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## One-Pot Synthesis of Symmetrical Diaryl Trithiocarbonates through Copper-Catalyzed Coupling of Aryl Compounds, Sodium Sulfide, and Carbon Disulfide

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Dedicated to Professor Carmen Nájera

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In this study, a protocol for the synthesis of symmetrical diaryl trithiocarbonates through the one-pot copper-catalyzed coupling reaction of sodium sulfide, carbon disulfide, and aryl compounds in DMF solution is presented. This method al-

Introduction

Carbon–sulfur bonds commonly occur in pharmaceutically and biologically active compounds.<sup>[1]</sup> Among the variety of sulfur compounds, trithiocarbonates are very important because of their wide range of applications, which include their use as pharmaceutical agents and agrochemicals, and they are also used as lubricating agents in oil additives.<sup>[2]</sup> In addition, trithiocarbonates are generally used as reversible addition–fragmentation chain-transfer (RAFT) agents in free-radical polymerization processes.<sup>[3]</sup>

The limited number of synthetic methods available for the preparation of dialkyl trithiocarbonates involve reactions of thiols with either thiophosgene or chlorodithioformates<sup>[4,5]</sup> and two-step reactions of thiols with carbon disulfide and alkyl halides.<sup>[6]</sup> The dialkylation of the in situ generated trithiocarbonate anion in the reaction of CS<sub>2</sub> with Cs<sub>2</sub>CO<sub>3</sub>,<sup>[7]</sup> KF/Al<sub>2</sub>O<sub>3</sub>,<sup>[8]</sup> nBu<sub>4</sub>NOH,<sup>[9]</sup> K<sub>3</sub>PO<sub>4</sub>,<sup>[10]</sup> and so forth<sup>[11]</sup> has also been reported. Recently, the one-pot synthesis of trithiocarbonates from the reaction of 1,1'thiocarbonyl diimidazole with thiols and its application in the controlled radical polymerization of vinyl monomers was reported.<sup>[12]</sup> Moreover, the preparation of alkyl aryl trithiocarbonates by reaction of bis(thiocarbonyl) disulfide with azo compounds was reported.<sup>[13]</sup> However, a literature search indicated that there is only one report on the synthesis of symmetrical diaryl trithiocarbonates through the reaction of thiophosgene with aryl thiols in basic media.<sup>[4]</sup> lows the synthesis of symmetrical diaryl trithiocarbonates without the use of highly toxic thiophosgene, and also, commercially available aryl halides were used instead of less available, toxic thiols.

This method is not very popular, as thiol compounds are foul smelling and a limited number of aryl thiols are commercially available. Also, thiophosgene is a highly toxic liquid that has been used as the chemical weapon known as Lacrimite. The handling of this chemical needs precaution, and protective equipment including rubber gloves, safety goggles, and breathing equipment should be used.<sup>[14]</sup> Diaryl trithiocarbonates have also been produced in very small quantities, as byproducts, in the reaction of sodium iodide with carbon disulfide and aryldiazonium fluoroborate in a free-radical process.<sup>[15]</sup> Hence, the design and development of a new strategy for the preparation of diaryl trithiocarbonates seems to be of paramount importance.

#### **Results and Discussion**

In recent years, transition-metal catalysis has intensely changed the face of modern organic chemistry by introducing a variety of novel synthetic methods. Carbon–heteroatom bond-formation reactions are one of the great achievements of transition-metal-catalyzed reactions, and C(aryl)–S bond formation by the direct coupling of aryl halides and thiols or an in situ generated thiolate moiety<sup>[16]</sup> has received wide attention.<sup>[17]</sup>

Herein, a novel protocol for the synthesis of symmetrical diaryl trithiocarbonates through a copper-catalyzed onepot coupling reaction of carbon disulfide, sodium sulfide, and aryl compounds in DMF at 100–130 °C is examined. In preliminary experiments, the one-pot reaction of sodium sulfide (1.1 mmol), carbon disulfide (5 mmol), and iodobenzene (2 mmol) as a model reaction was studied under different reaction conditions by using various solvents such as  $H_2O$ , toluene, and DMF and also by using different cop-

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per sources such as CuI, CuCl, and CuSO<sub>4</sub> in the presence or absence of  $Et_3N$  (Table 1).

Table 1. Effects of solvent, copper catalyst, and base.

		copper catalyst Na <sub>2</sub> S, CS <sub>2</sub>	S	
		solvent (5 mL) 100 °C	s s	
Entry	Catalyst	Conditions <sup>[a]</sup>	Solvent	Yield <sup>[b]</sup> [%]
1	CuCl	А	DMF	67
2	CuCl	А	toluene	trace
3	CuI	А	$H_2O$	60
4	CuI	А	toluene	trace
5	CuI	А	DMF	81
6	$CuSO_4$	А	$H_2O$	43
7	CuSO <sub>4</sub>	А	DMF	65
8	CuI	В	DMF	80
9	_	С	DMF	0
10	CuI	D	DMF	20
11	CuI	E	DMF	15

[a] Conditions A: Na<sub>2</sub>S (1.1 mmol), CS<sub>2</sub> (5 mmol), iodobenzene (2 mmol), CuX (5 mol-%). Conditions B: Na<sub>2</sub>S (1.1 mmol), CS<sub>2</sub> (5 mmol), iodobenzene (2 mmol), CuI (5 mol-%), Et<sub>3</sub>N (2.4 mmol). Conditions C: Na<sub>2</sub>S (1.1 mmol), CS<sub>2</sub> (5 mmol), iodobenzene (2 mmol). Conditions D: CS<sub>2</sub> (5 mmol), Cs<sub>2</sub>CO<sub>3</sub> (1 mmol), iodobenzene (2 mmol), CuI (5 mol-%). Conditions E: K<sub>3</sub>PO<sub>4</sub> (1 mmol), CS<sub>2</sub> (5 mmol), iodobenzene (2 mmol), iodobenzene (2 mmol), CuI (5 mol-%). [b] Isolated yield.

The results indicate that among the various copper sources and solvents tested, CuI and DMF were the most effective for this reaction (Table 1, entry 5). However, the presence of  $Et_3N$  did not show any significant effect on the yield of the reaction (Table 1, entry 8).

In the absence of the catalyst, the reaction did not show significant progress (Table 1, entry 9). For comparison, two recently reported methods for the preparation of symmetrical dialkyl trithiocarbonates were used for the copper-catalyzed synthesis of symmetrical diaryl trithiocarbonates with the use of CuI as the catalyst and DMF as the solvent at 100 °C. By employing  $CS_2/Cs_2CO_3$ ,<sup>[7]</sup> in the presence of CuI and iodobenzene the corresponding diphenyl trithiocarbonate was obtained in low yield (20%; Table 1, entry 10). Also, in the case of K<sub>3</sub>PO<sub>4</sub>,<sup>[10]</sup> the diphenyl trithiocarbonate was produced in 15% yield (Table 1, entry 11).

Subsequently, reactions of various aryl iodides such as iodobenzene, 4-iodotoluene, 4-iodoanisole, 2-iodotoluene, 2-iodoanisole, 4-iodobenzonitrile, and 1-iodonaphthalene were studied under the above-optimized conditions (Table 2). The reactions proceeded well, and the corresponding diaryl trithiocarbonates were obtained in high yields. 2-Iodothiophene as a heterocyclic aryl iodide was found to react successfully, and the desire trithiocarbonate was produced in 85% yield (Table 2, entry 4). Also, 4bromonitrobenzene and 4-bromobenzonitrile as active bromoaryl substrates gave the desired trithiocarbonates in 62 and 70% yield, respectively (Table 2, entries 7 and 8). Phenolic derivatives such as phenyl tosylate, phenyl triflate, 4-nitrophenyl triflate and 4-nitrophenyl tosylate were also found to react smoothly to afford the corresponding products in 82-87% yield (Table 2, entries 9–12). In a previous report,<sup>[4]</sup> the preparation of diphenyl trithiocarbonates as

Table 2. One-pot synthesis of structurally different symmetrical diaryl trithiocarbonates by the copper-catalyzed coupling reactions of aryl compounds, carbon disulfide, and sodium sulfide.



[a] Isolated yield.



the sole compound was demonstrated. Notably, the <sup>1</sup>H NMR spectra of the products and those of their diaryl sulfide analogues are similar, but the protons of the diaryl trithiocarbonates are shifted upfield relative to the protons of the diaryl sulfides (see the Supporting Information).

To probe the scope of the presented protocol for the onepot synthesis of unsymmetrical diaryl and alkyl aryl trithiocarbonates, the reaction of iodobenzene in the presence of 1-iodo-4-nitrobenzene and the reaction of iodobenzene in the presence of *n*-butyl bromide were studied. The results show that in both cases symmetrical diaryl trithiocarbonates and dialkyl trithiocarbonates were formed; the formation of unsymmetrical alkyl aryl trithiocarbonates was not observed.

The utility of this system was further illustrated by the flexibility of being able to scale up the reaction by using 20 mmol of iodobenzene, Na<sub>2</sub>S (11 mmol), CS<sub>2</sub> (50 mmol), and CuI (5 mol-%) at 100 °C. The reaction was performed with success within an appropriate reaction time and afforded the corresponding phenyl trithiocarbonate in 75% yield.

#### Conclusions

In conclusion, in this study, a protocol for the synthesis of symmetrical diaryl trithiocarbonate in a practical and safe way was reported. The coupling of carbon disulfide, sodium sulfide, and aryl compounds, including aryl iodides, activated aryl bromides, and phenyl tosylate and/or triflate, catalyzed by CuI provided the trithiocarbonates in one pot.

### **Experimental Section**

General Procedure for the Synthesis of Diaryl Trithiocarbonates: Na<sub>2</sub>S (1.1 mmol) powder was added to a stirring mixture of CS<sub>2</sub> (5 mmol) and DMF (2 mL) at room temperature. After 15 min, CuI (5 mol-%) and the aryl compound (2 mmol) were added to the red-colored reaction mixture, which was stirred and heated at 100–130 °C for the appropriate length of time. Then, the reaction mixture was cooled to room temperature and extracted with EtOAc. Evaporation of the solvent yielded the crude diaryl trithiocarbonate, which was purified by flash column chromatography on silica gel (EtOAc/*n*-hexane).

**Supporting Information** (see footnote on the first page of this article): Characterization data, copies of the <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra, HRMS data, and FTIR spectra of the products.

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