A Copper-Catalyzed Synthesis of Symmetrical Diarylsulfanes

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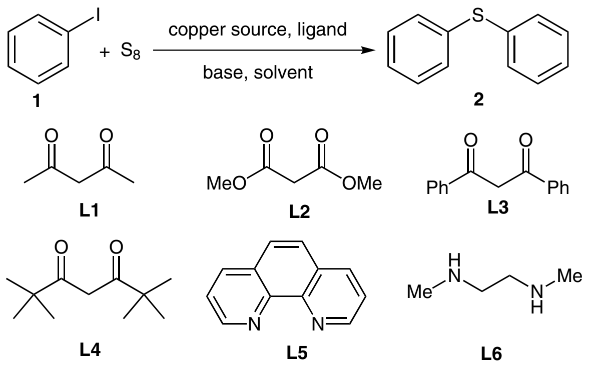
Abstract: A room-temperature, copper-catalyzed synthesis of symmetrical diarylsulfanes has been developed. The reaction proceeds from aryl iodides and elemental sulfur (S_8) by the action of copper(I) salts in the presence of *N*-ethyl-*N*-isopropylpropan-2-amine to afford the corresponding diarylsulfanes in good yields.

Key words: S-arylation, copper(I) iodide, diarylsulfanes, sulfur

Cross-coupling reactions performed between aryl halides and various nucleophiles in the presence of copper catalysts are powerful methods for carbon–heteroatom bond formation.[1,2] The importance of the aryl–sulfur bond stems from its presence in molecules of pharmaceutical and material interest. For example, diarylthioether moieties have been found in numerous drugs.[3] A common method for the synthesis of diarylsulfanes is the transition-metal-catalyzed cross-coupling reaction between aryl halides and thiophenoles. Different transition metals including palladium,[4,5] nickel,[6,7] iron,[8,9] and copper[10–13] have been reported to catalyze the formation of diarylsulfanes. Less common strategies for the synthesis of thioether moieties involve the use of thioureas,[14] disulfides,[15] 2-(iodoaryl)thioureas,[16] thoicyanates,[17] and aryl halides in the presence of copper catalysts. Recently, we have developed an efficient copper-catalyzed C–N cross-coupling.[18] Herein, we report a route to C–S cross-coupling at room temperature. To the best of our knowledge, no synthetic routes by copper catalysis at ambient temperature aimed to the synthesis of symmetrical diarylsulfanes have been reported.

Initially, the reaction between iodobenzene (3 mmol) and elemental sulfur (1.1 mmol), in the presence of copper(I) iodide (10 mol%), acetylacetone (1.1 mmol), and *N*-ethyl-*N*-isopropylpropan-2-amine (EIPA, 2 mmol) in DMSO at 25 °C was selected as a model for the synthesis of symmetrical diarylsulfanes (Table 1). Changing the solvent to DMSO led to good yields, but the use of other solvents resulted in significantly reduced yields. Bases other than EIPA afforded lower yields, and copper catalysts other than copper(I) iodide exhibited reduced activities. Among the ligands tested, acetylacetone showed a superior effect on the reaction yields (Table 1).

Table 1 Synthesis of Diarylsulfanes **2**[a]



Catalyst	Ligand	Base	Solvent	Yield (%)
CuI	**L1**	EIPA	DMSO	87
CuI	**L2**	EIPA	DMSO	33
CuI	**L3**	EIPA	DMSO	49
CuI	**L4**	EIPA	DMSO	76
CuI	**L5**	EIPA	DMSO	62
CuI	**L6**	EIPA	DMSO	62
CuI	**L1**	EIPA	DMF	64
CuI	**L1**	EIPA	NMP	32
CuI	**L1**	EIPA	MeCN	9
CuI	**L1**	EIPA	toluene	–
CuCl	**L1**	EIPA	DMSO	54
CuBr	**L1**	EIPA	DMSO	47
Cu_2O	**L1**	EIPA	DMSO	58
CuI	**L1**	Et_3N	DMSO	71
CuI	**L1**	DABCO	DMSO	43
CuI	**L1**	DBU	DMSO	61
CuI	**L1**	Cs_2CO_3	DMSO	10

[a] Reactions conditions: iodobenzene (2 mmol), S_8 (1.1 mmol), copper source (0.10 mmol), ligand (1.1 mmol), base (2.0 mmol), solvent (2 mL), 25 °C, 8 h, under argon.

After the optimized reaction conditions were established, a number of aryl iodides was examined to explore the scope of this reaction. As summarized in Table 2, various aryl iodides were converted into the corresponding diarylsulfanes in good yields.[19]

In conclusion, a novel copper-mediated procedure was developed for the preparation of symmetrical diarylsulfanes

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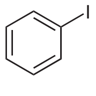
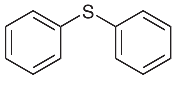
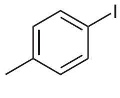
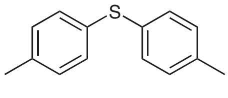
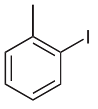
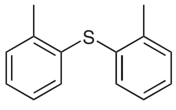
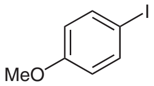
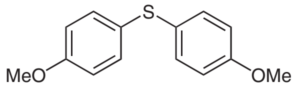
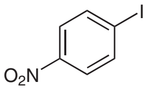
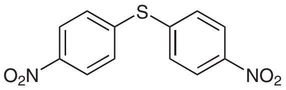
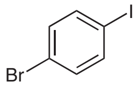
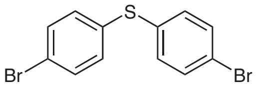
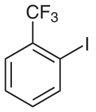
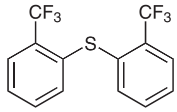
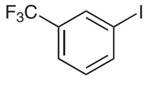
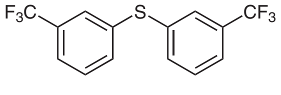
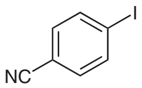
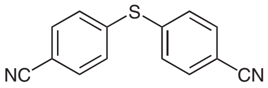
Table 2 Copper-Catalyzed C–S Coupling of Aryl Iodides with Elemental Sulfur

Entry	ArX	Product	Yield (%)
1	 **1a**	 **2a**	87
2	 **1b**	 **2b**	84
3	 **1c**	 **2c**	71
4	 **1d**	 **2d**	68
5	 **1e**	 **2e**	91
6	 **1f**	 **2f**	72
7	 **1g**	 **2g**	71
8	 **1h**	 **2h**	81
9	 **1i**	 **2i**	80

from aryl iodides at ambient temperature. This protocol, allowing the formation of two C–S bonds in a one-pot reaction, is distinguished by avoiding the use of foul smelling thiophenols and strong inorganic bases.

References and Notes

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(19) **General Procedure for the Synthesis of Products 2**
A mixture of aryl iodide (2 mmol), CuI (0.10 mmol), ligand (1.1 mmol), and S_8 (1.1 mmol) were added to an oven-dried reaction tube equipped with a septum. The reaction tube was evacuated and back-filled with argon. Under a counterflow of argon, EIPA (0.258 g, 2 mmol) and DMSO (2 mL) were added, and the mixture stirred at r.t. for 8 h. After complete disappearance of aryl iodide (monitored by TLC), H_2O (5 mL) was added, and the mixture was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic phases were dried (on $MgSO_4$) and filtered before evaporation of the solvent. The residue was purified on silica gel, eluting with PE–EtOAc (20:1), to give product **2**. Analytical and spectroscopic data for all derivatives, except **2g–i** have been reported previously.[19]

Bis(2-trifluoromethylphenyl)sulfane (2g)
Colorless oil; yield: 0.23 g (71%). IR (KBr): ν_{max} = 2915, 1591, 1443, 1313, 1264, 1170, 1128, 1034, 756 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.24 (2 H, d, ^3J = 8.0 Hz, 2 CH), 7.36–7.44 (4 H, m, 4 CH), 7.74 (2 H, d, ^3J = 7.5 Hz, 2 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 123.6 (2 CF_3, q, $^1J_{CF}$ = 272.0 Hz), 126.9 (2 CH, q, $^3J_{CF}$ = 5.5 Hz), 127.5 (2 CH), 131.0 (2 C, q, $^2J_{CF}$ = 30.2 Hz), 132.4 (2 CH), 134.7 (2 CH), 134.8 (2 C, q, $^3J_{CF}$ = 5.0 Hz). MS (EI, 70 eV): *m/z* (%) = 322 [M + 1], 301 (55), 252 (33), 233 (99), 184 (59), 157 (50), 133 (17), 108 (36).

Bis(3-trifluoromethylphenyl)sulfane (2h)
Colorless oil; yield: 0.26 g (81%). IR (KBr): ν_{max} = 2928, 1589, 1422, 1316, 1145, 755 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ = 7.46 (2 H, d, ^3J = 7.2 Hz, 2 CH), 7.49–7.55 (4 H, m, 4 CH), 7.62 (2 H, s, 2 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 123.6 (2 CF_3, q, $^1J_{CF}$ = 271 Hz), 124.4 (2 CH, q, $^3J_{CF}$ = 3.5 Hz), 127.7 (2 CH, q, $^3J_{CF}$ = 3.7 Hz), 129.9 (2 CH), 131.9 (2 C, q, $^2J_{CF}$ = 32.4 Hz), 134.2 (2 CH), 136.2 (2 C). MS (EI, 70 eV): *m/z* (%) = 322 [M + 1], 301 (26), 233 (69), 184 (35), 157 (40), 133 (11), 108 (25).

Bis(4-cyanophenyl)sulfane (2i)

Colorless solid; mp 174–176 °C; yield: 0.19 g (80%). IR (KBr): ν_{max} = 3424, 2370, 2218, 1582, 1482, 818 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.55 (4 H, d, ^3J = 8.4 Hz, 4 CH), 7.61 (4 H, d, ^3J = 8.4 Hz, 4 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 110.9 (2 C), 118.1 (2 CN), 126.5 (4 CH), 132.8 (4 CH), 142.1 (2 C). MS (EI, 70 eV): *m/z* (%) = 236 [M + 1], 204 (14), 166 (11), 134 (100), 107 (30), 90 (51), 82 (15), 75 (24), 69 (45), 63 (46), 57 (16), 51 (16).