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Thiol-free route to diaryl sulfides by Cu catalyzed coupling of sodium thiosulfate with aryl halides

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1. Introduction

Nowadays, organosulfur chemistry attracts extensive attention because sulfur containing building blocks are present in many natural products and pharmaceuticals [1-8]. The search for new methods for the synthesis of sulfides is a subject of much current interest. Traditional sulfide construction involves thiol alkylation or arylation [9-18], or the treatment of an organometallic reagent with a disulfide molecule [19-23]. However, the drawbacks of these methods include the utilization of environmentally unfavorable and odorous thiols as starting materials or generating them as byproducts. Thiols are also air sensitive and are readily oxidized by atmospheric oxygen. To overcome these problems, various sulfur-transfer reagents for in situ generation of thiols have been employed such as thiourea [24-28], potasium thioacetate [29], carbon disulfide [30-34], metal sulfides [35,36], sulfonyl hydrazide [37,38], ethyl xanthogenate [39], thiocyanate [40], thioacetamide [41], and S₈ [42–51]. Recently, Na₂S₂O₃, which is readily available as a stable solid and does not have any smell, was successfully

ABSTRACT

A method for the synthesis of diaryl sulfides from aryl halides in polyethylene glycol was reported. Inodorous $Na_2S_2O_3$ ·5H₂O, which is readily available as a stable salt, is an effective source of sulfur in the presence of CuI as catalyst.

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used for the in situ generation of thiol or thiolate. In 2013, Jiang's group [52] reported the first Pd catalyzed coupling reaction using $Na_2S_2O_3$ as the sulfur reagent to get a substituted 1,4-benzothiazine derivate.

Since then, this group has studied several intramolecular or intermolecular C-S bond formation reactions using Na₂S₂O₃ in the presence of different metal catalysts. In 2014, they developed a method for making aromatic sulfides by Pd catalyzed cross coupling of aryl halides, alkyl halides, and Na₂S₂O₃·5H₂O [53]. They also introduced a practical approach to construct thioethers using aromatic amines and alkyl halides as starting materials along with a catalyst system composed of CuSO₄·5H₂O/bipy/Na₂S₂O₃·5H₂O [54]. In another work, Jiang and coworkers [55] developed a procedure for sulfide synthesis by cross coupling of 1-aryltriazenes, Na₂S₂O₃ and alkyl halides, which employed CuSO4 as a catalyst, BF3-Et2O as a promoter and water as solvent at room temperature under air. In 2014, a combination of Pd(dppf)Cl₂ and dppf using odorless Na₂S₂O₃ as the sulfur source in DMF at 140 °C was used by Hou et al. [56] to synthesize 2-aminobenzo[b]-thiophene com-



Article

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pounds. Lately, Rostami et al. [42] reported the thio-arylation reactions of alkyl halides with nitroarenes using $Na_2S_2O_3 \cdot 5H_2O$ as a sulfide surrogate and Cu salts as catalyst. In most of these methods, Pd complex catalysts were employed for the thio-arylation of aryl halides. In this regard, developing a catalyst system other than Pd is of interest. To date, thioetherification of aryl halides in the presence of a copper based catalyst system and $Na_2S_2O_3 \cdot 5H_2O$ as a convenient and environmentally friendly source of sulfur has not been reported.

2. Experimental

2.1. General

All chemicals used were purchased from the Fluka, Merck, or Aldrich chemical companies. The products were characterized by the comparison of their spectral and physical data with those of reference samples.

2.2. Typical procedure for the synthesis of diphenylsulfane from iodobenzene

A mixture of Na₂S₂O₃·5H₂O (1.1 mmol, 0.273 g), iodobenzene (2.0 mmol, 0.22 mL), CuI (20 mol%, 0.038 g) and DMAP (20 mol%, 0.024 g) was added to a flask containing PEG-200 (1 mL). The mixture was heated at 120 °C with stirring and the reaction was followed by TLC analysis. After completion of the reaction, which was detected by TLC (12 h), the mixture was cooled to room temperature and the coupled product was extracted with ethyl acetate (3×3 mL). The solvent was evaporated and the crude mixture was purified by column chromatography over silica gel using *n*-hexane as the eluent to give pure diphenylsulfane as a colourless liquid in 94% yield.

Diphenylsulfane (Table 2, entry 1). ¹H NMR (250 MHz, CDCl₃): $\delta_{\rm H}$ = 7.25–7.16 (m, 10H). Anal. Calcd. for (C₁₂H₁₀S): C, 77.38; H, 5.41; S, 17.21. Found: C, 77.30; H, 5.35; S, 17.35.

Di-p-tolylsulfane (Table 2, entry 2). ¹H NMR (250 MHz, CDCl₃): $\delta_{\rm H}$ = 7.20–7.16 (m, 4H), 6.77–6.71 (m, 4H), 2.33 (s, 6H). Anal. Calcd. for (C₁₄H₁₄S): C, 78.46; H, 6.58; S, 14.96. Found: C, 78.61; H, 6.52; S, 14.87.

Bis(4-methoxyphenyl)sulfane (Table 2, entry 3). ¹H NMR (250 MHz, CDCl₃): $\delta_{\rm H}$ = 7.38–7.30 (m, 4H), 6.78–6.74 (m, 4H), 3.72 (s, 6H). Anal. Calcd. for (C₁₄H₁₄O₂S): C, 68.26; H, 5.73; S, 13.02. Found: C, 68.16; H, 5.70; S, 13.15.

4,4'-Thiodibenzonitrile (Table 2, entry 10). ¹H NMR (250 MHz, CDCl₃): $\delta_{\rm H}$ = 7.56–7.52 (m, 4H), 7.36–7.32 (m, 4H). Anal. Calcd. for (C₁₄H₈N₂S): C, 71.16; H, 3.41; N, 11.86; S, 13.57. Found: C, 71.28; H, 3.37; N, 11.95; S, 13.40.

3. Results and discussion

As a continuation of our ongoing research on organosulfur chemistry [57–62], we were interested in examining CuI as the pre-catalyst for the thio-arylation of aryl halides in the presence of $Na_2S_2O_3$ ·5H₂O. To test this, we performed the reaction of iodobenzene (2.0 mmol) with $Na_2S_2O_3$ ·5H₂O (1.1 mmol) in the presence of CuI (20 mol%) as catalyst and DMAP

(4-dimethylaminopyridine) (20 mo%) as ligand in DMSO at 120 °C under atmospheric conditions. The desired product was obtained in 95% yield after 12 h (Table 1, entry 1). Performing the reaction in toluene, CH₃CN and H₂O under reflux conditions did not result in the desired product, but left the starting materials intact (Table 1, entries 2-4). Moreover, when the reaction was performed in polyethylene glycol (PEG-200), which is an eco-friendly media, similar results were obtained to the DMSO results (Table 1, entry 5). Polyethylene glycols (PEGs) and their derivatives are non-toxic, cheap and easily available, and thermally stable and recoverable, and are a suitable medium for environmentally friendly and safe chemical reactions. Therefore, the subsequent reactions were performed in PEG-200. Lowering the temperature from 120 to 100 °C resulted in a longer reaction time and a lower yield (Table 1, entry 6). When the temperature of the reaction was raised to 140 °C, no improvement of the product yield and reaction rate was observed (Table 1, entry 7). Control experiments confirmed that no conversion occurred without a catalyst (Table 1, entry 8). It was further observed that increasing the catalyst loading beyond 20 mol% did not affect the reaction appreciably, while in the presence of 10 mol% of the catalyst, the reaction did not reach completion even after 24 h (Table 1, entries 9 and 10). The presence of a ligand was necessary for the reaction and the reaction did not occur under ligand-free conditions (Table 1, entry 11). The reaction was also tested with other ligands such as L-proline and DABCO. While L-proline gave 30% of yield (Table 1, entry 12), DABCO failed to give any product (Table 1, entry 13).

Having identified the optimal conditions (Table 1, entry 5), the substrate scope of this reaction was investigated. As shown in Table 2, aryl iodides bearing both electron-withdrawing and electron-donating groups, such as the nitro (Table 2, entry 5), methyl (Table 2, entry 2), methoxy (Table 2, entry 3) and amino

Table 1

Optimization of the reaction parameters for the reaction of iodobenzene (2.0 mmol) with $Na_2S_2O_3 \cdot 5H_2O$ (1.1 mmol) in the presence of CuI as catalyst.

	I + Na	₂ S ₂ O ₃ •5H ₂	O <u>CuI, Li</u> Solver	$\frac{\text{gand}}{\text{nt}, \Delta}$	S_	
Entry	Catalyst (mol%)	Solvent	Т (°С)	Ligand (20 mol%)	Time (h)	Yield * (%)
1	20	DMSO	120	DMAP	12	95
2	20	Toluene	Reflux	DMAP	24	_
3	20	CH₃CN	Reflux	DMAP	24	_
4	20	H_2O	100	DMAP	24	—
5	20	PEG	120	DMAP	12	94
6	20	PEG	100	DMAP	24	50
7	20	PEG	140	DMAP	12	94
8	_	PEG	120	DMAP	24	—
9	30	PEG	120	DMAP	12	95
10	10	PEG	120	DMAP	24	60
11	20	PEG	120	_	24	_
12	20	PEG	100	L-proline	24	30
13	20	PEG	140	DABCO	24	_

* Isolated yield.

Table 2

Synthesis of diaryl sulfides from aryl halides catalyzed by CuI in the presence of $Na_2S_2O_3$ - $5H_2O$ in PEG-200.

		CuI, DMAP		\searrow
z ·	+ $Na_2S_2O_3 \cdot 5H_2O$ -	PEG200, 120 °C	z	Ľ, z
Entry	ArX	Time (h)	Yield * (%)	Ref.
1		12	94	[28]
2	H ₃ C	. I 14	85	[28]
3	H ₃ CO	_ I 15	85	[28]
4	H ₂ N	- I 15	80	[41]
5	O ₂ N	I 11	90	[28]
6	CH ₃	48	_	_
7	Br	14	93	[28]
8	H ₃ C	Br 15	81	[28]
9	H ₂ N	Br 17	85	[41]
10	NC	Br 12	88	[41]
11	O ₂ N	Br 12	89	[28]
12	NC	Cl 48	_	

Reaction conditions: aryl halide (2.0 mmol), Na₂S₂O₃·5H₂O (1.1 mmol), DMAP (20 mol%), CuI (20 mol%), PEG-200 (1 mL), 120 °C. * Isolated yield.

groups (Table 2, entry 4) all worked well to give products in excellent yields. However, in case of electron-releasing groups, a slightly longer reaction time was required for the completion of the reaction. As shown in entry 6 in Table 2, the target product was not obtained in the case of 2-methyliodobenzene even after prolonged reaction time, which was probably due to the steric hindrance on the substrate. Aryl bromides bearing electron-withdrawing and electron-donating groups as well as aryl iodides afforded the desired products in excellent yields.



Scheme 1. Mechanism for symmetric sulfide synthesis.

Slightly longer reaction times compared with the iodo-analogues were required (Table 2, entries 7–11). This catalyst system was not efficient for chloro arenes. When the catalyst system was applied for 4-chlorobenzonitrile, the reaction did not proceed at all and the starting material was isolated intact after an appropriate reaction time (Table 2, entry 12).

On the basis of the literature [53–55], a reaction pathway is presented in Scheme 1. First, a Cu(III) species was generated by the oxidative addition of Cu(I) to the C–X bond of aryl halide. The Cu(III) species subsequently reacted with Na₂S₂O₃ to give intermediate **I**. Reductive elimination of intermediate **I** produced the aryl thiolsulfate along with the CuI catalyst. Then, the aryl thiolsulfate reacted with the arylated Cu(III) halide (generated in situ from aryl halide and CuI) to give intermediate **II**, which was transform to **III** by releasing SO₃. Finally, the subsequent reductive elimination from **III** yielded diaryl sulfide and regenerated the CuI catalyst.

4. Conclusions

Cu catalyzed coupling of aryl halides and Na₂S₂O₃·5H₂O was developed which gave symmetrical diaryl sulfides in excellent yields. A variety of functional groups on the aryl halides were tolerated. Na₂S₂O₃·5H₂O was used as a sulfur source. This is an odorless, stable, commercially available, easily handled and environmentally friendly salt. This route to sulfides avoids the use of thiol as the coupling partner or byproduct, which avoided its facile oxidation and unpleasant smell. The use of a green solvent and an inexpensive catalyst are the other advantages of this system.

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References

- [1] T. Kondo, T. Mitsudo, Chem. Rev., 2000, 100, 3205–3220.
- [2] S. V. Ley, A. W. Thomas, Angew. Chem. Int. Ed., 2003, 42, 5400–5449.
- [3] A. Q. Acton, ed., Sulfur Compounds: Advances in Research and Application, ScholarlyEditions, Atlanta, GA, 2012.
- [4] A. Mishra, C. Q. Ma, P. Bäuerle, *Chem. Rev.*, 2009, 109, 1141–1276.
- [5] D. P. Nair, M. Podgórski, S. Chatani, T. Gong, W. Xi, C. O. Fenoli, C. N. Bowman, *Chem. Mater.*, **2014**, 26, 724–744.
- [6] E. Block, Angew. Chem. Int. Ed. Engl., 1992, 31, 1135–1178.
- [7] D. Y. Lin, S. Z. Zhang, E. Block, L. C. Katz, *Nature*, 2005, 434, 470–477.
- [8] S. F. Nielsen, E. O. Nielsen, G. M. Olsen, T. Liljefors, D. Peters, J. Med. Chem., 2000, 43, 2217–2226.
- [9] M. E. Peach, in: S. Patai, ed., *The Chemistry of the Thiol Group*, John Wiley & Sons, London, **1974**, 721.
- [10] J. Yin, C. Pidgeon, Tetrahedron Lett., 1997, 38, 5953–5954.
- [11] I. P. Beletskaya, V. P. Ananikov, Chem. Rev., 2011, 111, 1596–1636.
- [12] C. C. Eichman, J. P. Stambuli, *Molecules*, **2011**, 16, 590–608.
- [13] P. Bichler, J. A. Love, Top. Organomet. Chem., 2010, 31, 39-64.
- [14] J. F. Hartwig, Acc. Chem. Res., 2008, 41, 1534–1544.
- [15] T. Kondo, T. Mitsudo, *Chem. Rev.*, **2000**, 100, 3205–3220.
- [16] H. J. Xu, Y. F. Liang, X. F. Zhou, Y. S. Feng, Org. Biomol. Chem., 2012, 10, 2562–2568.
- [17] H. J. Xu, Y. F. Liang, Z. Y. Cai, H. X. Qi, C. Y. Yang, Y. S. Feng, J. Org. Chem., 2011, 76, 2296–2300.
- [18] H. J. Xu, Y. Q. Zhao, T. Feng, Y. S. Feng, J. Org. Chem., 2012, 77, 2878–2884.
- [19] F. G. Bordwell, P. J. Boutan, J. Am. Chem. Soc., 1957, 79, 717–722.
- [20] W. Klose, K. Schwarz, J. Heterocycl. Chem., 1982, 19, 1165-1167.
- [21] M. Tazaki, S. Nagahama, M. Takagi, *Chem. Lett.*, **1988**, 339–342.
- [22] M. Shimazaki, M. Takahashi, H. Komatsu, A. Ohta, K. Kajii, Y. Kodama, Synthesis, 1992, 555–557.
- [23] P. F. Wang, X. Q. Wang, J. J. Dai, Y. S. Feng, H. J. Xu, Org. Lett., 2014, 16, 4586–4589.
- [24] H. Firouzabadi, N. Iranpoor, M. Gholinejad, Adv. Synth. Catal., 2010, 352, 119–124.
- [25] M. Kuhn, F. C. Falk, J. Paradies, Org. Lett., 2011, 13, 4100-4103.

- [26] H. Firouzabadi, N. Iranpoor, M. Gholinejad, A. Samadi, J. Mol. Catal. A, 2013, 377, 190–196.
- [27] M. Gholinejad, B. Karimi, F. Mansouri, J. Mol. Catal. A, 2014, 386, 20–27.
- [28] S. Roy, P. Phukan, Tetrahedron Lett., 2015, 56, 2426–2429.
- [29] N. Park, K. Park, M. Jang, S. Lee, J. Org. Chem., 2011, 76, 4371–4378.
- [30] F. Wang, S. J. Cai, Z. P. Wang, C. J. Xi, Org. Lett., 2011, 13, 3202–3205.
- [31] P. Zhao, F. Wang, C. J. Xi, Synthesis, 2012, 44, 1477–1480.
- [32] P. Zhao, Q. Liao, H. Gao, C. J. Xi, Tetrahedron Lett., 2013, 54, 2357–2361.
- [33] P. Zhao, H. Yin, H. X. Gao, C. J. Xi, J. Org. Chem., 2013, 78, 5001–5006.
- [34] H. Firouzabadi, N. Iranpoor, A. Samadi, *Tetrahedron Lett.*, 2014, 55, 1212–1217.
- [35] Y. M. Li, C. P. Nie, H. F. Wang, X. Y. Li, F. Verpoort, C. Y. Duan, *Eur. J. Org. Chem.*, **2011**, 2011, 7331–7338.
- [36] W. You, X. Y. Yan, Q. Liao, C. J. Xi, Org. Lett., 2010, 12, 3930–3933.
- [37] N. Singh, R. Singh, D. S. Raghuvanshi, K. N. Singh, *Org. Lett.*, **2013**, 15, 5874–5877.
- [38] S. R. Guo, W. M. He, J. N. Xiang, Y. Q. Yuan, Chem. Commun., 2014, 50, 8578–8581.
- [39] D. J. C. Prasad, G. Sekar, Org. Lett., 2011, 13, 1008-1011.
- [40] F. Ke, Y. Y. Qu, Z. Q. Jiang, Z. K. Li, D. Wu, X. G. Zhou, Org. Lett., 2011, 13, 454–457.
- [41] M. Z. Cai, R. Y. Yao, L. Chen, H. Zhao, J. Mol. Catal. A, 2014, 395, 349–354.
- [42] A. Rostami, A. Rostami, A. Ghaderi, J. Org. Chem., 2015, 80, 8694–8704.
- [43] Y. W. Jiang, Y. X. Qin, S. W. Xie, X. J. Zhang, J. H. Dong, D. W. Ma, Org. Lett, 2009, 11, 5250–5253.
- [44] H. F. Wang, L. L. Jiang, T. Chen, Y. M. Li, Eur. J. Org. Chem., 2010, 2010, 2324–2329.
- [45] M. Martinek, M. Korf, J. Srogl, Chem. Commun., 2010, 46, 4387–4389.
- [46] J. H. Cheng, C. L. Yi, T. J. Liu, C. F. Lee, *Chem. Commun.*, 2012, 48, 8440–8442.
- [47] D. Singh, A. M. Deobald, L. R. S. Camargo, G. Tabarelli, O. E. D. Rodrigues, A. L. Braga, *Org. Lett.*, **2010**, 12, 3288–3291.
- [48] H. Y. Chen, W. T. Peng, Y. H. Lee, Y. L. Chang, Y. J. Chen, Y. C. Lai, N. Y. Jheng, H. Y. Chen, *Organometallics*, **2013**, 32, 5514–5522.
- [49] C. Chen, Y. Xie, L. L. Chu, R. W. Wang, X. G. Zhang, F. L. Qing, Angew. Chem. Int. Ed., 2012, 51, 2492–2495.

Graphical Abstract

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- [50] F. Shibahara, T. Kanai, E. Yamaguchi, A. Kamei, T. Yamauchi, T. Murai, *Chem. Asian J.*, **2014**, 9, 237–244.
- [51] N. Taniguchi, *Tetrahedron*, **2012**, 68, 10510–10515.
- [52] Z. J. Qiao, H. Liu, X. Xiao, Y. N. Fu, J. P. Wei, Y. X. Li, X. F. Jiang, Org. Lett., 2013, 15, 2594–2597.
- [53] Z. J. Qiao, J. P. Wei, X. F. Jiang, Org. Lett., **2014**, 16, 1212–1215.
- [54] Y. M. Li, J. H. Pu, X. F. Jiang, Org. Lett., **2014**, 16, 2692–2695.
- [55] Y. H. Zhang, Y. M. Li, X. M. Zhang, X. F. Jiang, Chem. Commun., 2015, 51, 941–944.
- [56] C. W. Hou, Q. He, C. H. Yang, Org. Lett., **2014**, 16, 5040–5043.

- [57] H. Firouzabadi, N. Iranpoor, M. Abbasi, *Tetrahedron Lett.*, **2010**, 51, 508–509.
- [58] M. Abbasi, M. R. Mohammadizadeh, H. Moosavi, N. Saeedi, *Synlett*, 2015, 26, 1185–1190.
- [59] M. Abbasi, A. Jabbari, J. Iran. Chem. Soc., 2016, 13, 81–86.
- [60] H. Firouzabadi, N. Iranpoor, M. Abbasi, Bull. Chem. Soc. Jpn., 2010, 83, 698–702.
- [61] M. Abbasi, D. Khalili, J. Iran. Chem. Soc., 2015, 12, 1425–1430.
- [62] M. Abbasi, M. R. Mohammadizadeh, Z. K. Taghavi, J. Iran. Chem. Soc., 2013, 10, 201–205.