*J. Org. Chem.* **1992**, *57*, 2751-2753 **2751**

# Novel Redox Reactions between Diaryl Disulfides and Iodoarenes

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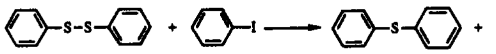
*Received November 26, 1991*

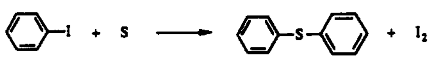
## Introduction

Thermolysis of diphenyl disulfide at high temperatures (ca. 250 °C) produces diphenyl sulfide and elemental sulfur (eq 1).[1] Diphenyl disulfide can also be formed by heating diphenyl sulfide with an excess of sulfur.[1]

(1)



(2)

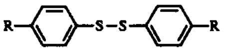


(3)

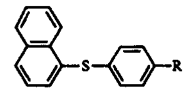
However, we have recently found that in the presence of iodobenzene thermolysis of diphenyl disulfide yielded diphenyl sulfide and elemental iodine (eq 2).[2] Iodoarenes do not form iodine under the same thermolysis conditions. It has also been reported that diphenyl sulfide and iodine are the products from the reaction of iodobenzene and elemental sulfur at 230–270 °C (eq 3).[3] Preliminary results have proved that diphenyl sulfide in eq 2 was not formed by extrusion of sulfur from the disulfide (eq 1) and subsequent reaction with iodobenzene (eq 3).[2] We report herein further studies on the thermolysis of various functionalized diaryl disulfides.

## Results and Discussion

**1. Synthesis of Diaryl Disulfides.** The disulfides **1a**–**1d** and **1f** are commercially available. The disulfide **1i** was prepared by treatment of a diazotized solution of 4-aminobenzoic acid with sodium disulfide. Bis(4-bromophenyl) disulfide (**1g**) was synthesized according to the known procedure, starting from thiophenol.[4] The disulfide **1e** was made either from 4-fluorothiophenol by oxidation with bromine or from 4-fluorobenzenesulfonyl chloride using Olah's method (Scheme I).[5] Thus, 4-fluorobenzenesulfonyl chloride was treated with chlorotrimethylsilane in the presence of dry sodium iodide and a catalytic amount of tetra-*n*-butylammonium iodide in methylene chloride at room temperature. The reaction was easily followed by HPLC. The disulfide **1e** could be obtained in about 80% yield after purification by distillation. Alternatively, 4-fluorobenzenesulfonyl chloride can be reduced directly to the disulfide with concentrated hydriodic acid. Bis(4-iodophenyl) disulfide (**1h**) was prepared by the reaction of sodium iodide with the diazonium salt generated from diazotization of the disulfide **1d** (Scheme I).



**1**
a, R = H, e, R = F
b, R = CH$_3$ f, R = Cl
c, R = NO$_2$ g, R = Br
d, R = NH$_2$ h, R = I
i, R = CO$_2$H



**2**
a, R = F; b, R = Cl; c, R = CO$_2$H

### Scheme I

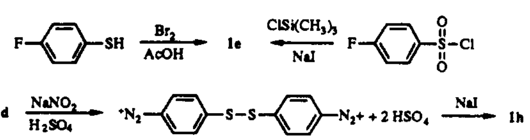
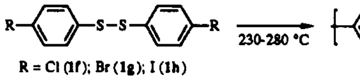


**Table I. Reactions of Diaryl Disulfides and 1-Iodonaphthalene**

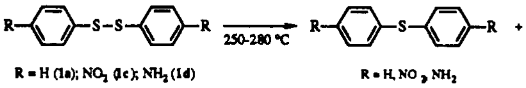
| disulfide 1, R | product 2, R | mol ratio SS:I | yield (%) | mp (°C) |
|---|---|---|---|---|
| e, F | a, F | 0.53:2.2 | 74.6 | (liquid) |
| f, Cl | b, Cl | 1.0:2.2 | 58.2 | 42-44 |
| i, CO$_2$H | c, CO$_2$H | 1.0:2.2 | 71.4 | 165-166 |

**2. Thermolysis of Diaryl Disulfides.** Thermolysis of diaryl disulfides containing chloro, bromo, and iodo groups leads to the formation of linear poly(phenylene sulfide) (eq 4).[6] The molecular weight of the polymer decreases with increasing bond dissociation energy of the carbon–halogen bond from C–I to C–Cl.



(4)

High molecular weight poly(phenylene sulfide) was readily formed by heating disulfide **1h** at 250–280 °C. Disulfides bearing electron-withdrawing fluoro (**1e**) and carboxylic acid (**1i**) groups were recovered as starting disulfides after 24 h of thermolysis at 245 °C. The disulfides **1c** and **1d** behaved similarly to **1a**, undergoing an extrusion reaction to yield the corresponding symmetric sulfide and elemental sulfur (eq 5). Only a small amount of the extruded product, *p*-tolyl sulfide, was detected from thermolysis of the disulfide **1b**.



(5)

Resin-like residues as main products could be due to the subsequent reaction of the extruded sulfur with the reactive methyl groups, since it has been reported that heating toluene and elemental sulfur at high temperature produces stilbene and hydrogen sulfide.[7]

**3. Thermolysis of Diaryl Disulfides in the Presence of Iodoarenes.** Under the same thermolysis conditions the diaryl disulfides **1** react rapidly with an iodoarene such as 1-iodonaphthalene to form the sulfides **2**, along with the evolution of iodine. The redox reaction begins around 210–230 °C, with the iodide being oxidized to elemental iodine and the disulfide being reduced to the sulfide. When the substituents are iodo and bromo groups, heating the disulfides at 250–280 °C gives the corresponding phenylene sulfide polymers. Instead of reacting with itself to form a polymer the disulfide **1f** (R = Cl) reacted preferably with 1-iodonaphthalene to yield 4-(chlorophenyl)-1-naphthyl sulfide as a major product. Thermolysis of the disulfides **1c** and **1b** in the presence of 1-iodonaphthalene only led to the formation of complex mixtures and iodine, indicating that the redox reaction between the disulfide and iodoarene took place. However, the nitro and methyl groups also participated in the reaction, which caused side reactions to occur. It was found that if the substituents are fluoro or carboxylic acid groups,

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(1) Harpp, D. N.; Kader, H. A.; Smith, R. A .*Sulfur Lett.* **1982**, *1*(2), 59 and references cited therein.

(2) Wang, Z. Y.; Hay, A. S. *Tetrahedron Lett.* **1990**, *31*, 5685.

(3) Rule, M. U.S. Patent 4,792,634, Dec 20, 1988; *Chem. Abstr.* **1988**, *110*, 195126.

(4) Handlovits, C. E. *Macromol. Synth.* **1968**, *3*, 132.

(5) Olah, G. A.; Narang, S. C.; Field, L. D.; Salem, G. F. *J. Org. Chem.* **1980**, *45*, 4792.

(6) Wang, Z. H.; Hay, A. S. *Macromolecules* **1991**, *24*, 333.

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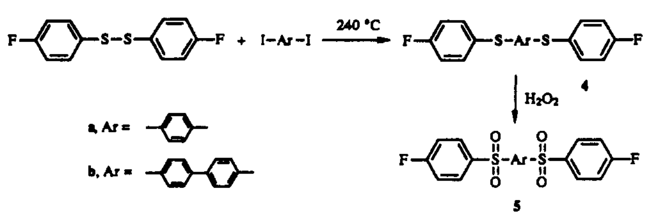
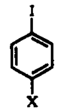
0022-3263/92/1957-2751$03.00/0

Scheme II



the reaction proceeded cleanly to yield the corresponding substituted sulfides in moderate to high yields. The results from the reactions of some functionalized disulfides and 1-iodonaphthalene are presented in Table I.

Similarly, the choice of iodoarenes is limited. Several iodoarenes when reacted with bis(4-fluorophenyl) disulfide failed to give the desired sulfide products in reasonable yields. In all cases, elemental iodine was formed and a complex mixture was obtained. For **3a**, it was observed by HPLC that in the early stages of the reaction there was 94% of a new product formed. But, further reaction led to a complex product mixture. This is probably due to the subsequent reaction of extruded sulfur from an excess of disulfide present in the reaction mixtures with the methyl group. In the case of **3b** and **3c**, the chloro and nitro groups were replaced, which initiated other side reactions. Failure to obtain a clean product from the reaction of **3d** and bis(4-fluorophenyl) disulfide is most likely caused by further iodination of the phenol with the resulting iodine at elevated temperatures. The reaction with **3e** acid proceeded very slowly.



| 3 | X |
|---|---|
| a | $CH_3$ |
| b | Cl |
| c | $NO_2$ |
| d | OH |
| e | $CO_2H$ |

Bis(4-fluorophenyl) disulfide also reacts with diiodoarenes such as 1,4-diiodobenzene and 4,4′-diiodobiphenyl, as diphenyl disulfide does,[2] to yield the corresponding bissulfides **4a** and **4b**. The bissulfide intermediates can either be isolated or further oxidized to the corresponding bissulfones with hydrogen peroxide (Scheme II). Thermal stability studies of bis(4-fluorophenyl) disulfide indicate that this disulfide starts to decompose (possible sulfur extrusion) at temperatures above 250 °C. Thus, the reaction temperature was kept at a maximum of 230 °C to ensure minimal or no decomposition. Due to these relatively high temperatures, the sublimable 1,4-diiodobenzene was kept in solution by using a high boiling solvent. We have found that diphenyl ether and diphenyl sulfide are suitable solvents. In nitrogen-containing solvents such as *N*-methylpyrrolidinone, *N*,*N*-dimethylacetamide, triphenylamine, and quinoline, no redox reactions occur between the diaryl disulfides and iodoarenes; however, under these conditions the disulfides are decomposed. High-boiling ketone and sulfone solvents like benzophenone and diphenyl sulfone cannot be used because they react with the disulfides.

The sulfones **5a** and **5b** are useful monomers for the synthesis of poly(arylene ether sulfone)s. 4,4-Bis(4-chlorobenzenesulfonyl)biphenyl, an analogue of **5b**, has been prepared by direct sulfonation of chlorobenzene with 4,4′-biphenyldisulfonyl chloride and used for making high-temperature polymers.[8] However, the sulfone **5a** could not be synthesized in the same way by sulfonation of fluorobenzene because of the unavailability of 1,4-benzenedisulfonyl chloride from the direct chlorosulfonation of benzene. Although this sulfone has previously been noted as a side product of another reaction,[9] it has never been synthesized on a preparative scale.

In conclusion, diaryl disulfides containing carboxy (**1i**), fluoro (**1e**), and chloro (**1f**) functionalities react cleanly with iodoarenes in diphenyl ether or neat at temperatures ranging from 220 to 280 °C to yield either symmetric or unsymmetric diaryl sulfides in good yields.

## Experimental Section

**General Method.** All compounds were purified by recrystallization or vacuum distillation, and the purity was confirmed by high-pressure liquid chromatography (HPLC). A Milton Roy HPLC instrument with a Spherisorb ODS2 reversed-phase column (250 × 4.6 mm, 5 $\mu$m) was used. The UV detector was set at 254-nm wavelength and the eluent was methanol at a flow rate of 1.0 mL/min.

**Bis(4-carboxyphenyl) Disulfide (1i).** An amorphous solid (yield, 50 g, 70%) with a melting point above 320 °C was obtained, according to the known procedure,[10] by treatment of a diazotized solution of 4-aminobenzoic acid (69 g) with a solution of sodium disulfide prepared by addition of sodium hydroxide (20 g) in water (50 mL) to a hot solution of sodium sulfide (130 g) in water (150 mL).[11]

**Bis(4-bromophenyl) Disulfide (1g).** It was prepared according to the known procedure[4] and purified by recrystallization from absolute ethanol: mp 92–93 °C.

**Bis(4-chlorophenyl) Disulfide (1f).** Iodine (17.55 g, 69 mmol) was added to a solution of 4-chlorothiophenol (20.0 g, 138 mmol) in acetic acid (45 mL), and the mixture was stirred at room temperature for 24 h. The dark brown reaction mixture was poured into a stirred concentrated aqueous solution of sodium bisulfite (300 mL). After 30 min, the solid was filtered by suction and rinsed with aqueous sodium bisulfite and water. The product was recrystallized from absolute ethanol to yield a pale yellow crystalline solid (19.16 g, 96.7%): mp 67.5–69.5 °C (lit.[5] mp 70 °C).

**Bis(4-fluorophenyl) Disulfide (1e).** (a) Bromine (6.5 g, 40.7 mmol) was added dropwise over a 5-min period to 4-fluorothiophenol (8.2 g, 64.1 mmol). The flask was set aside until cessation of HBr formation (~2 h). The contents in the flask were then distilled under vacuum. The product was obtained as a yellow liquid: 6.32 g (77.1%, 99.6% pure by HPLC); bp 141 °C (1.5 mmHg) (lit.[12] bp 131 °C (1.0 mmHg)).

(b) To a stirred suspension of (4-fluorophenyl)benzenesulfonyl chloride (31.04 g, 0.16 mol), sodium iodide (140 g, 0.934 mol), and tetra-*n*-butylammonium iodide (1.0 g) in methylene chloride (150 mL) was slowly added chlorotrimethylsilane (120 mL). The reaction mixture was stirred at room temperature for 2 days and diluted with methylene chloride (1.0 L). The mixture was filtered to remove salts, and the filtrate was washed with concentrated sodium bisulfite solution until the organic phase was free of iodine color. After further washing with concentrated sodium bicarbonate solution and water, the solvent was removed under vacuum at 40–60 °C. The residue was distilled under vacuum and the fraction with boiling point 140–150 °C (1.5 mmHg) was collected, which contained the product as a yellow liquid: 15.90 g (78.3%, 99% pure by HPLC).

**Bis(4-iodophenyl) Disulfide (1h).** To a stirred suspension of 4-aminophenyl disulfide (7.452 g, 30.0 mmol, technical grade)

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(8) Balanda, P. B.; Cummings, D.; Mohanty, D. K. *Polym. Preprints* **1990**, *31*(2), 671.

(9) Granoth, I.; Kalir, A.; Pelah, Z.; Bergmann, E. D. *Isr. J. Chem.* **1970**, *8*(4), 613.

(10) Smiles, S.; Harrison, D. C. *J. Chem. Soc.* **1922**, *121*, 2022.

(11) A reviewer has pointed out that the arylation of sodium disulfide with diazonium salts can be hazardous and explosions have been reported. See: Hogg, D., Sulphenic Acids and their Derivatives. *Comprehensive Organic Chemistry*; Pergamon Press: Oxford, U.K., 1979; Vol. 3, p 285.

(12) Brookes, R. F.; Cranham, J. E.; Greenwood, D.; Stevenson, H. A. *J. Sci. Food Agr.* 1957, *8*, 561.

in water (250 mL) was slowly added sulfuric acid (60 mL) at 0 °C, followed by the addition of a solution of sodium nitrite (4.5 g) in water (15 mL). The resulting yellow solution was stirred at 0 °C for 15 min and then slowly added to a solution of sodium iodide (20 g) and iodine (20 g) in water (30 mL) at 0 °C. During the addition methylene chloride (about 50 mL) was added to keep the products in solution. After being stirred at room temperature overnight, the mixture was diluted with methylene chloride (400 mL) and the two phases were partitioned. The organic phase was washed successively with concentrated sodium bisulfite solution and sodium bicarbonate solution and water. After the solution was dried over anhydrous sodium sulfate, the solvent was removed under vacuum. Purification of the residual yellow solids from ethanol afforded bis(4-iodophenyl) disulfide as a yellow amorphous solid: 8.25 g (58.5 %; >99% pure by HPLC); mp 122–123 °C (lit.[13] mp 124.5–125.5 °C).

**4-Fluorophenyl 1-Naphthyl Sulfide (2a).** Bis(4-fluorophenyl) disulfide (0.134 g, 0.53 mmol) and 1-iodonapthalene (0.572 g, 2.25 mmol) were placed in a Pyrex test tube (1.0 × 15 cm) which was heated to 270 °C in a sand bath. A gentle stream of nitrogen was introduced into the test tube through a Pasteur pipette. Completion was signaled when iodine was no longer produced (1–1.5 h). The reaction mixture was chromatographed on a silica gel column eluted with petroleum ether to give the product as a clear colorless liquid: 200 mg (74.6%); MS ($m/e$) 254 ($M^{\bullet+}$, 100); $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 6.97 (t, 2 H), 7.26 (q, 2 H), 7.42 (t, 1 H), 7.53 (m, 3 H), 7.86 (m, 2 H), 8.38 (m, 1 H).

**4-Chlorophenyl 1-Naphthyl Sulfide (2b).** Bis(4-chlorophenyl) disulfide (0.290 g, 1.01 mmol) and 1-iodonaphthalene (0.548 g, 2.16 mmol) were reacted as above. The reaction mixture was chromatographed on a silica gel column eluted with petroleum ether to afford the product as white, needle-like crystals: 320 mg (58%); mp 42–44 °C; MS ($m/e$) 270 ($M^{\bullet+}$, 100); $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 7.01 (d, $J$ = 8.6 Hz, 2 H), 7.11 (d, $J$ = 8.6 Hz, 2 H), 7.34–7.48 (m, 3 H), 7.63 (d, $J$ = 6.3 Hz, 1 H), 7.83 (m, 2 H), 8.26 (m, 1 H).

**4-(1-Naphthylthio)benzoic Acid (2c).** Bis(4-carboxyphenyl) disulfide (608 mg, 2.0 mmol), 1-iodonaphthalene (559 mg, 2.2 mmol), and diphenyl ether (1.0 mL) were placed in a test tube. The reaction mixture was heated at 260–270 °C for 3 h. Vigorous evolution of iodine was noted after heating for 10 min. The crude reaction mixture was chromatographed, eluting with chloroform. The product was isolated as a pale yellow solid: 400 mg (71.4%); mp 165–166 °C; $^1$H NMR (200 MHz, acetone-$d_6$/DMSO-$d_6$) $\delta$ 7.6 (d, 2 H), 8.0–8.2 (m, 4 H), 8.3–8.6 (m, 4 H), 8.8 (m, 1 H); MS ($m/e$) 280 ($M^{\bullet+}$, 100).

**1,4-Bis(4-fluorobenzenesulfonyl)benzene (5a).** Bis(4-fluorophenyl) disulfide (13.33 g, 0.0524 mol), 1,4-diiodobenzene (16.50 g, 0.050 mol), and diphenyl ether (10 mL) were placed in a 250-mL three-necked flask and heated to 220 °C in an aluminum heating block. The flask was equipped with a condenser, a magnetic stirrer, and a pipette through which a gentle stream of nitrogen was bubbled into the reaction mixture. The reaction was allowed to proceed for 4 days (69% yield by HPLC). Immediately thereafter, the contents were dissolved in acetic acid at 100 °C in a 500-mL Erlenmeyer flask. A 30-fold excess of 30% hydrogen peroxide (120 mL) was added in small portions with stirring after which the contents were left to react completely for 1 day at about 50 °C. The resulting pale beige, amorphous solid was filtered and rinsed with cold water. Yield: 15.95 g (81%, 85% pure by HPLC). After purification by recrystallization from acetic acid the pure sulfone was obtained in 61% yield: mp 258–260 °C (lit.[9] mp 260 °C); $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 7.2 (t, 4 H, Ar-H ortho to F), 7.9 (q, 4 h, Ar-H meta to F), 8.1 (s, 4 H, Ar-H ortho to sulfone). Anal. Calcd: C, 54.82; H, 3.07; S, 16.26; F, 9.63. Found: C, 54.88; H, 3.22; S, 16.17; F, 9.93.

**Acknowledgment.** This work was supported by the General Electric Co. and the Natural Sciences and Engineering Research Council of Canada.

**Registry No.** **1d**, 722-27-0; **1e**, 405-31-2; **1f**, 1142-19-4; **1g**, 5335-84-2; **1h**, 6345-64-8; **1i**, 1155-51-7; **2a**, 139564-31-1; **2b**, 127567-57-1; **2c**, 139564-32-2; **5a**, 139564-33-3; $p$-$FC_6H_4SO_2Cl$, 349-88-2; $p$-$N_2^+C_6H_4SSC_6H_4$-$p$-$N_2^+\cdot 2HSO_4^-$, 139564-34-4; 1-iodonaphthalene, 90-14-2; 4-aminobenzoic acid, 150-13-0; 4-chlorothiophenol, 106-54-7; 4-fluorothiophenol, 371-42-6; 1,4-diiodobenzene, 624-38-4.

**Supplementary Material Available:** $^1$H NMR spectra of **2a–c** (3 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(13) Lukashevich, V. O. *Dokl. Akad. Nauk S.S.S.R.* **1950**, *103*, 627; *Chem. Abstr.* **1950**, *50*, 5556i.

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# Stereoselective Synthesis of Tetrasubstituted α,β-Unsaturated Esters[†]

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*Received November 21, 1991*

The stereoselective synthesis of tetrasubstituted α,β-unsaturated esters[1] has met with limited success despite the number of methods available for their general synthesis.[2] While the Arbusov–Wittig[3] and the Peterson reactions[4] are still the best methods available today for their synthesis, they almost always yield a mixture of *E* and *Z* isomers. Furthermore, both methods give low yields when enolizable or bulky ketones are used as one of the substrates.

Although stereoselective synthesis of trisubstituted α,β-unsaturated esters has been reported,[5] these methods have not been extended to tetrasubstituted unsaturated esters. Recently in this laboratory, considerable efforts were directed toward developing a practical stereoselective synthesis of (*E*)-3,4-diphenyl-2-methyl-2-butenoic acid, ethyl ester (**1**), the precursor for the asymmetric synthesis of Darvon alcohol[6] viz. (2*S*,3*R*)-4-(dimethylamino)-1,2-diphenyl-3-methyl-2-butanol. The only reported synthesis[7] of this ester gives an isolated yield of 16%.[8] Our efforts to improve the yield of **1** by resorting to conventional methods available for the synthesis of unsaturated esters met with limited success. As an example, the Peterson reaction of lithio ethyl (trimethylsilyl)propionate[9] with deoxybenzoin give **1** in only 28% yield.

We now report a highly stereoselective synthesis of **1** by the direct $S_N2'$ alkylation of lithium diphenylcuprate[10] with ethyl 2-chloro-2-methyl-3-phenyl-3-butenoate[11] (**2**) in THF (Scheme I).

Ethyl 2-methyl-3-phenyl-2-butenoate[12] obtained as a mixture of *E* and *Z* isomers (65:35) was treated with $Ca(OCl)_2$/AcOH at ice-bath temperature to give the α-chloro-β,γ-unsaturated ester **2** in 92% isolated yield.[11]

Reaction of this halo ester **2** with $Ph_2CuLi$ in THF at ice-bath temperature gave exclusively the desired *E* ester **1** (no trace of *Z* isomer was detected by proton NMR or HPLC) in 89% isolated yield after silica gel flash column chromatography.

Extension of this reaction to other halo esters and dialkyl/diaryl cuprates gave in every instance exclusive $S_N2'$ alkylation, although stereoselectivity dropped slightly in most cases. The results are tabulated in Table I.

It is interesting to note that stereoselectivity drops when the less bulky lithium dimethylcuprate is used as the nucleophile and that the highest stereoselectivity is achieved

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[†] Presented in part at the 203rd National Meeting of the American Chemical Society, San Francisco.

0022-3263/92/1957-2753$03.00/0 © 1992 American Chemical Society