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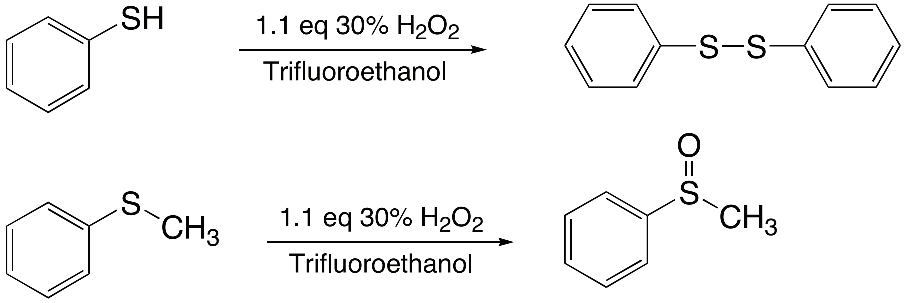
MILD AND SELECTIVE OXIDATION OF SULFUR COMPOUNDS IN TRIFLUOROETHANOL: DIPHENYL DISULFIDE AND METHYL PHENYL SULFOXIDE

[(Disulfide, diphenyl- and Benzene, (methylsulfinyl)-)]



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Checked by Jonathan Tripp and Dennis P. Curran.

1. Procedure

A. Diphenyl disulfide. In a 100-mL, round-bottomed flask equipped with a magnetic stirrer are placed 11.0 g (10.25 ml, 0.1 mol) of benzenethiol and 50 mL of trifluoroethanol (Note 1). The mixture is stirred and cooled in an ice bath (Note 2) and 12.5 mL (3.73 g, 0.11 mol) of 30% aqueous hydrogen peroxide (Note 3) is added dropwise over a period of 15 min through an addition funnel. After completion of the addition, the ice bath is removed and the reaction mixture is allowed to stir at room temperature for 24 h. Diphenyl disulfide is sparingly soluble in trifluoroethanol and precipitates out of solution. The solids are collected on a Buchner funnel and dried under vacuum to afford 10.6 g of diphenyl disulfide (97%) (Note 4). Sodium sulfite 2.52 g (0.02 mol) is added to the mother liquor to decompose the excess peroxide and the mixture is heated in a water bath at 50 °C for 30 min. A starch iodide test is negative. The liquid is transferred to a 100-mL, round-bottomed flask, fitted with a distillation unit having a Vigreux column (5 cm). The flask is heated in an oil bath and the solvent is distilled to recover the trifluoroethanol (Note 5).

B. Methyl phenyl sulfoxide. To a 100-mL, round-bottomed flask equipped with a magnetic stirrer are added 12.4 g (0.1 mol) of thioanisole and 50 mL of trifluoroethanol (Note 1). The mixture is stirred and cooled in an ice bath (Note 6) and 12.5 mL (3.73 g, 0.11 mol) of 30% aqueous hydrogen peroxide is added dropwise over 30 min using an addition funnel (Note 7). After completion of the addition, the ice bath is removed and the reaction mixture is stirred at room temperature for 8 h (Note 8). Sodium sulfite (2.52 g, 0.02 mol) is added to decompose the excess hydrogen peroxide and the mixture is heated in a water bath at 50 °C for 30 min (a starch iodide test is negative). The flask is fitted with a distillation unit having a Vigreux column (5 cm) and heated with an oil bath to remove the solvent by distillation (Note 5). Ether (100 mL) is added to the residue and the mixture is dried over 28 g of magnesium sulfate. Solids are removed by filtration and washed with ether (2 × 50 mL). The combined filtrate and washings are concentrated under vacuum to afford 14.9 g of a slightly yellow oil that crystallizes upon cooling in an ice bath. The crude sulfoxide is transferred to a 25-mL distillation flask with the aid of a small amount of dichloromethane. After removal of solvent, simple short path distillation (Note 9) of the crude product affords 12.8 g (91%) of pure methyl phenyl sulfoxide (Notes 10, 11).

2. Notes

1. Both benzenethiol and phenyl methyl sulfide are sparingly soluble in trifluoroethanol.
2. During the addition of hydrogen peroxide, the temperature of the reaction mixture increases. The submitters report that the addition can be done carefully without an ice bath and that no overoxidation is observed.
3. 30% Aqueous hydrogen peroxide is purchased from Fluka Chemical Company and handled with caution.
4. The product's physical and spectroscopic properties are: mp 52-53 °C; 1H NMR δ: 7.5-7.6 (m, 10 H); MS m/z 218 (M+), 109.
5. Initially trifluoroethanol is obtained (37-38 mL, bp 77-79 °C). Subsequently, a fraction (11-13 mL), containing a mixture of trifluoroethanol and water, is collected at 85-87 °C. The 19F NMR spectrum of this fraction was identical to that of trifluoroethanol. The recovered

trifluoroethanol can be reused for the oxidation of sulfides.

6. When the addition of hydrogen peroxide is carried out at room temperature, the submitters reported that the reaction is exothermic and that 3-4% of the sulfone is formed.

7. When 2 equivalents of hydrogen peroxide are used, the submitters report that 0-2% of the sulfone is obtained. When phenyl methyl sulfoxide is oxidized under similar conditions, no sulfone is observed, even after 24 h.

8. The submitters report that oxidation of phenyl methyl sulfide to phenyl methyl sulfoxide also can be achieved selectively by using hexafluoroisopropyl alcohol (HFIP) as the solvent; the reaction is complete after 10 min.

9. The technique of adding a small amount of activated carbon to the distillation pot afforded a colorless distillate.

10. A fore-fraction is not obtained.

11. The product's physical and spectroscopic properties are: bp 78-79 °C (0.1 mm); 1H NMR (CDCl3) δ: 2.7 (s, 3 H); 7.5-7.7 (m, 5 H); MS m/z 140 (M+), 125, 97, 77.

3. Discussion

Methods of preparation. Diphenyl disulfide can be prepared by the action of hydrogen peroxide in acidic or basic media,[2] iodine-hydrogen iodide,[3] Sm/BiCl3 in water,[4b] FeCl3/NaI,[4c] and by using bromine-aqueous potassium hydrogen carbonate.[4] Methyl phenyl sulfoxide has also been prepared from thioanisole by the action of hydrogen peroxide in methanol,[5] mCPBA,[5b] peroxytrifluoroacetic acid[6] and sodium periodate.[7]

Merits of preparation. Selective oxidative transformation of thiols to disulfides is of interest for both biological[8] and synthetic reasons.[2] Most of the existing methods involve the use of metal catalysts or halogenated reagents, which lead to the formation of side-products.

Organic sulfoxides are useful intermediates for the construction of many chemically and biologically significant molecules.[9] Most of the current methods for the oxidation of sulfides to sulfoxides[10] suffer from over-oxidation to sulfones. Even when controlling the reaction temperature, it is difficult to avoid over-oxidation in most of the reported procedures.

The present procedure is based on the use of fluoroalkyl alcohols as solvents in oxidation reactions. The method is efficient and versatile, and produces disulfides and sulfoxides under mild conditions. These reactions have also been developed using hexafluoroisopropyl alcohol (HFIP) as solvent with a large variety of substrates (alkyl sulfides, alkyl thiols, vinyl sulfides, fluorinated vinyl sulfides, thioglucosides) by Bégué et al.[11,12] Replacement of HFIP with trifluoroethanol, a more common and less expensive solvent, also allows the use of mild conditions and affords high yields of disulfides and sulfoxides without contamination. 30% Aqueous hydrogen peroxide is inexpensive and, since water is the sole byproduct, this method is environmentally friendly.

Cooling is advisable during the addition of hydrogen peroxide, but the remainder of the reaction can be carried out at ambient temperature. This method may be useful for large-scale reactions since trifluoroethanol can be recovered.

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Appendix

Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

Benzenethiol (8,9); (108-98-5)
Diphenyl disulfide: Disulfide, diphenyl (9); (882-33-7)
Hydrogen peroxide (H2O2) (9); (7722-84-1)
Methyl phenyl sulfoxide: Benzene, (methylsulfinyl)- (9); (1193-82-4)
Thioanisole: Benzene, (methylthio)- (9); (100-68-5)
Trifluoroethanol: Ethanol, 2,2,2-trifluoro- (6,8,9); (75-89-8)