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# Selective and Simple Phase Transfer Catalyzed Synthesis of Disulfides from Thiols†

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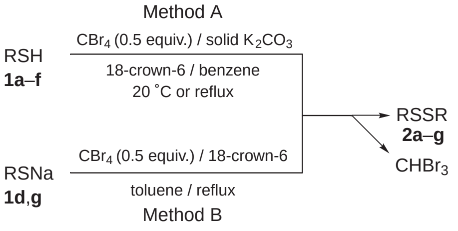
Two novel methods of synthesis of disulfides from thiols or their Na salts in the phase transfer catalytic system $CBr_4$/18-crown-6/benzene or toluene are developed and the products isolated in 67–88% yields.

Synthesis of disulfides from thiols is an important process from both synthetic and biochemical points of view.[1] The main type of these reactions is the oxidation of thiols in the presence of molecular oxygen,[2–4] DMSO,[5,6] metal oxide,[7] metal ions,[8] nitric oxide,[9] sodium perborate,[10] thallium(III) acetate,[11] bromine,[12] iodine,[13] borohydride exchange resin,[14] calcium hypochlorite and silica gel,[15] DMSO/alumina,[16] and $NaIO_3$/alumina,[17] $MnO_2$.[18]

**Table 1** Synthesis of disulfides (**2a–g**) from thiols (**1a–g**)

| Compound | R | Method | $T/{}^\circ C$ | $t$/h | Isolated yield(%) | Yield(%) |
|---|---|---|---|---|---|---|
| **1a** | $(CH_3)_2CH$ | A | 20 | 6 | 83 | 82[3] |
| **1b** | $CH_3(CH_2)_4$ | A | 20 | 6 | 79 | 85[19] |
| **1c** | Ph | A | 20 | 6 | 78 | 82[3] |
| **1d** | $PhCH_2$ | A | 20 | 7 | 83 | 89[11] |
| **1d** | $PhCH_2$ | B | 110 | 3 | 88 | 89[11] |
| **1e** | 2-pyridyl | A | 80 | 6 | 67 | 75[10] |
| **1f** | 2-pyrimidyl | A | 80 | 5 | 80 | 85[20] |
| **1g** | 8-quinolyl | B | 110 | 3 | 68 | —[21] |

We have developed two novel and simple phase transfer catalytic (PTC) methods for the synthesis of aliphatic, aromatic and heterocyclic disulfides (**2a**–**g**) from the corresponding thiols (**1a**–**g**) (see Experimental). Both methods included oxidation of thiols (**1a**–**f**) by $CBr_4$/solid $K_2CO_3$/18-crown-6/benzene (method A, Scheme 1) or by sodium thiolates (**1d**,**g**) by $CBr_4$/18-crown-6/toluene (method B) (Table 1). In all cases bromoform was formed. This suggests that the reactions of dimerization proceed *via* brominated thiols (RSBr), not detectable due to their rapid decomposition.



**Scheme 1**

The structure of the disulfides was confirmed by data of $^1H$ NMR and mass spectra.

Thus, two simple, convenient and general methods for the synthesis of disulfides, especially for heterocyclic ones, which are difficult to obtain by other methods, have been developed.

## Experimental

GC analysis was performed on a Chrom-5 instrument equipped with a flame-ionization detector using a glass column packed with 5% OV-101/Chromosorb W-HP (80–100 mesh) (1.2 m × 3 mm). Thiols, carbon tetrabromide and 18-crown-6 were Fluka products.

*Typical Procedure. Synthesis of* **2**. *Method A*.—Finely powdered $K_2CO_3$ (1.66 g, 12 mmol) was added to a solution of **1a**–**f** (4 mmol), $CBr_4$ (0.663 g, 2 mmol), 18-crown-6 (52 mg, 0.2 mmol) in benzene (7 ml). The reaction mixture was stirred 5–7 h at room temperature (under reflux for the thiols **1e**,**f**) (GC and GC/MS control). Any solid substance was filtered off and the filtrate was evaporated under reduced pressure. The residue was purified by column chromatography using benzene as eluent for disulfides **2a**–**d** and benzene/ethyl acetate (1 : 1) for **2e**–**f**.

*Method B*.—Na-salt of thiols **1d**,**g** (2.5 mmol) was added to the solution of $CBr_4$ (0.41 g, 1.25 mmol) and 18-crown-6 (66 mg, 0.25 mmol) in toluene (4 ml) and the reaction mixture was boiled under reflux for 3 h. Any solid substance was filtered off and the filtrate was evaporated at reduced pressure. The residue was purified by column chromatography on silica gel.

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