 Hz
PPM0 0.55196 ppm/cm
HZ0 260.85104 Hz/cm

Table 1, entry 15

Table 1, entry 16

Current Data Parameters
 NAME AMB11107
 EXPNO 2
 PROCNO 1
 F2 - Acquisition Parameters
 Date_ 20040902
 Time 15.06
 INSTRUM spect
 PULPROG zgpg30
 TD 65536
 SOLVENT CDCl3
 NS 16
 DS 2
 SWH 5950.204 Hz
 FIDRES 0.165552 Hz
 AQ 2.7356011 SEC
 RG 143.7
 DM 83.400 USEC
 DE 6.00 USEC
 TE 300.0 K
 D1 1.5000000 SEC
 ===== CHANNEL f1 =====
 NUC1 1H
 P1 10.10 USEC
 PL1 -3.00 dB
 SFO1 399.602388 MHz
 F2 - Processing parameters
 SI 32768
 SF 399.600105 MHz
 WDW no
 SSB 0
 LB 0.00 Hz
 GB 0
 PC 1.00
 1D NMR plot parameters
 CX 23.00 cm
 CY 12.50 cm
 F1 42.22 ppm
 F2 -1.5524 ppm
 F2 -609.25 Hz
 PPH0 0.85189 ppm/cm
 HZCN 260.85104 Hz/cm

Table 1, entry 17

Table 1, entry 18

Appendix B – SFC Traces

Appendix C – GLC Traces

RUN# 852 MAY 5, 1982 19:19:05

AREAX

RT	AREA	TYPE	WIDTH	AREAX
1.960	39676000	SPB	.077	89.03325
16.489	4887130	PB	.106	10.96675

TOTAL AREA=4.4563E+07
MUL FACTOR=1.0000E+00

RUN# 853 MAY 5, 1982 19:40:52

AREAX

RT	AREA	TYPE	WIDTH	AREAX
1.977	39074848	SPB	.076	80.45168
7.378	9494298	PB	.069	19.54833

TOTAL AREA=4.8568E+07
MUL FACTOR=1.0000E+00

RUN# 855 MAY 6, 1982 16:52:51

AREAX

RT	AREA	TYPE	WIDTH	AREAX
1.970	39542176	SPB	.075	81.71734
2.594	48152	BB	.033	.09951
7.690	8769062	PB	.069	18.12283
9.500	29575	BB	.002	.06112

TOTAL AREA=4.8309E+07
MUL FACTOR=1.0000E+00

RUN# 849 MAY 3, 1982 18:24:48

AREAX

RT	AREA	TYPE	WIDTH	AREAX
1.959	27236112	SPB	.053	67.32374
7.301	13219328	BB	.465	32.67627

TOTAL AREA=4.0455E+07

MUL FACTOR=1.0000E+00

RUN# 858 MAY 6, 1982 22:24:03

AREAX

RT	AREA	TYPE	WIDTH	AREAX
2.111	36828704	SPB	.071	58.66797
6.169	140881	PB	.002	.22447
7.335	25799594	SPB	.094	41.10755

TOTAL AREA=6.2761E+07

MUL FACTOR=1.0000E+00

RUN# 854 MAY 5, 1982 20:02:39

AREAX

RT	AREA	TYPE	WIDTH	AREAX
1.956	39265696	SPB	.076	93.16861
17.316	2079077	PB	.107	6.03140

TOTAL AREA=4.2145E+07

MUL FACTOR=1.0000E+00

♦ RUN # 061 MAY 7, 1982 19:42:33

START

RUN# 061 MAY 7, 1982 19:42:33

AREAX

RT	AREA	TYPE	WIDTH	AREA%
2.122	44186496	SHB	.086	84.99286
10.771	7801981	PB	.132	15.00713

TOTAL AREA=5.1988E+07
MUL FACTOR=1.0000E+00