Research Article

CuI-Catalyzed: One-Pot Synthesis of Diaryl Disulfides from Aryl Halides and Carbon Disulfide

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A new application of carbon disulfide in the presence of $\text{KF}/\text{Al}_2\text{O}_3$ is reported for the synthesis of organic symmetrical diaryl disulfides. These products were synthesized by one-pot reaction of aryl halides with the *in situ* generated trithiocarbonate ion in the presence of copper under air atmosphere.

1. Introduction

Carbon disulfide is a very important reagent for which many and varied uses have been reported in chemistry and also serves as an industrial and chemical nonpolar solvent [1–3]. The compound is frequently used as a building block in synthetic chemistry for the preparation of trithiocarbonates [4–9], dithio- and monothio-carbamates and carbonates [10, 11], thiourea [12, 13], and other organic compounds containing sulfur or thiocarbonyl ($\text{C}=\text{S}$) moiety [14–16]. Interestingly, carbon disulfide is also used for the synthesis of diaryl disulfides from diazonium salts under conditions of radicalic pathway [17, 18].

In continuation of our efforts to synthesize organic compounds containing sulfur and to use carbon disulfide in organic reactions [4–6, 19, 20], we report a method for the direct synthesis of symmetrical diaryl disulfides via domino coupling reactions of aryl halides with the trithiocarbonate anion. However, recently symmetrical diaryl trithiocarbonates are synthesized from the reaction of Na_2S and CS_2 with Ar-X in the presence of CuI [21]. In our process, $\text{KF}/\text{Al}_2\text{O}_3$ was used as a strong, recyclable, and heterogeneous base, which has a history of use in both synthetic methodology reactions [22–27] and the *in situ* production of the trithiocarbonate ion from carbon disulfide [4].

Organic disulfides are also valuable compounds in synthetic chemistry, industry, and biochemistry [28, 29]. They

are typically prepared by oxidation of the corresponding thiols [30–36]. There are a limited number of methods for the direct synthesis of disulfides from aryl halides [20, 37].

2. Results and Discussion

To find the optimal reaction conditions in terms of temperature and type of copper source, the coupling reaction of the carbon disulfide with iodobenzene was examined in the presence of $\text{KF}/\text{Al}_2\text{O}_3$ under air (Scheme 1).

The trithiocarbonate anion was prepared by the *in situ* reaction of three equivalents of carbon disulfide in the presence of 1.0 gram of KF (40% by weight)/ Al_2O_3 in DMF. First, the effect of different copper salts was examined. As is shown in Table 1, copper iodide can catalyze the synthesis of diphenyl disulfide from phenyl iodide better than that from the other salts tested (Table 1, entry 4). As strong bases are commonly used for CS_3^{2-} preparation [10, 11], Cs_2CO_3 and KOH were also tested to evaluate the efficiency of $\text{KF}/\text{Al}_2\text{O}_3$. They catalyze the reaction under optimized reaction conditions, but not as well as $\text{KF}/\text{Al}_2\text{O}_3$ as the reaction yields were 65% and 35%, respectively.

It can be deduced from the previous literature reports that the temperature and the nature of an added ligand significantly affect the progress of coupling reactions of sulfur-containing compounds because some of them have not

SCHEME 1

X = Br, I

SCHEME 2

TABLE 1: Optimization of the reaction temperature and screening of copper sources^a.

Entry	Copper salt	Temp. (°C)	Isolated yield (%)
1	CuCl	110	65
2	CuBr	110	72
3	Cu ₂ O	110	52
4	CuI	110	95
5	CuI	100	88
6	CuI	80	83
7	CuI	60	77
8	CuI	25	15

^aGeneral reaction conditions: carbon disulfide (6.0 mmol), KF/Al₂O₃ (1.0 g, 40% KF by weight), copper sources (0.32 mmol), and iodobenzene (2.0 mmol), in DMF (4 mL) for 5 h.

been carried out at room temperature and/or in the absence of a ligand [38, 39]. In our studies on the reaction, the best result was obtained at 110°C. However, significant progress of the reaction was also observed at lower temperatures (Table 1, entries 6 and 7). In addition, the reaction also proceeded well in the absence of a ligand. It seems that CS₃²⁻ acts as both a ligand and a sulfur source.

It was expected that some symmetrical diaryl trithiocarbonate and thiol would be generated as by-products with the desired diaryl disulfide. However, no traces of these compounds were found at the end of the reaction. Thus, a large number of derivatives of symmetrical diaryl disulfides were synthesized in good to excellent yields under optimal conditions (Scheme 2, Table 2). Aryl bromides also reacted under these conditions, but not as well as aryl iodides.

A wide range of diaryl disulfides was synthesized according to the nature and position of the attachment of the substituents on the aryl groups. Thus, the products bearing different substituents, both electron-withdrawing and electron-donating, were obtained at the *ortho*-, *para*-, and *metapositions*.

Symmetrical diheteroaryl disulfides were readily synthesized from the corresponding heteroaryl halides (Table 2, entries 7 and 8). The optimal reaction conditions were also tested for the synthesis of symmetrical dialkyl disulfides (Table 2, entry 13) but were proved to be ineffective in yielding the dibenzyl disulfide and dibenzyl trithiocarbonate (as the major product); dibenzyl sulfide was obtained in 76% and 16% yields, respectively. Interestingly, a high chemoselectivity is observed in the coupling reactions (Table 2, entries 11 and 5). It is the case of 1-bromo-2,4-difluorobenzene to bis-(2,4-difluoro phenyl) disulfide (Table 2, entry 11) and 1-bromo-4-iodobenzene to bis-(4-bromo phenyl) disulfide (Table 2, entry 5) yielded as the main products. The reactivity of carbon-halide (C-X) bonds in aryl halides (Ar-X) probably

depends on the nature of the halides. As was seen, the reactivity of carbon-X bonds is in the order of C-I > C-Br > C-F (Table 2, entries 4 and 10, 7 and 8, 5, 11).

Although we cannot yet clearly delineate the catalytic reaction pathway for the synthesis of diaryl disulfides from aryl halides and CS₃²⁻, it is possible that this reaction proceeds through an addition/oxidation Cu(I)-catalyst reaction of trithiocarbonate anion to aryl halides to generate an aryl trithiocarbonate ion *via* Ullman-type mechanism and then the fragmentation of formed aryl trithiocarbonate anion into carbon disulfide and aryl thiolate [40], which is followed by thiolate oxidation to corresponding disulfides in the presence of KF/Al₂O₃ [41, 42]. Aryl (alkyl) halides are activated *via* a Cu(I)/Cu(II) redox couple single electron transfer (SET) [43].

3. Conclusion

In summary, in this study, carbon disulfide was used as an inexpensive and readily available source of sulfur in the presence of KF/Al₂O₃. The reaction proceeds well under air. This strategy provides a new method for the direct synthesis of symmetrical diaryl disulfides from aryl halides and CS₃²⁻. Other advantages of this process are the ability to reuse the recyclable base KF/Al₂O₃, ease of performing and controlling the reaction as well as purification of the product, and the avoidance of expensive and/or dangerous reagents.

4. Experimental

4.1. Direct Synthesis of Diaryl Disulfides from Aryl Halides and Trithiocarbonate Ion: General Procedure. 6 mmol of carbon disulfide and 2 mmol of aryl halide were added to a two-neck flask containing 4 mL of DMF and 1.0 gram of KF (40% by weight)/Al₂O₃ [4, 44]. The mixture was vigorously stirred for 15 minutes at room temperature on a hot-plate magnetic stirrer, so that it was blood red in color. Then 0.32 mmol (60 mg) of CuI was added, and the reaction continued at 110°C under air atmosphere and in a condenser until the reaction was completed (5 h). The reaction progress was controlled by TLC. The reaction mixture was then filtered, the filtrate was evaporated under vacuum, CH₂Cl₂ (20 mL) was added, and the mixture washed with H₂O (2 * 15 mL). The organic layer was dried over anhydrous Na₂SO₄. The solvent was evaporated to give the crude diaryl disulfide, which was purified by plate chromatography (silica gel, *n*-hexane: ethyl acetate 20:1). All the products are known compounds and were characterized by comparison of NMR spectral data and melting points with those reported in the literature.

TABLE 2: CuI-catalyzed and KF/Al₂O₃ mediated, direct synthesis of diaryl disulfides from aryl halides and CS₂²⁻ at 110°C.

Entry	Aryl halide	Diaryl disulfide	Yield (%) ^a
1			95
2			91
3			93
4			85 ^b
5			81 ^b
6			83
7			83
8			65
9			82 ^b
10			60
11			62 ^b

TABLE 2: Continued.

Entry	Aryl halide	Diaryl disulfide	Yield (%) ^a
12			95 ^b
13			Trace

^aYield of the isolated product. ^bA small amount of the corresponding diaryl sulfide derivative was formed as by-product (5–10%).

4.2. Selected Spectral Data for Representative Disulfides. *Diphenyl Disulfide* (Table 2, entry 1). mp = 59–60°C (59–61°C lit. [31]). ¹H NMR (CDCl₃, 400 MHz): δ = 7.24–7.36 (m, 6H), 7.54 (m, 4H). ¹³C NMR (CDCl₃, 100 MHz): δ = 127.2, 127.5, 129.1, 137.0.

Bis(4-methoxyphenyl) Disulfide (Table 2, entry 2). mp = 42–43°C (42–43°C lit. [34, 35]). ¹H NMR (CDCl₃, 400 MHz): δ = 3.82 (s, 6H), 6.87 (d, *J* = 8.8 Hz, 4H), 7.32 (d, *J* = 8.8 Hz, 4H). ¹³C NMR (CDCl₃, 100 MHz): δ = 55.4, 114.7, 127.4, 132.8, 159.0.

Bis(thiophen-2-yl) Disulfide (Table 2, entry 7). mp = 54–55°C (54–56°C lit. [36]). ¹H NMR (CDCl₃, 400 MHz): δ = ¹H NMR (CDCl₃, 400 MHz): δ 6.97–7.00 (m, 2H), 7.22–7.25 (m, 2H), 7.36–7.38 (m, 2H). ¹³C NMR (CDCl₃, 100 MHz): δ = 115.4, 120.7, 129.7, 155.4.

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