Supporting Information

Three-Component Coupling Reactions of Thioformamides with Organolithium and Grignard Reagents Leading to Formation of Tertiary Amines and a Thiolating Agent

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General Remarks: The IR spectra were obtained on a JASCO FT-IR spectrophotometer. The ^1H NMR spectra were recorded on a JEOL α -400 (400 MHz) in CDCl_3 . Chemical shifts of protons were reported in δ values referred to tetramethylsilane as an internal standard in CDCl_3 , and the following abbreviations were used: s: singlet, d: doublet, t: triplet, m: multiplet. The ^{13}C NMR spectra were measured on a JEOL α -400 (100 MHz) in CDCl_3 . The mass spectra (MS) and high resolution mass spectra (HRMS) were taken on a JEOL JNM 700 mass spectrometer.

Materials: Dehydrated diethyl ether (Et_2O), dehydrated tetrahydrofuran (THF), phenyllithium in cyclohexane- Et_2O , ethylmagnesium bromide in THF, methyllithium in Et_2O , phenylmagnesium bromide in THF, vinylmagnesium bromide in THF, *t*-butyllithium in pentane, furan, and phthaloyl dichloride were purchased from Kanto Chemical Co., Ltd. Benzyl bromide, *n*-butyllithium solution in hexane, ferrocene, and lithium chloride anhydrous were purchased from Nacalai Tesque Inc. *N*-Formylmorpholine was purchased from Tokyo Chemical Industry Co., Ltd. Benzoyl chloride was purchased from Wako Pure Chemical Industries, Ltd. Lawesson's reagent, 1-piperazinecarboxaldehyde, di-*tert*-butyl dicarbonate, *N,N*-dimethylthioformamide, 4-methoxyphenylmagnesium bromide in THF, 4-(*N,N*-dimethyl)anilinemagnesium bromide in THF, 3-methoxyphenylmagnesium bromide in THF, 2-bromopyridine, allylmagnesium bromide in Et_2O , 4-fluorophenylmagnesium bromide in THF, 4-chlorobromobenzene, *i*-propylmagnesium chloride in THF, 2-thienyllithium in THF, and cyclohexylmagnesium bromide in Et_2O were purchased from Aldrich Chemical Company, Inc. Silica gel used on column chromatography was run on silica gel 60 of Kanto Chemical Co., Ltd. All manipulations were carried out under argon atmosphere.

The experimental procedures for the synthesis of **1b–1d**, **4a–4t**, **9**, **10** and their spectroscopic properties are shown below.

***N*-Morpholincarbothioaldehyde (1b)**

To a dichloromethane (10 mL) solution of *N*-formylmorpholine (2.0 mL, 20 mmol) was added Lawesson's reagent (4.0 g, 10 mmol) at room temperature, and the mixture was stirred at this temperature for 3 h. To the resulting mixture was added silica gel (25 g) and concentrated in vacuo. The residue was purified by column chromatography (SiO_2 , hexane/ EtOAc / Et_3N = 1 : 1 : 0.01) to give **1b** (2.61 g, 99%) as a white solid; mp 66.5–67.0 °C; IR (KBr) 2967, 2924, 2905, 2856, 1510, 1230, 1111, 1025, 1011, 850, 630, 507 cm^{-1} ; ^1H NMR (CDCl_3) δ 3.63 (m, 2H, CH_2), 3.71 (m, 4H, CH_2), 4.05 (m, 2H, CH_2), 9.21 (s, 1H,

CH); ^{13}C NMR (CDCl_3) δ 45.4, 55.0, 66.0, 66.8 (CH_2), 186.7 ($\text{C}=\text{S}$); MS (EI) m/z 131 (M^+); HRMS (EI) Calcd for $\text{C}_5\text{H}_9\text{NOS}$ (M^+); 131.0405, Found: 131.0395.

4-(Thioxomethyl)-1-piperazinecarboxylic acid 2,2-dimethylethyl ester (1c)

To a THF (20 mL) solution of 1- piperazinecarboxaldehyde (2.05 mL, 20 mmol) was added di-*tert*-butyl dicarbonate (4.37 g, 20 mmol) at room temperature, and the mixture was stirred at this temperature for 2 h. The solvents were removed in vacuo and the crude product was dissolved in dichloromethane (10 mL). To this was added Lawesson's reagent (4.04 g, 10 mmol), and the reaction mixture was stirred for 2 h at room temperature again. To the resulting mixture was added silica gel (25 g), and it was concentrated in vacuo. The residue was purified by column chromatography (SiO_2 , hexane/EtOAc/ Et_3N = 1 : 1 : 0.01) to afford **1c** (2.78 g, 60%) as a white solid; mp 129.8-130.4 °C; IR (KBr) 2977, 1684, 1507, 1431, 1361, 1236, 1180, 1071, 908, 763 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.46 (s, 9H, OCMe_3), 3.49-3.54 (m, 4H, CH_2NCH_2), 3.60-3.62 (m, 2H, CH_2NCH_2), 4.02-4.05 (m, 2H, CH_2NCH_2), 9.28 (s, 1H, CH); ^{13}C NMR (CDCl_3) δ 28.4 (CMe_3), 44.9, 54.6 (NCH_2), 80.9 (OCMe_3), 154.3 ($\text{C}=\text{O}$), 187.2 ($\text{C}=\text{S}$); MS (EI) m/z 230 (M^+); HRMS (EI) Calcd for $\text{C}_{10}\text{H}_{18}\text{N}_2\text{O}_2\text{S}$ (M^+) 230.1089, found: 230.1112.

1-(Thioxomethyl)-4-(phenylmethyl)piperazine (1d)

To a dichloromethane (20 mL) solution of 1- piperazinecarboxaldehyde (2.05 mL, 20 mmol) was added benzyl bromide (2.61 mL, 22 mmol) and triethylamine (27.8 mL, 200 mmol) at room temperature, and the mixture was stirred at this temperature for 3 h. The resulting mixture was quenched with water. The organic layer was separated, and the aqueous layer was extracted with dichloromethane. The organic layer

collected was washed with saturated NH_4Cl solution, water and brine and dried over MgSO_4 . The solvent was removed in vacuo, and the crude product was dissolved in dichloromethane (10 mL). Lawesson's reagent (4.04 g, 10 mmol) was added, and the reaction mixture was stirred for 1 h at room temperature again. To the resulting mixture was added silica gel (25 g), and it was concentrated in vacuo. The residue was purified by column chromatography (SiO_2 , hexane/EtOAc/ Et_3N = 1 : 1 : 0.01) to afford **1d** (3.48 g, 79%) as a white solid; IR (KBr) 3450, 3027, 2956, 2917, 2804, 2762, 1509, 1435, 1399, 1354, 1343, 1243, 1216, 1201, 1137, 1116, 1029, 1006, 990, 957, 915, 805, 749, 701 cm^{-1} ; ^1H NMR (CDCl_3) δ 2.45-2.47 (m, 4H, CH_2NCH_2), 3.49 (s, 2H, CH_2), 3.56-3.58 (m, 2H, CH_2NCH_2), 4.00-4.02 (m, 2H, CH_2NCH_2), 7.19-7.26 (m, 5H, Ar), 9.14 (s, 1H, CH); ^{13}C NMR (CDCl_3) δ 44.9, 51.7, 52.9, 55.0 (NCH_2), 62.5 (CH_2), 127.5, 128.4, 129.0, 137.2 (Ar), 186.3 ($\text{C}=\text{S}$); MS (EI) m/z 220 (M^+); HRMS (EI) Calcd for $\text{C}_{12}\text{H}_{16}\text{N}_2\text{S}$ (M^+) 220.1034,

found: 220.1027.

α -Ethyl-*N,N*-dimethylbenzenemethanamine (4a) (FA271)

To a solution of *N,N*-dimethylthioformamide (**1a**) (0.087 mL, 1.0 mmol) in Et₂O (2.0 mL) was added slowly 1.04 M solution of phenyllithium in cyclohexane-Et₂O (1.06 mL, 1.1 mmol) at -78 °C. After the addition was complete, the mixture was stirred for 0.5 h at room temperature. To this was added 1.0 M solution of ethylmagnesium bromide in THF (2.0 mL, 2.0 mmol) at room temperature, and this mixture was stirred at this temperature for 2 h. The resulting mixture was poured into a saturated aqueous solution of NH₄Cl, and extracted with Et₂O. The organic layer was purified by acid-base workup, dried over MgSO₄ and concentrated in vacuo to give the amine **4a** (0.148 g, 91%) as a colorless oil; IR (neat) 3027, 2961, 2875, 2816, 2770, 1452, 702 cm⁻¹; ¹H NMR (CDCl₃) δ 0.72 (t, J = 7.6 Hz, 3H, Me), 1.67-1.78 (m, 1H, CH₂), 1.88-1.98 (m, 1H, CH₂), 2.18 (s, 6H, NMe₂), 3.04 (dd, J = 9.5, 4.6 Hz, 1H, CH), 7.20-7.26 (m, 3H, Ar), 7.30-7.34 (m, 2H, Ar); ¹³C NMR (CDCl₃) δ 10.9 (Me), 26.1 (CH₂), 43.0 (NMe₂), 72.6 (CH), 126.9, 127.9, 128.6, 140.7 (Ar); MS (EI) m/z 163 (M⁺); HRMS (EI) Calcd for C₁₁H₁₇N (M⁺-CH₂CH₃); 134.0970, Found: 134.0918.

4-Methoxy-*N,N*-dimethyl- α -phenylbenzylamine (4b) (FA223)

To a solution of *N,N*-dimethylthioformamide (**1a**) (0.087 mL, 1.0 mmol) in THF (1.0 mL) was added slowly 1.04 M solution of phenyllithium in cyclohexane-Et₂O (1.44 mL, 1.5 mmol) at -78 °C. After the addition was complete, the mixture was stirred for 0.5 h at room temperature. To this was added 0.5 M solution of 4-methoxyphenylmagnesium bromide in THF (4.0 mL, 2.0 mmol) at room temperature, and this mixture was stirred at this temperature for 2 h. The resulting mixture was poured into a saturated aqueous solution of NH₄Cl, and extracted with Et₂O. The organic layer was purified by acid-base workup, dried over MgSO₄ and concentrated in vacuo to give the amine **4b** (0.230 g, 95%) as a colorless oil; IR (neat) 2950, 2815, 2770, 1610, 1510, 1453, 1248, 1179, 1038, 819, 700 cm⁻¹; ¹H NMR (CDCl₃) δ 2.18 (s, 6H, NMe₂), 3.74 (s, 3H, OMe), 4.02 (s, 1H, CH), 6.81 (d, J = 8.1 Hz, 2H, Ar), 7.14-7.18 (m, 1H, Ar), 7.24-7.34 (m, 4H, Ar), 7.41 (d, J = 8.1 Hz, 2H, Ar); ¹³C NMR (CDCl₃) δ 44.7 (NMe₂), 55.2 (OMe), 77.3 (CH), 113.8, 126.8, 127.6, 128.5, 128.8, 135.6, 143.4, 158.5 (Ar); MS (EI) m/z 241 (M⁺); HRMS (EI) Calcd for C₁₆H₁₉NO (M⁺) 241.1467, found: 241.1450.

4-(Dimethylamino)-*N,N*-dimethyl- α -phenylbenzenemethanamine (4c) (FA224)

To a solution of *N,N*-dimethylthioformamide (**1a**) (0.087 mL, 1.0 mmol) in THF (1.0 mL) was added slowly 1.04 M solution of phenyllithium in cyclohexane-Et₂O (1.44 mL, 1.5 mmol) at -78 °C. After the addition was complete, the mixture was stirred for 0.5 h at room temperature. To this was added 0.5 M solution of 4-(*N,N*-dimethyl)anilinemagnesium bromide in THF (4.0 mL, 2.0 mmol) at room temperature, and this mixture was stirred at this temperature for 2 h. The resulting mixture was poured into a saturated aqueous solution of NH₄Cl, and extracted with Et₂O. The

organic layer was dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography (SiO₂, hexane/EtOAc/Et₃N = 5 : 1 : 0.01) to give the amine **4c** (0.232 g, 91%) as a white solid; mp 88.2-88.7 °C; IR (KBr) 3022, 2986, 2949, 2890, 2811, 2767, 1613, 1522, 1443, 1355, 1206, 1016, 802, 724, 699 cm⁻¹; ¹H NMR (CDCl₃) δ 2.12 (s, 6H, NMe₂), 2.82 (s, 6H, NMe₂), 3.90 (s, 1H, CH), 6.58 (d, *J* = 8.3 Hz, 2H, Ar), 7.05-7.20 (m, 5H, Ar), 7.34 (d, *J* = 8.3 Hz, 2H, Ar); ¹³C NMR (CDCl₃) δ 40.6 (NCH₃), 44.8 (NCH₃), 77.4 (CH), 112.5, 126.5, 127.5, 128.3, 128.5, 131.3, 144.2, 149.5 (Ar); MS (EI) *m/z* 254 (M⁺); HRMS (EI) Calcd for C₁₇H₂₂N₂ (M⁺) 254.1783, found: 254.1760.

3-Methoxyl-*N,N*, α -trimethylbenzenemethanamine (**4d**) (FA198)

The amine **4d** was synthesized by utilizing the procedure described for **4b**. The reaction of thioformamide **1a** (1.0 mmol) with methyllithium (1.1 mmol), and 3-methoxyphenylmagnesium bromide (2.0 mmol) gave the amine **4d** (0.153 g, 85%) as a yellow oil; IR (neat) 2975, 2860, 2816, 2767, 1600, 1486, 1455, 1434, 1283, 1256, 1154, 1044, 785, 702 cm⁻¹; ¹H NMR (CDCl₃) δ 1.28 (d, *J* = 6.6 Hz, 3H, Me), 2.12 (s, 6H, NMe₂), 3.12 (q, *J* = 6.6 Hz, 1H, CH), 3.72 (s, 3H, OMe), 6.69-6.72 (m, 1H, Ar), 6.79-6.81

(m, 2H, Ar), 7.12-7.16 (m, 1H, Ar); ¹³C NMR (CDCl₃) δ 20.4 (Me), 43.3 (NMe₂), 55.1 (OMe), 66.1 (CH), 112.2, 112.9, 119.9, 129.1, 145.8, 159.5 (Ar); MS (EI) *m/z* 179 (M⁺); HRMS (EI) Calcd for C₁₁H₁₇NO (M⁺-CH₃); 164.1075, Found: 164.1051.

N,N-Dimethyl- α -phenylfurfurylamine (**4e**) (FA267)

To a solution of *N,N*-dimethylthioformamide (**1a**) (0.087 mL, 1.0 mmol) in THF (1.0 mL) was added slowly 2-furyllithium prepared from furan (0.116 mL, 1.6 mmol) and 1.6 M solution of *n*-butyllithium in hexane (0.94 mL, 1.5 mmol) in THF (2.0 mL) at -15 °C via cannula at -78°C. After the addition was complete, the mixture was stirred for 0.5 h at room temperature. To this was added 0.93 M solution of

phenylmagnesium bromide in THF (2.2 mL, 2.0 mmol) at room temperature, and this mixture was stirred at room temperature for 2 h. The resulting mixture was poured into a saturated aqueous solution of NH_4Cl , and extracted with Et_2O . The organic layer was purified by acid-base workup, dried over MgSO_4 and concentrated in vacuo to give the amine **4e** (0.174 g, 86%) as a brown oil; IR (neat) 2984, 2951, 2864, 2819, 2774, 1714, 1601, 1494, 1453, 1149, 1012, 735, 702 cm^{-1} ; ^1H NMR (CDCl_3) δ 2.20 (s, 6H, NMe_2), 4.31 (s, 1H, CH), 6.21 (d, $J = 2.9$ Hz, 1H, Ar), 6.29 (dd, $J = 2.9, 1.7$ Hz, 1H, Ar), 7.23-7.34 (m, 3H, Ar), 7.36 (d, $J = 1.7$ Hz, 1H, Ar), 7.44-7.46 (m, 2H, Ar); ^{13}C NMR (CDCl_3) δ 43.7 (NMe_2), 69.6 (CH), 107.8, 109.9, 127.4, 128.3, 128.3, 139.9, 141.9, 154.8 (Ar); MS (EI) m/z 201 (M^+); HRMS (EI) Calcd for $\text{C}_{13}\text{H}_{15}\text{NO}$ (M^+) 201.1154, found: 201.1135.

***N,N*-Dimethyl- α -phenyl-2-pyridinemethanamine (**4f**) (FA286)**

To a solution of 2-pyridyllithium prepared from 2-bromopyridine (0.116 mL, 1.6 mmol) and 1.4 M solution of *t*-butyllithium in pentane (2.14 mL, 3.0 mmol) in THF (2.0 mL) at -78°C was added slowly *N,N*-dimethylthioformamide (**1a**) (0.087 mL, 1.0 mmol) via syringe at -78°C . After the addition was complete, the mixture was stirred for 0.5 h at -20°C . To this was added 1.08 M solution of phenylmagnesium bromide in THF (1.9 mL, 2.0 mmol), and this mixture was stirred at room temperature for 2 h. The resulting mixture was poured into a saturated aqueous solution of NH_4Cl , and extracted with Et_2O . The organic layer was dried over MgSO_4 and concentrated in vacuo. The residue was purified by column chromatography (SiO_2 , hexane/ $\text{EtOAc}/\text{Et}_3\text{N} = 1 : 1 : 0.01$) to give the amine **4f** (0.135 g, 64%) as a brown oil; IR (neat) 3060, 2986, 2951, 2865, 2819, 2775, 1588, 1569, 1468, 1433, 1023, 748, 702 cm^{-1} ; ^1H NMR (CDCl_3) δ 2.20 (s, 6H, NMe_2), 4.26 (s, 1H, CH), 7.05-7.07 (m, 1H, Ar), 7.17-7.21 (m, 1H, Ar), 7.26-7.30 (m, 2H, Ar), 7.50-7.61 (m, 4H, Ar), 8.50-8.51 (m, 1H, Ar); ^{13}C NMR (CDCl_3) δ 44.5 (NMe_2), 79.5 (CH), 121.8, 121.9, 127.1, 128.0, 128.4, 136.5, 141.8, 149.1, 162.5 (Ar); MS (EI) m/z 212 (M^+); HRMS (EI) Calcd for $\text{C}_{12}\text{H}_{10}\text{N}$ ($\text{M}^+ - \text{NMe}_2$) 168.0813, found: 168.0785.

(Dimethylaminophenylmethyl)ferrocene (4g**)¹⁾ (FA153)**

To a solution of *N,N*-dimethylthioformamide (**1a**) (0.087 mL, 1.0 mmol) in THF (1.0 mL) was added slowly ferrocenyllithium prepared from ferrocene (0.409 g, 2.2 mmol) and 1.6 M solution of *t*-butyllithium in pentane (1.23 mL, 2.0 mmol) in THF- Et_2O (2.0 mL) at -10°C via cannula at -78°C . After the addition was complete, the mixture was stirred for 0.5 h at room temperature. To this was added 1.0 M solution of phenylmagnesium bromide in THF (2.0 mL, 2.0 mmol) at room

temperature, and this mixture was stirred at reflux for 5 h. The resulting mixture was poured into a saturated aqueous solution of NH_4Cl , and extracted with Et_2O . The residue was purified by column chromatography (SiO_2 , hexane/ EtOAc / Et_3N = 1 : 1 : 0.01) to give the amine **4g** (0.156 g, 49%) as a brown solid; ^1H NMR (CDCl_3) δ 2.01 (s, 6H, NMe_2), 3.64 (s, 5H, Fc), 3.71 (s, 1H, CH), 4.01-4.13 (m, 4H, Fc), 6.14 (d, J = 3.2 Hz, 1H, Ar), 7.21-7.43 (m, 5H, Ar); ^{13}C NMR (CDCl_3) δ 44.5 (NMe_2), 66.4, 67.2, 68.5, 68.7 (Fc), 70.5 (CH), 72.4, 90.2 (Fc), 127.1, 128.0, 128.5, 143.3 (Ar).

1-Dimethylaminopropylferrocene (**4h**)¹⁾ (FA162)

To a solution of *N,N*-dimethylthioformamide (**1a**) (0.087 mL, 1.0 mmol) in THF (1.0 mL) was added slowly ferrocenyllithium prepared from ferrocene (0.409 g, 2.2 mmol) and 1.6 M solution of *t*-butyllithium in pentane (1.23 mL, 2.0 mmol) in THF- Et_2O (2.0 mL) at -10°C via cannula at -78°C . After the addition was complete, the mixture was stirred for 0.5 h at room temperature. To this was added 0.91 M solution of ethylmagnesium bromide in THF (2.2 mL, 2.0 mmol) at room temperature, and this mixture was stirred at reflux for 5 h. The resulting mixture was poured into a saturated aqueous solution of NH_4Cl , and extracted with Et_2O . The residue was purified by column chromatography (SiO_2 , hexane/ EtOAc / Et_3N = 3 : 1 : 0.01) to give the amine **4h** (0.179 g, 66%) as a dark brown solid; ^1H NMR (CDCl_3) δ 1.03 (t, J = 7.6 Hz, 3H, Me), 1.65 (m, 1H, CH_2), 1.93 (s, 7H, CH_3 , CH_2), 3.18 (dd, J = 10.7, 3.4 Hz, 1H, CH), 3.88-4.09 (m, 9H, Ar); ^{13}C NMR (CDCl_3) δ 12.3 (Me), 24.4 (CH_2), 40.5 (NMe_2), 64.8, 66.8, 67.1, 67.3, 68.5 (Ar), 69.3 (CH), 85.6 (Ar).

4-[(4-Methoxyphenyl)phenylmethyl]morpholine (**4i**)²⁾ (FA220)

To a solution of thioformamide **1b** (0.131 g, 1.0 mmol) in THF (2.0 mL) was added slowly 1.04 M solution of phenyllithium in cyclohexane- Et_2O (1.44 mL, 1.5 mmol) at -78°C . After the addition was complete, the mixture was stirred for 0.5 h at room temperature. To this was added 0.5 M solution of 4-methoxyphenylmagnesium bromide in THF (4.0 mL, 2.0 mmol) at room temperature, and this mixture was stirred at this temperature for 2 h. The resulting mixture was poured into a saturated aqueous solution of NH_4Cl , and extracted with Et_2O . The organic layer was purified by acid-base workup, dried over MgSO_4 and concentrated in vacuo to give the amine **4i** (0.266 g, 94%) as a yellow oil; ^1H NMR (CDCl_3) δ 2.34 (brs, 4H, CH_2NCH_2), 3.53-3.70 (m, 4H, CH_2OCH_2), 3.72 (s, 3H, OMe), 4.13 (s, 1H, CH), 6.76-6.80 (m, 2H, Ar), 7.12-7.40 (m, 7H, Ar); ^{13}C NMR (CDCl_3) δ 52.7 (NCH_2), 55.2 (OMe), 67.2 (OCH_2), 76.0 (CH), 113.9, 126.9, 127.8, 128.5, 129.0, 134.4, 142.7, 158.6 (Ar).

4-[1-Phenyl-3-butenyl]morpholine (**4j**) (FA236)

The amine **4j** was synthesized by utilizing the procedure described for **4i**. The reaction of thioformamide **1b** (1.0 mmol) with phenyllithium (1.5 mmol), and allylmagnesium bromide (2.0 mmol) gave the amine **4j** (0.207 g, 95%) as a colorless oil; IR (neat) 3075, 3028, 2958, 2853, 2807, 1640, 1492, 1450, 1271, 119, 1005, 913, 703 cm^{-1} ; 1H NMR ($CDCl_3$) δ 2.37-2.48 (m, 4H, CH_2NCH_2), 2.48-2.69 (m, 2H, CH_2), 3.30 (dd, $J = 8.8$, 4.9 Hz, 1H, NCH), 3.67 (t, $J = 4.6$ Hz, 4H, CH_2OCH_2), 4.89-4.98 (m, 2H, $CH=CH_2$), 5.59 (ddt, $J = 15.1, 10.1, 7.2$ Hz, 1H, $CH=CH_2$), 7.22-7.32 (m, 5H, Ar); ^{13}C NMR ($CDCl_3$) δ 37.1 (CH_2), 50.1 (NCH_2), 67.2 (OCH_2), 70.4 (CH), 116.5 ($CH=CH_2$), 127.2, 128.1, 128.6 (Ar), 135.0 ($CH=CH_2$), 140.2 (Ar); MS (EI) m/z 176 ($M^+ - CH_2CH=CH_2$); HRMS (EI) Calcd for $C_{11}H_{14}NO$ ($M^+ - CH_2CH=CH_2$) 176.075, found: 176.1076.

4-[1-(4-Methoxyphenyl)pentyl]morpholine (**4k**) (FA222)

The amine **4k** was synthesized by utilizing the procedure described for **4i**. The reaction of thioformamide **1b** (1.0 mmol) with *n*-butyllithium (1.5 mmol), and 4-methoxyphenylmagnesium bromide (2.0 mmol) gave the amine **4k** (0.247 g, 94%) as a colorless oil; IR (neat) 3061, 3026, 2991, 2951, 2862, 2816, 2771, 1610, 1510, 1453, 1247, 1179, 1038, 728, 700 cm^{-1} ; 1H NMR ($CDCl_3$) δ 0.80 (t, $J = 7.3$ Hz, 3H, Me), 0.97-1.12 (m, 2H, CH_2), 1.16-1.29 (m, 2H, CH_2), 1.63-1.89 (m, 2H, CH_2), 2.32-2.41 (m, 4H, CH_2NCH_2), 3.12-3.14 (m, 1H, CH), 3.60-3.65 (m, 4H, CH_2OCH_2), 3.78 (s, 3H, OMe), 6.83 (d, $J = 8.5$ Hz, 2H, Ar), 7.18 (d, $J = 8.5$ Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$) δ 14.0 (Me), 22.8, 28.6, 32.2 (CH_2), 51.1 (NCH_2), 55.2 (OMe), 67.3 (OCH_2), 70.1 (CH), 113.4, 127.7, 129.7, 158.7 (Ar); MS (EI) m/z 263 (M^+); HRMS (EI) Calcd for $C_{16}H_{25}NO_2$ (M^+) 263.1885, found: 263.1864.

[4-(4-Fluorophenyl)phenylmethyl]-1-piperazinecarboxylic acid 1,1-dimethylethyl ester (**4l**) (FA083)

To a solution of thioformamide **1c** (0.230 g, 1.0 mmol) in THF (1.0 mL) was added slowly 1.04 M solution of phenyllithium in cyclohexane-Et₂O (1.1 mL, 1.1 mmol) at -78 °C. After the addition was complete, the mixture was stirred for 0.5 h at room temperature. To this was added 1.0 M solution of 4-fluorophenylmagnesium bromide in THF (1.1 mL, 1.1 mmol) at room temperature, and this mixture was stirred at reflux for 5 h.

The resulting mixture was poured into a saturated aqueous solution of NH_4Cl , and extracted with Et_2O . The organic layer was dried over MgSO_4 and concentrated in vacuo. The residue was purified by column chromatography (SiO_2 , hexane/ $\text{EtOAc}/\text{Et}_3\text{N} = 10 : 1 : 0.01$) to give the amine **4l** (0.334 g, 90%) as a white solid; mp 129.9-130.5 °C; IR (KBr) 2980, 2821, 1686, 1507, 1454, 1424, 1363, 1247, 1221, 1166, 1125, 1001, 870, 700, 561 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.36 (s, 9H, OCMe_3), 2.25 (brs, 4H, CH_2NCH_2), 3.33-3.36 (m, 4H, CH_2NCH_2), 4.14 (s, 1H, CH), 6.89 (t, $J = 8.8$ Hz, 2H, Ar), 7.10-7.14 (m, 1H, Ar), 7.19-7.25 (m, 2H, Ar), 7.28-7.32 (m, 4H, Ar); ^{13}C NMR (CDCl_3) δ 28.4 (CMe_3), 51.7 (NCH_2), 75.3 (CH), 79.5 (OCMe_3), 115.3, 115.5, 127.2, 127.8, 128.7 (Ar), 129.3 (d, $J = 31.2$ Hz, CF), 138.2, 142.2 (Ar), 154.8 (C=O); MS (EI) m/z 370 (M^+); HRMS (EI) Calcd for $\text{C}_{22}\text{H}_{27}\text{FN}_2\text{O}_2$ (M^+): 370.2057, found: 370.2030.

[4-(4-Chlorophenyl)phenylmethyl]-1-piperazinecarboxylic acid 1,1-dimethylethyl ester (**4m**)

(FA187)

The amine **4m** was synthesized by utilizing the procedure described for **4l** from thioformamide **1c** (1.0 mmol), phenyllithium (1.1 mmol), and 4-chlorophenylmagnesium chloride (1.1 mmol) prepared from 4-bromochlorobenzene and *i*-PrMgCl·LiCl. The crude product was purified by column chromatography (SiO_2 , hexane/ $\text{EtOAc}/\text{Et}_3\text{N} = 10 : 1 : 0.01$) to give the amine **4m** (0.329 g, 85%) as a white solid; mp 140.4-140.9 °C IR; (KBr) 2977, 2918, 2888, 2856, 2818, 1685, 1491, 1453, 1424, 1246,

1164, 1124, 1000, 871, 756 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.34 (s, 9H, OCMe_3), 2.22 (brs, 4H, CH_2NCH_2), 3.32-3.34 (m, 4H, CH_2NCH_2) 4.11 (s, 1H, CH), 7.07-7.27 (m, 9H, Ar); ^{13}C NMR (CDCl_3) δ 28.3 (OCMe_3), 51.5 (NCH_2), 75.2 (CH), 79.4 (OCMe_3), 127.2, 127.7, 128.6, 128.6, 129.1, 132.6, 141.0, 141.7 (Ar), 154.7 (C=O); MS (EI) m/z 386 (M^+); HRMS (EI) Calcd for $\text{C}_{22}\text{H}_{27}\text{ClN}_2\text{O}_2$ (M^+) 386.1761, found: 386.1741.

[4-(4-Methoxyphenyl)phenylmethyl]-1-piperazinecarboxylic acid 1,1-dimethylethyl ester (**4n**)

(FA079)

The amine **4n** was synthesized by utilizing the procedure described for **4l** from thioformamide **1c** (1.0 mmol), phenyllithium (1.1 mmol), and 4-methoxyphenylmagnesium bromide (1.1 mmol). The crude product was purified by column chromatography (SiO_2 , hexane/ $\text{EtOAc}/\text{Et}_3\text{N} = 10 : 1 : 0.01$) to give the amine **4n** (0.326 g, 85%) as a white solid; mp 114.9-115.6 °C; IR (KBr) 2968, 2862, 2813, 1693, 1509, 1410, 1366, 1244, 1169, 1119, 996, 867, 811, 786, 742, 704 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.36 (s, 9H, OCMe_3), 2.25 (brs, 4H, CH_2NCH_2), 3.32-3.35 (m, 4H, CH_2NCH_2),

3.68 (s, 3H, OMe), 4.11 (s, 1H, CH), 6.74 (d, $J = 8.1$ Hz, 2H, Ar), 7.08-7.12 (m, 1H, Ar), 7.18-7.24 (m, 4H, Ar), 7.32 (d, $J = 8.1$ Hz, 2H, Ar); ^{13}C NMR (CDCl_3) δ 28.4 (CMe_3), 51.7 (NCH_2), 55.2 (OMe), 75.4 (CH), 79.5 (OCMe_3), 113.9, 126.9, 127.8, 128.5, 129.0, 134.5, 142.8 (Ar), 154.9 (C=O), 158.6 (Ar); MS (EI) m/z 382 (M^+); HRMS (EI) Calcd for $\text{C}_{23}\text{H}_{30}\text{N}_2\text{O}_3$ (M^+): 382.2257, found: 382.2253.

[4-(2-Thienyl)phenylmethyl]-1-piperazinecarboxylic acid 1,1-dimethylethyl ester (4o) (FA141)

The amine **4o** was synthesized by utilizing the procedure described for **4l** from thioformamide **1c** (1.0 mmol), 2-thienyllithium (1.1 mmol), and phenylmagnesium bromide (1.1 mmol). The crude product was purified by column chromatography (SiO_2 , hexane/EtOAc/ Et_3N = 10 : 1 : 0.01) to give the amine **4o** (0.298 g, 83%) as a yellow solid; mp 122.3-130.0 °C; IR (KBr) 3085, 2966, 2925, 2855, 2816, 1691, 1453, 1414, 1364, 1288, 1247, 1163, 1121, 996, 704 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.42 (s, 9H, OCMe_3), 2.38 (m, 4H, CH_2NCH_2), 3.41-3.43 (m, 4H, CH_2NCH_2), 4.63 (s, 1H, CH), 6.88-6.90 (m, 2H, Ar), 7.20-7.43 (m, 6H, Ar); ^{13}C NMR (CDCl_3) δ 28.4 (OCMe_3), 51.3 (NCH_2), 70.9 (CH), 79.5 (OCMe_3), 125.2, 125.4, 126.3, 127.5, 128.3, 128.5, 140.9, 146.6 (Ar), 154.8 (C=O); MS (EI) m/z 358 (M^+); HRMS (EI) Calcd for $\text{C}_{20}\text{H}_{26}\text{N}_2\text{O}_2\text{S}$ (M^+) 358.1715, found: 358.1714.

[4-(2-Thienyl)propyl]-1-piperazinecarboxylic acid 1,1-dimethylethyl ester (4p) (FA142)

The amine **4p** was synthesized by utilizing the procedure described for **4l** from thioformamide **1c** (1.0 mmol), 2-thienyllithium (1.1 mmol), and ethylmagnesium bromide (1.1 mmol). The crude product was purified by column chromatography (SiO_2 , hexane/EtOAc/ Et_3N = 10 : 1 : 0.01) to give the amine **4p** (0.260 g, 84%) as an orange oil; IR (neat) 2972, 2931, 2873, 2814, 1698, 1455, 1421, 1365, 1281, 1247, 1172, 1120, 1000, 867, 813, 698 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.81 (t, $J = 7.3$ Hz, 3H, Me), 1.35 (s, 9H, OCMe_3), 1.64-1.91 (m, 2H, CH_2), 2.32-2.36 (m, 4H, CH_2NCH_2), 3.32-3.34 (m, 4H, CH_2NCH_2), 3.57 (dd, $J = 8.3, 5.9$ Hz, 1H, CH), 6.77 (d, $J = 3.4$ Hz, 1H, Ar), 6.90 (dd, $J = 5.1, 3.4$ Hz, 1H, Ar), 7.15 (d, $J = 5.1$ Hz, 1H, Ar); ^{13}C NMR (CDCl_3) δ 11.4 (CH_3), 26.9 (CH_2), 28.4 (CMe_3), 49.3 (NCH_2), 66.3 (CH), 79.5 (OCMe_3), 124.2, 125.8, 126.2, 143.1 (Ar), 154.7 (C=O); MS (EI) m/z 310 (M^+); HRMS (EI) Calcd for $\text{C}_{16}\text{H}_{26}\text{N}_2\text{S}$ (M^+): 310.1715, Found: 310.1723.

1-(1-Phenylpropyl)-4-(phenylmethyl)piperazine (4q) (FA230)

To a solution of thioformamide **1d** (0.220 g, 1.0 mmol) in THF (2.0 mL) was added slowly 1.04 M

solution of phenyllithium in cyclohexane-Et₂O (1.44 mL, 1.5 mmol) at -78 °C. After the addition was complete, the mixture was stirred for 0.5 h at room temperature. To this was added 1.0 M solution of ethylmagnesium bromide in THF (2.0 mL, 2.0 mmol) at room temperature, and this mixture was stirred at this temperature for 2 h. The resulting mixture was poured into a saturated aqueous solution of NH₄Cl, and extracted with Et₂O. The organic layer was dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography (SiO₂, hexane/EtOAc/Et₃N = 3 : 1 : 0.01) to give the amine **4q** (0.227 g, 77%) as a yellow oil; A yellow oil (0.227 g, 77%); IR (neat) 3390, 3027, 2961, 2932, 2857, 2808, 2766, 1493, 1453, 1473, 1353, 1313, 1290, 1150, 1006, 842, 762, 736, 700 cm⁻¹; ¹H NMR (CDCl₃) δ 0.64 (t, *J* = 7.3 Hz, 3H, Me), 1.60-1.90 (m, 2H, CH₂), 2.37 (brs, 8H, CH₂NCH₂), 3.09 (dd, *J* = 9.3, 4.9 Hz, 1H, CH), 3.4 (s, 2H, CH₂), 7.12-7.24 (m, 10H, Ar); ¹³C NMR (CDCl₃) δ 10.8 (CH₃), 25.6 (CH₂), 50.4, 53.5 (NCH₂), 63.1 (CH₂), 71.8 (CH), 126.9, 127.0, 128.0, 128.2, 128.8, 129.3, 138.1, 140.5 (Ar); MS (EI) *m/z* 294 (M⁺); HRMS (EI) Calcd for C₂₀H₂₆N₂ (M⁺): 294.2096, found: 294.2107.

1-(1-Phenyl-3-butenyl)-4-(phenylmethyl)piperazine (**4r**) (FA237)

The amine **4r** was synthesized by utilizing the procedure described for **4q** from thioformamide **1d** (1.0 mmol), phenyllithium (1.5 mmol), and allylmagnesium bromide (2.0 mmol). The crude product was purified by column chromatography (SiO₂, hexane/EtOAc/Et₃N = 5 : 1 : 0.01) to give the amine **4r** (0.263 g, 86%) as a pale yellow oil; IR (neat) 3387, 3062, 3027, 2932, 2808, 2766, 1639, 1601, 1493, 1453, 1350, 1289, 1139, 1007, 911, 740, 700 cm⁻¹; ¹H NMR (CDCl₃) δ 2.37 (brs, 8H, CH₂NCH₂), 2.41-2.61 (m, 2H, CH₂), 3.26-3.30 (dd, *J* = 8.8, 5.4 Hz, 1H, CH), 3.39 (s, 2H, CH₂), 4.80-4.89 (m, 2H, CH=CH₂), 5.52 (ddt, *J* = 14.7, 10.0, 8.8 Hz, 1H, CH=CH₂), 7.12-7.23 (m, 10H, Ar); ¹³C NMR (CDCl₃) δ 37.3 (CH₂), 50.2, 53.4 (NCH₂), 63.1 (CH₂), 69.8 (CH), 116.3 (CH=CH₂), 126.9, 127.0, 128.0, 128.1, 128.7, 129.3 (Ar), 135.7 (CH=CH₂), 138.1, 140.0 (Ar); MS (EI) *m/z* 306 (M⁺); HRMS (EI) Calcd for C₂₁H₂₆N₂ (M⁺): 306.2096, found: 306.2083.

1-[1-(2-Furyl)-2-propenyl]-4-(phenylmethyl)piperazine (**4s**) (FA235)

To a solution of thioformamide **1d** (0.220 g, 1.0 mmol) in THF (2.0 mL) was added slowly 2-furyllithium prepared from furan (0.116 mL, 1.6 mmol) and 1.6 M solution of *n*-butyllithium in hexane (0.94 mL, 1.5 mmol) in THF (2.0 mL) at -15 °C via cannula at -78°C. After the addition was complete, the mixture was stirred for 0.5 h at room temperature. To

this was added 1.0 M solution of vinylmagnesium bromide in THF (2.0 mL, 2.0 mmol) at room temperature, and this mixture was stirred at room temperature for 2 h. The resulting mixture was poured into a saturated aqueous solution of NH_4Cl , and extracted with Et_2O . The organic layer was dried over MgSO_4 and concentrated in vacuo. The residue was purified by column chromatography (SiO_2 , hexane/ EtOAc / Et_3N = 3 : 1 : 0.01) to give the amine **4s** (0.195 g, 69%) as a brown oil; IR (neat) 2934, 2810, 2767, 1496, 1455, 1295, 1149, 1074, 1009, 926, 798, 736, 699 cm^{-1} ; ^1H NMR (CDCl_3) δ 2.36-2.41 (m, 8H, CH_2NCH_2), 3.42 (s, 2H, CH_2), 3.87 (d, J = 8.3 Hz, 1H, CH), 5.13 (d, J = 10.3 Hz, 1H, $\text{CH}=\text{CH}_2$), 5.15 (d, J = 17.1 Hz, 1H, $\text{CH}=\text{CH}_2$), 5.96 (ddd, J = 17.1, 10.3, 8.3 Hz, 1H, $\text{CH}=\text{CH}_2$), 6.09 (d, J = 3.4 Hz, 1H, Ar), 6.22 (dd, J = 3.4, 2.0 Hz, 1H, Ar), 7.12-7.22 (m, 5H, Ar), 7.28-7.29 (m, 1H, Ar); ^{13}C NMR (CDCl_3) δ 50.4, 53.0 (NCH_2), 62.9 (CH_2), 66.7 (CH), 107.7, 109.9 (Ar), 118.0 ($\text{CH}=\text{CH}_2$), 126.9, 128.1, 129.1 (Ar), 135.7 ($\text{CH}=\text{CH}_2$), 137.9, 141.8, 153.6 (Ar); MS (EI) m/z 282 (M^+); HRMS (EI) Calcd for $\text{C}_{18}\text{H}_{22}\text{N}_2\text{O}$ (M^+) 282.1732, Found: 282.1739.

1-[1-(2-Furyl)-cyclohexylmethyl]-4-(phenylmethyl)piperazine (**4t**) (FA240)

The amine **4t** was synthesized by utilizing the procedure described for **4s** from thioformamide **1d** (1.0 mmol), 2-furyllithium (1.1 mmol), and cyclohexylmagnesium bromide (2.0 mmol). The crude product was purified by column chromatography (SiO_2 , hexane/ EtOAc / Et_3N = 10 : 1 : 0.01) to give the amine **4t** (0.234 g, 69%) as a colorless oil; IR (neat) 2929, 2850, 2811, 2765, 1496, 1450, 1148, 1009, 910, 733, 699 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.71-0.87 (m, 2H, CH_2), 1.04-1.31 (m, 4H, CH_2), 1.54-1.99 (m, 5H, CH_2 , CH), 2.23-2.41 (m, 8H, CH_2NCH_2), 3.10 (d, J = 10.3 Hz, 1H, CH), 3.38 (s, 2H, CH_2), 5.95 (d, J = 2.9 Hz, 1H, Ar), 6.20 (dd, J = 3.4, 2.0 Hz, 1H, Ar), 7.12-7.20 (m, 5H, Ar), 7.24 (m, 1H, Ar); ^{13}C NMR (CDCl_3) δ 26.2, 26.8, 30.6, 30.7, 37.3 (*c*-hex), 49.3, 53.5 (NCH_2), 63.2 (CH_2), 67.6 (CH), 108.2, 109.5, 126.9, 128.1, 129.2, 138.1, 141.2, 153.5 (Ar); MS (EI) m/z 338 (M^+); HRMS (EI) Calcd for $\text{C}_{22}\text{H}_{30}\text{N}_2\text{O}$ (M^+); 338.2358, Found: 338.2343.

Benzenecarbothioic acid (**9**) (FA275)

To a solution of *N,N*-dimethylthioformamide (**1a**) (0.087 mL, 1.0 mmol) in THF (1.0 mL) was added slowly 1.0 M solution of phenyllithium in cyclohexane- Et_2O (1.0 mL, 1.0 mmol) at -78°C . After the addition was complete, the mixture was stirred for 0.5 h at room temperature. To this was added 0.93 M solution of phenylmagnesium bromide in THF (1.08 mL, 1.0 mmol) at room temperature, and this mixture was stirred for 2 h at reflux. Benzoyl chloride (0.116 mL, 1.0 mmol) was added and the reaction mixture was stirred again for 2 h at room temperature. The resulting mixture was poured into a saturated aqueous

solution of NH_4Cl , and were separated to organic layer **I** and the aqueous layer. The aqueous layer was acidified with aq. HCl (1N, 10mL), and extracted with Et_2O to give organic layer **II**. It was dried over MgSO_4 and concentrated in vacuo. Thiobenzoic acid **9** was obtained as a gray yellow oil (0.127 g, 92%); ^1H NMR (CDCl_3) δ 4.72 (brs, 1H, SH), 7.45-7.49 (m, 2H, Ar), 7.59-7.63 (m, 1H, Ar), 7.89-7.92 (m, 2H, Ar); ^{13}C NMR (CDCl_3) δ 127.9, 128.7, 133.9, 136.6 (Ar), 190.2 (C=O).

***N,N*-Dimethyl- α -phenyl-benzenemethaneamine (**4u**) (FA275)**

The organic layer **I** was purified by acid-base workup, dried over MgSO_4 and concentrated in vacuo to give the amine **4u** (0.178 g, 84%) as a pale yellow solid; mp 69.8-70.3 °C; IR (KBr) 3025, 2982, 2947, 2863, 2816, 2763, 1491, 1452, 1433, 1181, 1152, 1019, 764, 746, 708 cm^{-1} ; ^1H NMR (CDCl_3) δ 6.10 (s, 6H, NMe_2), 4.05 (s, 1H, CH), 7.14-7.18 (m, 2H, Ar), 7.24-7.28 (m, 4H, Ar), 7.41-7.44 (m, 4H, Ar); ^{13}C NMR (CDCl_3) δ 44.7 (NMe_2), 78.0 (CH), 126.8, 127.7, 128.4, 143.4 (Ar); MS (EI) m/z 211 (M^+); HRMS (EI) Calcd for $\text{C}_{15}\text{H}_{17}\text{N}$ (M^+); 211.1361, Found: 211.1334.

Benzo[*c*]thiophene-1,3-dione (10**) (FA279)**

To a solution of *N,N*-dimethylthioformamide (**1a**) (0.087 mL, 1.0 mmol) in THF (1.0 mL) was added slowly 1.0 M solution of phenyllithium in cyclohexane- Et_2O (1.0 mL, 1.0 mmol) at -78 °C. After the addition was complete, the mixture was stirred for 0.5 h at room temperature. To this was added 0.93 M solution of phenylmagnesium bromide in THF (1.08 mL, 1.0 mmol) at room temperature, and this mixture was stirred for 2 h at reflux. Phthaloyl dichloride (0.144 mL, 1.0 mmol) was added and the reaction mixture again stirred for 2h at room temperature. The resulting mixture was poured into a saturated aqueous solution of NH_4Cl , and extracted with Et_2O . The organic layer was dried over MgSO_4 and concentrated in vacuo. The residue was purified by column chromatography (SiO_2 , hexane/ CH_2Cl_2 = 3 : 1) to give the anhydride **10** (0.107 g, 65%) as a white solid; ^1H NMR (CDCl_3) δ 7.77-7.81 (m, 2H, Ar), 7.93-7.97 (m, 2H, Ar); ^{13}C NMR (CDCl_3) δ 123.7, 135.0, 138.7 (Ar), 189.8 (C=O).

The reaction mixture of *N,N*-dimethylthioformamide (**1a**) (1 mmol) and phenyllithium (**2a**) (1 mmol) was concentrated in vacuo to give **5a** (Scheme 3). The copies of ^1H and ^{13}C NMR spectra of **5a** measured in 1,4-dioxane- d_8 are shown in the next page. Because of the use of cyclohexane-Et₂O solution of **2a**, the signals due to cyclohexane are also observed in each spectrum.

Scheme 3. Reaction of *N,N*-Dimethylthioformamide (**1a**) with Phenyllithium (**2a**) Leading to **5a**

- 1) Tappe, K.; Knochel, P. *Tetrahedron: Asymmetry* **2004**, 15, 91.
- 2) Kai, S.; Showalter, H. D. H. *J. Org. Chem.* **1999**, 64, 4972.