

Bis(4-methoxyphenyl)disulfide Formation through Copper Catalysts

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The formation of disulfide as a by-product in the reactions using the heterogeneous copper catalysts – metal (conductor) and oxides (semiconductor) is described, respectively the conditions of eliminating of this unwanted product. A lot of various methods and conditions have been tried and at some reactions also various types of copper catalysts (metal, copper(I) oxide, copper(II) oxide) were used.

Disulfides rise very easily by oxidation from their thiols. Using thiols for the synthesis is often a great problem, because disulfides may be very significant by-products. A lot of various methods of formation of bis(4-methoxyphenyl)disulfide from 4-methoxybenzenethiol (as the main product or as a by-product) have been described.

Some problem arose at the synthesis of aromatic thiols substituted by substituent with positive mesomeric effect in the benzene ring using various copper catalysts at the same time. These compounds were oxidized respectively dehydrogenized to their disulfides. The reactions of thiols and thiolates with transition metals and their ions in higher oxidation groups are very quick reactions [1]. The metal copper (conductor) and its oxides (semiconductors) show high oxidative respectively dehydrogenative activity. Especially copper semiconductors in which copper has oxidative number II have been used in organic technology for oxidation, oxychloration, and as mild dehydrogenative agents. They have been used *e.g.* for the production of methanol, butadiene, acrolein, methacrolein, acetic anhydride, vinyl acetate, dichloroethane, vinyl chloride [2]. 4-Methoxybenzenethiol was chosen as a model substance for easy oxidability resp. for its easy dehydrogenation. On this substrate the margin of ability of copper heterogeneous catalysts is tested to oxidize resp. dehydrogenize aromatic thiols with the substituent in position 4 of the aromatic core showing positive mesomeric effect on respective disulfides and thus to eliminate them from the main reaction.

In the lower mentioned works besides disulfide different quantities of the other oxidation products (sul-

fonic acids, sulfone) appeared. On the other hand, the reactions carried out on copper heterogeneous catalysts always lead to disulfide as the only product of oxidation resp. dehydrogenation.

4-Methoxybenzenethiol (*I*) was oxidized to its bis(4-methoxyphenyl)disulfide (*II*) (Scheme 1). This product was formed in 70 % yield by means of some methods. Preparation of thio derivatives and therefore various conditions of rising their disulfides are described in this paper. Bis(4-methoxyphenyl)disulfide could be synthesized in various synthetic pathways with various yielding: bis(4-methoxyphenyl)disulfide could be prepared as the main product by *e.g.* hydrogen peroxide [3] (98 %), sodium hypochlorite [4] (92 %), sodium iodate [5] (98 %), DMSO [6, 7] (98 %), sodium iodide [8] (97 %), copper(II) nitrate [9] (99 %), aqueous potassium hydroxide, potassium ferricyanide [10] (93 %), sodium perborate tetrahydrate [11, 12] (78 %), chromium trioxide [13] (76 %), and as a by-product using *e.g.* chlorotrimethylsilane [14] (80 %), 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2,2,2]octane bis(tetrafluoroborate) [15] (58 %), toluene-4-sulfonyl iodide [16] (37 %), *meso*-tetraphenylporphyrin [17] (13 %).

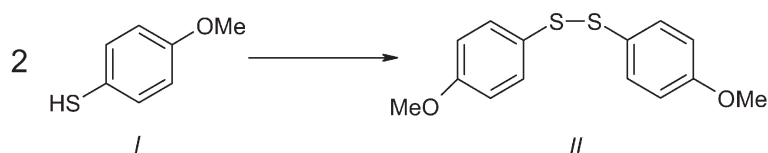
The experiment was realized in different solvents with atmospheric oxygen, under the atmosphere of nitrogen or argon. Different types of copper heterogeneous catalysts were tested with the copper component in different oxidizing state. The catalysts were applied in powder form, the smooth dispersion of the effective component was prepared by means of coagulative or impregnating procedures.

The used copper materials are specified in Table 1 and in Experimental.

Table 1. Conditions and Yields of Performed Reactions

Method	Conditions	Atmosphere	Yield/%
1a	Na, ethanol, Cu ^a	Oxygen	51
1b	Na, ethanol, Cu ^a	Nitrogen	43
2a	KOH(aq), Cu ^a	Oxygen	69
2b	KOH(aq), Cu ^a	Nitrogen	63
3a	K ₂ CO ₃ , Et-Me ketone, Cu ^a	Oxygen	56
3b	K ₂ CO ₃ , Et-Me ketone, Cu ^a	Nitrogen	49
3c	K ₂ CO ₃ , Bu-Me ketone, Cu ^a	Oxygen	72
3d	K ₂ CO ₃ , Bu-Me ketone, Cu ^a	Nitrogen	65
4a	Bu-Me ketone, Cu ^a	Nitrogen	49
4b	Bu-Me ketone, Cu ^b	Nitrogen	32
4c	Bu-Me ketone, Cu ^b	Argon	23
5	Bu-Me ketone, Cu ₂ O ^c	Argon	9
6	Bu-Me ketone, CuO ^d	Argon	27
7	K ₂ CO ₃ , DMF, Cu ₂ O ^c	Argon	5
8	Xylene, Cu ₂ O ^c	Argon	1

a is wire, *b* metal on "silicate" support, *c* is powder, *d* oxide on "silicate" support.

*Scheme 1*

The reactions were performed under various conditions and the yields are mentioned in Table 1. All the reactions were carried out on copper heterogeneous catalysts with copper component in different oxidation state: Cu⁰ (metal – conductor), Cu^I (semiconductor), Cu^{II} (semiconductor). On the basis of the experiments carried out it is evident that the activity of copper in the form of metal and semiconductor was confirmed by relatively low temperatures (ethanol 78 °C). Using the same type of catalyst the yield of disulfide is higher if the temperature is higher. Cu^{II} in accordance with all assumptions appears to be the most efficient dehydrogenative catalyst. Cu^I has the least dehydrogenative activity. Using the same type of catalyst the yield of disulfide is higher in polar solvents. If the precursor is used in the form of salt (sodium or potassium) the yields of disulfide are higher. The reaction process is facilitated by atmospheric oxygen (parallel oxidation reaction).

Carried out experiments proved that the lowest percentage of the formation of disulfide from thiophenols with the substituent in position 4 of the aromatic ring is achieved when using copper(I) oxide as heterogeneous catalyst. Inert atmosphere and using anhydrous nonpolar solvents help the reduction but it is not decisive.

EXPERIMENTAL

All organic solvents used for the synthesis were of anal. grade. The solvents were dried and freshly

distilled under argon atmosphere. Melting points were measured on Kofler block BOËTIUS PHMK 05 (VEB KOMBINAT NAGEMA, VEB Wagetechnik RAPIDO, Radebeul, Germany).

Flash chromatography was realized on Silica gel Kieselgel 60 (Merck). TLC was performed on Silufol UV 254 plates (Kavalier, Votice). Silica gel plates, besides detection under UV 254, were visualized in addition to the solution of bromothymol blue in NaOH (proof of thiol, sulfide, disulfide). Infrared spectra were measured in KBr pellets on IR-spectrometer Nicolet Impact 400. ¹H and ¹³C NMR spectra were recorded on Varian Mercury – Vx BB 300 (299.95 MHz – ¹H and 75.43 MHz – ¹³C) spectrometer (Bruker, Karlsruhe, Germany). Chemical shifts reported are given relative to internal Si(CH₃)₄.

Copper catalyst Cu^a – wire copper (ThermoQuest Italia S.p.A., code 338 35310), Cu₂O^c – powder of 97 % purity (Sigma-Aldrich, code 20,882-5), CuO^d – CHEROX 46-00, catalyst contents 40 % CuO on "silicate" support: SiO₂, MgO, CaCO₃ (Chemopetrol a.s., Litvínov), Cu^b – activated catalyst CHEROX 46-11 (the precursor of this catalyst is a product of Chemopetrol a.s., Litvínov) were used. Suspension of activated powder catalyst in an organic solvent was prepared. The catalyst is formed, metallic copper being finely dispersed on silicate support. CHEROX 46-11 was activated in organic solvent in autoclave under hydrogen atmosphere under the temperature of 180 °C and pressure 5 MPa.

Flash chromatography on silica gel provided bis(4-

methoxyphenyl)disulfide as lightly yellow solid compound, m.p. = 39.0–39.5 °C, R_f = 0.49 in petroleum ether–diethyl ether (φ_r = 3 : 1); thiol R_f = 0.88. IR spectrum (KBr), $\tilde{\nu}/\text{cm}^{-1}$: 1249 (C—O), 1590 (Ph), 2835 (O—CH₃), 2956 (CH₃). ¹H NMR spectrum (300 MHz, DMSO), δ : 7.38–7.42 (m AA'BB', 4H, CH_{arom}), 6.94–6.96 (m AA'BB', 4H, CH_{arom}), 3.76 (s, 3H, CH₃). ¹³C NMR spectrum (75 MHz, DMSO), δ : 159.92, 132.31, 127.14, 115.23, 55.53 corresponds to literature data. Yields obtained by various methods are given in Table 1.

Bis(4-methoxyphenyl)disulfide (II)

Method 1: Sodium (0.23 g) was dissolved in 20 cm³ of dry ethanol, then 4-methoxybenzenethiol (1.0 g; 8 mmol) was dissolved there, Cu^a (3.0 g) was added and the reaction mixture was stirred and refluxed for 3 h in the open air (1a) or under nitrogen (1b). Then the reaction mixture was filtered while hot and the filtrate evaporated *in vacuo*.

Method 2: Potassium hydroxide (1.4 g) was dissolved in 12 cm³ of H₂O, 4-methoxybenzenethiol (1.0 g; 8 mmol) and Cu^a (3.0 g) were added and the reaction mixture was stirred and refluxed for 3 h in the open air (2a) or under nitrogen (2b). Then the reaction mixture was extracted with ether and the combined extracts were dried over MgSO₄ and evaporated *in vacuo*.

Method 3: K₂CO₃ (0.7 g) was suspended in freshly distilled 20 cm³ of ethyl methyl ketone, respectively in butyl methyl ketone and 4-methoxybenzenethiol (1.0 g; 8 mmol) and Cu^a (3.0 g) were added. The reaction mixture was stirred and refluxed for 3 h in the open air (3a, 3c) or under nitrogen (3b, 3d). Then the reaction mixture was filtered while hot and the filtrate evaporated *in vacuo*.

Method 4: 4-Methoxybenzenethiol (1.0 g; 8 mmol) was dissolved in freshly distilled dry butyl methyl ketone (20 cm³) and copper catalyst was added; Method 4a: Cu^a (3.0 g); Method 4b, 4c: Cu^b (0.2 g). The reaction mixture was stirred and refluxed for 3 h (4a) and for 1 h (4b, 4c) under nitrogen or argon. Then the reaction mixture was filtered while hot and the filtrate evaporated *in vacuo*.

Methods 5, 6: 4-Methoxybenzenethiol (1.0 g; 8 mmol) was dissolved in freshly distilled dry butyl methyl ketone (20 cm³) and copper catalyst was added; Method 5: Cu₂O^c (1.0 g), Method 6: CuO^d (0.2 g). The reaction mixture was stirred and refluxed for 1 h under argon. Then the reaction mixture was filtered while hot and the filtrate evaporated *in vacuo*.

Method 7: K₂CO₃ (0.7 g) was suspended in 20 cm³ of freshly distilled dry DMF (20 cm³), 4-methoxybenzenethiol (1.0 g; 8 mmol) was dissolved

there and Cu₂O^c (1.0 g) was added. The reaction mixture was stirred and refluxed for 1 h under argon. Then the reaction mixture was filtered while hot and the filtrate evaporated *in vacuo*.

Method 8: 4-Methoxybenzenethiol (1.0 g; 8 mmol) was dissolved in freshly distilled dry xylene (20 cm³) and Cu₂O^c (1.0 g) was added. The reaction mixture was stirred and refluxed for 1 h under argon. Then the reaction mixture was filtered while hot and the filtrate evaporated *in vacuo*.

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