Supplementary Material (ESI) for Chemical Communications

Ascorbate Mediated Copper Catalyzed Reductive Cross-coupling of Disulfides with Aryl Iodides

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Supporting Information

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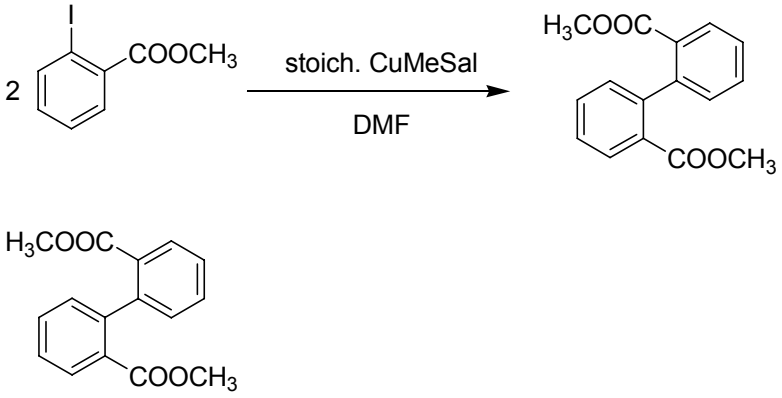
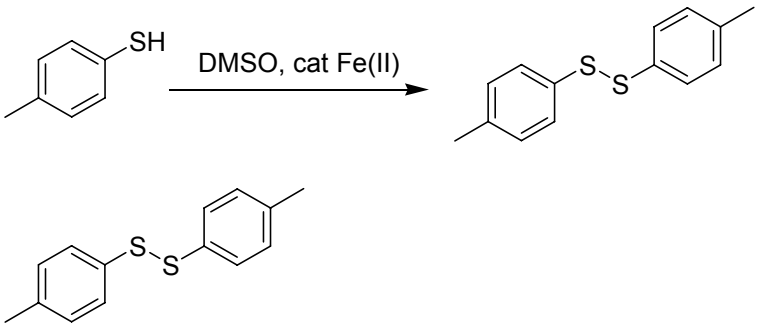
General Experimetal

^{1}H NMR and ^{13}C NMR spectra were recorded at 400MHz NMR spectrometer with solvent residual peak ($CDCl_3$: ^{1}H = 7.24 ppm, ^{13}C = 77.23 ppm; DMSO-d_6: ^{1}H = 2.50 ppm, ^{13}C = 39.51 ppm) as the internal reference unless otherwise noted. Data are reported in the following order: chemical shifts are given (δ); multiplicities are indicated br (broadened), s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), app (apparent); coupling constants, *J*, are reported in Hz. Reaction conversion was monitored with UPLC-MS and GC-MS. IR spectra were measured with FT-IR spectrometer (ATR technique); peaks are reported in cm^{-1}. High resolution mass spectra were obtained on a LTQ Orbitrap XL (ESI). Melting points were determined on a Boetius block and are not corrected. Column chromatography was carried out using silica gel 70-230 mesh, 60Å. Preparative TLC was performed on precoated silica gel plates (2 mm thick, 60F254) Analytical TLC was performed on precoated silica gel plates (0.25 mm thick, 60F254) and observed under UV light. Demineralized water used for reactions was deoxygenated under argon atmosphere by ultrasonic bath. Chemicals purchased from commercial sources were used as received unless otherwise noted. Copper (I) 3-methylsalicylate (CuMeSal) was prepared according to the previously reported procedure.[1]

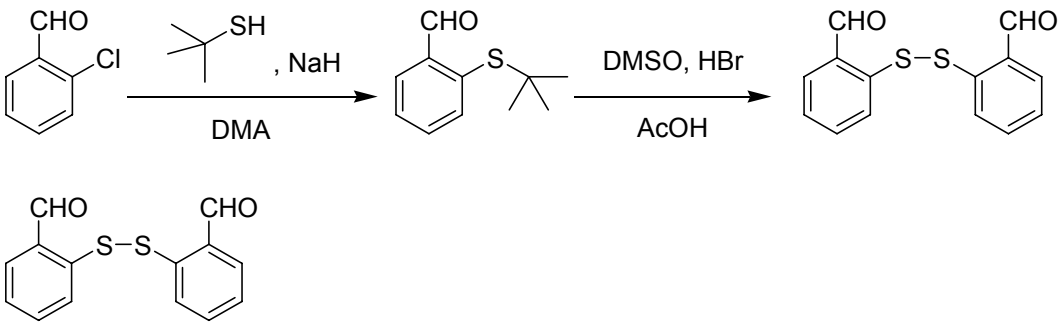


Dimethyl biphenyl-2,2'-dicarboxylate (3). Aryl iodide (59 mg, 0.225 mmol) and CuMeSal (107 mg, 0.5 mmol) were weighed into Schlenk flask and three times purged by vacuum-argon cycle. Then deoxygenated DMF (2 mL) was added. Reaction mixture was then stirred under argon atmosphere at 50 °C for 5 h. Water (20 mL) was added into reaction mixture and the product was three times extracted with diethyl ether (20 mL). Combined ether layers were washed with saturated solution of potassium carbonate (30 mL) and water (30 mL). Ether solution was dried with anhydrous magnesium sulfate, filtered through cottonwool and solvent was distilled off by rotary evaporator. Product obtained after extraction was then purified by preparative TLC (silica gel; dichloromethane:hexane:methanol = 1:1:0.01). The product was obtained as white crystals in 90% yield (27 mg). M.p. 74-75 °C, (lit.[2] 74 °C). ^{1}H NMR (400 MHz, CDCl3) δ 7.99 (dd, *J* = 1.2, 8.0, 2H), 7.54 – 7.49 (m, 2H), 7.44 – 7.38 (m, 2H), 7.19 (dd, *J* = 1.0, 7.6, 2H), 3.60 (s, 6H).



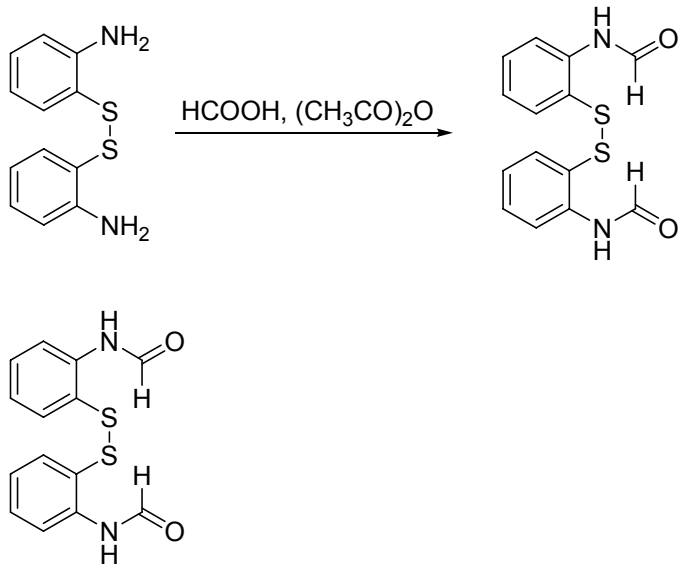
1,1'-Disulfanediylbis(4-methylbenzene) (1a). 4-Methylbenzenethiol (20 g, 0.161 mol), iron (II) acetate (1 mg , 6 μmol) was dissolved in dimethyl sulfoxide (11.4 mL, 0.161

mol) and stirred at 50 °C overnight. Reaction mixture was poured in water and white solid was collected on frit. Crude product was dried *in vacuo* and recrystallized from ethanol. Product was obtained as pale yellow crystals in 79% yield (15.72 g). M.p. 42 – 42.5 °C, (lit.[3] 45.5 °C). ^{1}H NMR (400 MHz, CDCl3) δ 7.39 – 7.33 (m, 4H), 7.08 (d, J = 8.0, 4H), 2.30 (s, 6H).



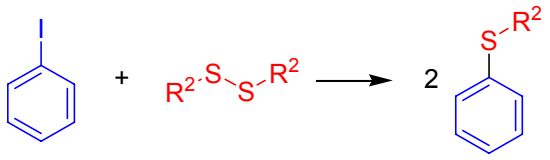
2,2'-disulfanediyldibenzaldehyde (1g). Sodium hydride (5.05 g, 0.12 mol, 57-63% oil disp.) was dissolved in DMA (100 mL) and cooled to 0 °C. *tert*-Butylthiol (14.7 mL, 0.13 mol) was added into the mixture dropwise. Then 2-Chlorobenzaldehyde (11.26 mL, 0.1 mol) was added by syringe dropwise into the stirred suspension and changed colour to yellow-brown. After 1 h the reaction mixture was poured into water (400 mL) and brine (50 mL) was added. Product was extracted with ethyl acetate (3 times 40 mL). Combined organic layers were washed with brine, dried over anhydrous magnesium sulfate and solvent distilled off by rotary evaporator. Product was obtained as pale oil in 99% yield (19.20 g). The product was used without further purification and characterization in next step. 2-(*tert*-Butylsulfanyl)benzaldehyde (18.00 g, 0.0927 mol) was dissolved in acetic acid (50 mL) and hydrobromic acid (50 mL) with DMSO (7.24 g, 0.0927 mol) was added. The raction mixture was then vigorously stirred at room temperature. After 4 h the mixture was poured into water and precipitate was collected on frit. The crude product was dried on air, washed with hexane and diethyl ether and dried *in vacuo*. The product was obtained as white crystals in 62% yield

(7.84 g). M. p. 144 – 145 °C, (lit.[4] 145 °C). ^{1}H NMR (400 MHz, CDCl3) δ 10.20 (s, 2H), 7.90 – 7.81 (m, 2H), 7.81 – 7.71 (m, 2H), 7.54 – 7.42 (m, 2H), 7.42 – 7.32 (m, 2H).



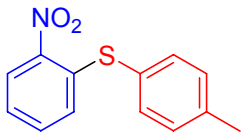
***N,N´*-(2,2´-Disulfanediylbis(2,1-phenylene))diformamide** (1i). Acetanhydride (7.5 mL) was placed into the flask and was cooled to 0 °C. Formic acid (85%, 2.8 mL) was added dropwise and cooling bath was removed. The reaction mixture was heated at 55 °C for 2 h. Then reaction mixture was allowed to cool to room temperature and THF (5 mL) was added. The reaction mixture was cooled to -20 °C and 2,2´-disulfanediyl-dianiline (4.9611 g; 0.02 mol) dissolved in THF (15 mL) was added dropwise. The product started to solidify after 5 min. After 20 min, diethyl ether was added into the reaction mixture and the solid was triturated. The solid was collected on frit, washed with diethyl ether and dried *in vacuo*. The product was obtained as white crystals in 94 % yield (5.7389 g). M.p. 163 – 166 °C, (lit.[5] 161 °C) . ^{1}H NMR (400 MHz, DMSO) δ 9.93 (s, 2H), 8.34 – 8.29 (m, 2H), 7.88 – 7.78 (m, 2H), 7.46 – 7.40 (m, 2H), 7.39 – 7.31 (m, 2H), 7.19 – 7.09 (m, 2H).

General procedure for thioether preparation.



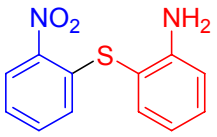
Aryl iodide (0.5 mmol), disulfide (0.3 mmol), CuMeSal (25 μmol), sodium ascorbate (1.25 mmol) and Brij 700 (50 μmol) was weighed into Schlenk flask and three times purged by vacuum-argon cycle. Then deoxygenated demineralised water (2 mL) was added. Reaction mixture was then stirred under argon atmosphere at 70 °C. Water (20 mL) with saturated solution of potassium carbonate (2 mL) was added into reaction mixture after depletion of aryl iodide. The product was extracted with diethyl ether (20 mL). Water portion was then three times extracted with diethyl ether (20 mL). Precipitate from the first extraction was removed, and three times dissolved with appropriate amount of water, extracted with diethyl ether (20 mL) and retroactively coagulated by potassium carbonate saturated solution. Combined ether layers were dried with anhydrous magnesium sulfate, filtered through cottonwool and solvent was distilled off by rotary evaporator.

Characterization of prepared thioethers

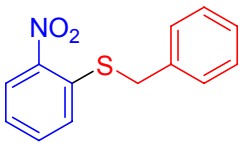


1-[(4-Methylphenyl)sulfanyl]-2-nitrobenzene (3a). Product obtained after extraction was then purified by column chromatography (silica gel; hexane:diethyl ether:acetone = 7:1:2). The product was obtained as yellow crystals in 83% yield (101 mg, in 2 days). M.p. 87

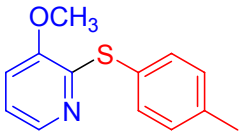
– 88.5 °C, (lit.[6] 88 – 89 °C) . ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (dd, J = 1.4, 8.3, 1H), 7.49 – 7.41 (m, 2H), 7.34 – 7.25 (m, 3H), 7.17 (ddd, J = 1.3, 7.2, 8.4, 1H), 6.84 (dd, J = 1.2, 8.2, 1H), 2.41 (s, 3H).



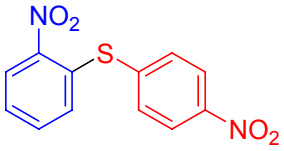
2-[(2-Nitrophenyl)sulfanyl]aniline (3b). Product obtained after extraction was then purified by column chromatography (silica gel; dichloromethane:hexane:methanol = 1:1:0,01). The product was obtained as ochre crystals in 71% yield (88 mg, in 6 days). M.p. 83 – 84°C, (lit.[7] 86 °C) . ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (dd, J = 1.4, 8.3, 1H), 7.42 (dd, J = 1.4, 7.7, 1H), 7.38 – 7.28 (m, 2H), 7.25 – 7.18 (m, 1H), 6.87 – 6.76 (m, 3H), 4.28 (s, 2H).



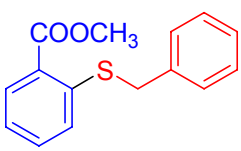
1-(Benzylsulfanyl)-2-nitrobenzene (3c). Product obtained after extraction was then purified by column chromatography (silica gel; hexane:diethyl ether:acetone = 7:1:2). The product was obtained as yellow crystals in 64% yield (78 mg, in 7 days). M.p. 81 – 81.5 °C, (lit.[8] 82 – 83 °C) . ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (dd, J = 1.4, 8.3, 1H), 7.53 – 7.47 (m, 1H), 7.46 – 7.38 (m, 3H), 7.35 – 7.25 (m, 3H), 7.24 – 7.20 (m, 1H), 4.18 (s, 2H).



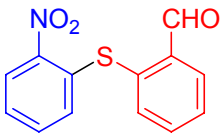
3-Methoxy-2-[(4-methylphenyl)sulfanyl]pyridine (3d). Product obtained after extraction was then purified by column chromatography (silica gel; hexane:diethyl ether:acetone = 7:1:2). The product was obtained as yellowish oil which solidified after drying *in vacuo* in 70% yield (82 mg, in 3 days). M.p. 69 – 70°C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (dd, J = 1.5, 4.5, 1H), 7.48 – 7.42 (m, 2H), 7.23 – 7.17 (m, 2H), 7.02 – 6.94 (m, 2H), 3.90 (s, 3H), 2.36 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 152.07, 149.28, 141.56, 138.74, 135.35, 130.02, 126.50, 120.46, 115.91, 55.89, 21.50. IR (ATR) 3057, 3018, 2967, 2933, 2835, 1575, 1558, 1455, 1406, 1299, 1285, 1265, 1202, 1086, 1060, 1005, 815, 785, 733, 686, 572, 534, 484, 399 cm^{-1}. HRMS (ESI) *m/z* calcd for $C_{13}H_{13}NNaOS$ $(M + Na)^+$ 254.0616, found 254.0610.



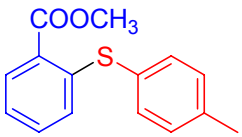
1-Nitro-2-[(4-nitrophenyl)sulfanyl]benzene (3e). Product obtained after extraction was then purified by column chromatography (silica gel; hexane:ethyl acetate = 4:1). The product was obtained as yellow crystals in 54% yield (75 mg, in 2 days). M.p. 160 – 163 °C, (lit.[9] 163 – 164 °C) . ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 – 8.21 (m, 2H), 8.18 (dd, J = 1.5, 8.2, 1H), 7.67 – 7.62 (m, 2H), 7.44 (ddd, J = 1.5, 7.4, 8.1, 1H), 7.35 (ddd, J = 1.3, 7.3, 8.5, 1H), 7.05 (dd, J = 1.2, 8.1, 1H).



Methyl 2-(benzylsulfanyl)benzoate (3f). Product obtained after extraction was then purified by column chromatography (silica gel; hexane:diethyl ether:acetone = 7:1:2). The product was obtained as white crystals in 39% yield (50 mg, in 7 days). M.p. 62 – 63 °C, (lit.[10] 61 – 62 °C) . ^{1}H NMR (400 MHz, CDCl3) δ 7.99 (dd, *J* = 1.3, 7.8, 1H), 7.43 (dd, *J* = 4.4, 11.5, 3H), 7.39 – 7.29 (m, 4H), 7.19 (ddd, *J* = 1.3, 7.2, 7.9, 1H), 4.19 (s, 2H), 3.93 (s, 3H).

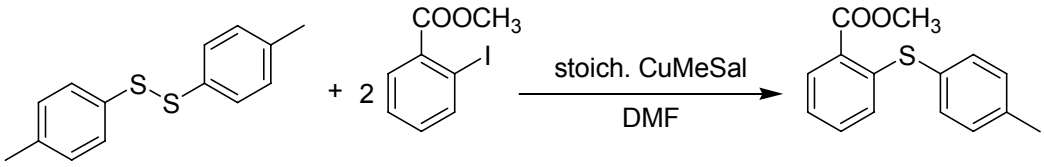


2-[(2-Nitrophenyl)sulfanyl]benzaldehyde (3g). Product obtained after extraction was then purified by column chromatography (silica gel; hexane:diethyl ether:acetone = 7:1:2). The product was obtained as beige crystals in 65% yield (83 mg, in 4 days.). M.p. 96.5 – 97.5°C, ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 10.42 (d, *J* = 0.6, 1H), 8.23 (dd, *J* = 1.5, 8.2, 1H), 8.09 – 8.04 (m, 1H), 7.71 – 7.66 (m, 1H), 7.66 – 7.60 (m, 2H), 7.38 – 7.33 (m, 1H), 7.29 – 7.24 (m, 1H), 6.75 (dd, *J* = 1.3, 8.1, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 191.47, 138.01, 137.66, 137.63, 135.44, 135.08, 134.09, 130.96, 130.03, 129.21, 126.27, 126.16. IR (ATR) 3064, 2921, 2852, 1678, 1588, 1566, 1504, 1451, 1334, 1302, 1260, 1194, 1104, 1040, 854, 822, 766, 732, 681, 630, 430 cm^{-1}. HRMS (ESI) *m/z* calcd for $C_{13}H_9NNaO_3S$ $(M + Na)^+$ 282.0201, found 282.0195.

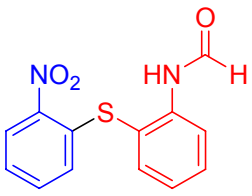


Methyl 2-[(4-methylphenyl)sulfanyl]benzoate (3h). Product obtained after extraction was then purified by column chromatography (silica gel; hexane:diethyl

ether:acetone = 7:1:2). The product was obtained as yellowish crystals in 66% yield (85 mg, in 3 days). M.p. 75 – 76 °C, (lit.[11] 76 – 77 °C) . ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 – 7.93 (m, 1H), 7.46 – 7.41 (m, 2H), 7.24 – 7.17 (m, 3H), 7.11 – 7.05 (m, 1H), 6.77 (dd, J = 0.9, 8.2, 1H), 3.94 (s, 3H), 2.39 (s, 3H).



Methyl 2-[(4-methylphenyl)sulfanyl]benzoate (3h). **Cu stoichiometric preparation**. 2-iodomethylbenzoate (0.130 g, 0.5 mmol,), bis(4-tolyl)disulfide (0.075 g, 0.3 mmol), and CuMeSal (0.265 g, 1.25 mmol) were placed into Schlenk flask and the flask was three times purged with argon. Then deoxygenated dry DMF (4 mL) was added. The reaction mixture was stirred under argon atmosphere at 50 °C. The conversion was followed by GC/MS chromatography. Water (30 mL) with saturated solution of potassium carbonate (2 mL) was added into the reaction mixture after 8 hours when all the iodide was consumed and the mixture was extracted by Et_2O (3x20 mL). The ether extract was dryed by $MgSO_4$, the volatiles were evaporated and the solid was purified by column chromatography giving the product as a yellowish crystaline solid (0.111g, 86% yield).



***N*-{2-[(2-Nitrophenyl)sulfanyl]phenyl}formamide** (3i).. Product obtained after extraction was then purified by column chromatography (silica gel; dichloromethane). The product was obtained as yellow crystals in 89% yield (122 mg, in 24 hrs.). M.p. 142 – 143 °C, (lit.[12] 143 °C) . ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.79 (s, 1H), 8.38 (d, J = 8.1, 1H), 8.29 (dd,

J = 0.8, 8.2, 1H), 8.18 (d, *J* = 1.4, 1H), 7.69 (dd, *J* = 1.4, 7.6, 1H), 7.65 – 7.51 (m, 2H), 7.44 – 7.34 (m, 1H), 7.34 – 7.24 (m, 1H), 6.63 (dd, *J* = 0.9, 8.2, 1H).

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