J. Indian Chem. Soc.,
Vol. LX, June 1983, pp. 570-571

Some Oxodisulfide Cleavage Reactions to form Disulfides and Trisulfides

P. K. SRIVASTAVA*, RAMESH CHANDRA and (MISS) MADHU BALA GUPTA

Department of Chemistry, Banaras Hindu University, Varanasi-221 005

Manuscript received 21 January 1982, accepted 20 May 1983

Some disulfide and trisulfide sulfinate salts were synthesized by "oxodisulfide cleavage" and tested as antithyroid agents.

RECENTLY the nature of reactions of disulfide, which for convenience are called "oxodisulfide cleavage", have been studied[1,2]. These investigations prompted us to extend this reaction with other thiols to synthesise a few more disulfides and to screen them for antithyroid activity. It was our hope that these sulfinate salts might have better solubility, adsorption, transportation and distribution in the body.

Results and Discussion

The present communication deals with the synthesis of di- and trisulfides having sulfinate moiety in 1,8 relationship on a napthyl system (I) and a 2,2'-relationship on a biphenyl system (II). Several thiols were used as their thiolate salts for synthesising disulfides. Disulfides were prepared by adding equimolar quantities of sodium salt of thiol in methanol to corresponding dioxide in the same solvent and trisulfides were prepared by adding Na_2S to the related dioxide in methanol. These sulfinate salts obtained as hydrates recyclised to their respective dioxides. This problem was solved by redissolving the sulfinate salts in methanol and reprecipitating by ether. Hydration was more of a problem with trisulfides than with disulfides, perhaps because of the two sulfinate moiety per molecule in the former rather than one. The structures of these compounds were confirmed on the basis of ir spectra and elemental analysis. The ir spectra (nujol) show characteristic strong bands at ~1640, ~ 3400 cm^{-1} (H_2O), ~ 970, ~ 1020 cm^{-1} ($-SO_2$).

All disulfide and trisulfide sulfinate salts were tested for antithyroid activity by using the method of Rawson *et al*[5]. Thiouracil was used as the standard compound. From the experimental data (Tables 1-3), it was observed that none of the compounds appeared to be more active than thiouracil.

The overall reactions are as follows :

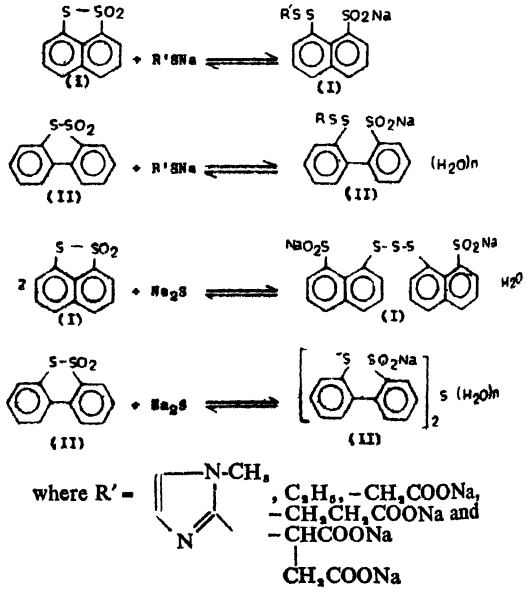
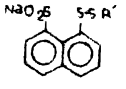


TABLE 1—CHARACTERISTIC OF SODIUM-8-(SUBSTITUTED DITHIO)-NAPTHALENE-1-SULPHINATES



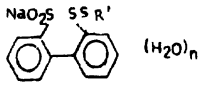
Sl. No.	R'	m.p.[d] °C	Molecular formula	Approximate estimated activity in rats (Thiouracil = 1.00)
1.	$-C_4H_5N_2$	187-88	$C_{14}H_{14}N_2NaO_2S_2$	1.00
2.	$-C_2H_5$	173-74	$C_{12}H_{13}NaO_2S_2$	0.86
3.	$-CH_2COOH$	159-60	$C_{12}H_{10}Na_2O_6S_2$	0.86
4.	$-CH_2CH_2COOH$	232-33	$C_{13}H_{12}Na_2O_6S_2$	0.97
5.	$-CHCOOH$ CH_2COOH	217-18	$C_{14}H_{12}Na_2O_7S_2$	0.82

d = melting with decomposition ; all compounds gave satisfactory elemental analyses ; yield ranged between 56 to 70%.

Experimental

All melting points were recorded on a Kofler hot stage apparatus and are uncorrected. IR spectra were measured in nujol on a Beckman IR-20 spectrophotometer.

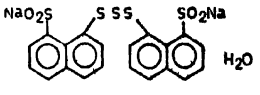
TABLE 2—CHARACTERISTIC OF SODIUM-2'-(SUBSTITUTED DITHIO)-2-BIPHENYL SULPHINATES



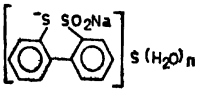
Sl. No.	R'	m.p.[d] °C	Molecular formula	Approximate estimated activity in rats (Thiouracil = 1.00)
6.	$-C_4H_5N_2$	178-79	$C_{16}H_{15}N_2NaO_3S_3$	0.98
7.	$-C_2H_5$	191-92	$C_{14}H_{15}NaO_3S_3$	0.99
8.	$-CH_2COOH$	163-64	$C_{14}H_{13}NaO_5S_3$	0.96
9.	$-CH_2CH_2COOH$	240-41	$C_{16}H_{14}Na_2O_6S_3$	0.91
10.	$-CHCOOH$ $\vert$ CH_2COOH	155-56	$C_{16}H_{12}Na_2O_7S_3$	0.97

d = melting with decomposition ; all compounds gave satisfactory elemental analyses ; yield ranged between 64 to 71%.

TABLE 3—CHARACTERISTIC OF DISODIUM 8,8'-TRITHIO*bis*-(1-NAPTHALENE SULPHINATE) (11) AND DISODIUM 2',2'-TRITHIO*bis*-(2-BIPHENYL SULPHINATE) (12)



11



12

Sl. No.	m.p [d] °C	Molecular formula	Approximate estimated activity in rats (Thiouracil = 1.00)
11.	230-31	$C_{20}H_{12}Na_2O_4S_6$	0.89
12.	178-79	$C_{16}H_{12}N_2NaO_3S_3$	0.82

d = melting with decomposition ; all compounds gave satisfactory elemental analyses ; yield ranged between 72 to 88%.

Naphthol (1, 8-cd)-1,2-dithiole-1,1-dioxide : It was prepared by the procedure of Zweig and Hoffman[3].

Dibenzo(c,e)-o-dithiin-5,5-dioxide : It was prepared by the known method[4].

Sodium 8-(1-methylimidazol-2-yl-dithio)-naphthalene-1-sulfinate : Napthol (1,8-cd)-1,2-dithiole-1, 1-dioxide (1.11 g ; 5.0 mmole) was dissolved in methanol (100 ml) and added dropwise with stirring during 0.5 hr to a solution, prepared by dissolving sodium (0.11 g ; 5.0 m mole) in methanol (10 ml) and mixing methimazole (0.56 g ; 4.95 mmole). Dry acetone was added until no more precipitate appeared. A solid product separated which was purified by adding ether to its solution in methanol at 0.5° until no more precipitate formed, yield 1 g (56%), m.p. 187-88.

Similarly, other sodium 8-(substituted dithio)-napthalene-1-sulphinate salts were prepared. Results are recorded in Table 1.

Sodium 2' - [(1-methylimidazolyl-2-yl)-dithio] 2-biphenyl sulfinate[2] : Dibenzo (c, e)-*o*-dithiin-5, 5-dioxide (1.24 g ; 5.0 mmole) was suspended in methanol (10 ml) and mixed intimately with methimazole (0.57 g ; 5.0 mmole) in methanol (10 ml). The reaction mixture was cooled at 0°. A solution of sodium (0.11 g ; 5.0 mmole) in methanol (10 ml) cooled at 0° was added dropwise to the reaction mixture. A large excess of ether (400 ml) was added to precipitate the sulfinate salt. It was dried for 25 hr at 25°, yield 1.31 g (64%), m.p. 178-79°.

Similarly, other sodium 2'-(substituted dithio)-2-biphenyl sulfinates were prepared. Results are recorded in Table 2.

*Disodium 8,8'-trithio*bis-(*1-napthalene sulfinate*)[2] (11) : A solution of commercial $Na_2S.9H_2O$ (2.9 mmole) in methanol (5 ml) was added slowly to naphthol (1,8-cd)-1,2-dithiole-1,1-dioxide (1.30 g ; 5.80 mmole) in methanol (25 ml) at 25° with stirring during 30 min. After the reaction was complete, dry ether (600 ml) at 0° was added to it. A white product was obtained and dissolved in a little methanol. It was further precipitated by adding dry ether to this solution, yield 1.28 g (72%), m.p. 230-31°.

Analytical results of the above salts are recorded in Table 3.

*Disodium 2',2'-trithio*bis (*2-biphenyl sulfinate*)[2] (12) : A solution of commercial $Na_2S.9H_2O$ (2.50 mmole) in methanol (10 ml) was added slowly to a suspension of dibenzo-(c,e)-*o*-dithiin-5,5-dioxide (1.24 g ; 5.0 mmole) in methanol (20 ml) at 0-5° with stirring. After the addition was complete ether (400 ml) was added at 0° when a white precipitate was obtained. It was decanted, dried, redissolved in methanol (3 ml) and reprecipitated with ether, yield 1.50 g (88%), m.p. 178-79°.

Analytical results of the above salt are recorded in Table 3.

Acknowledgement

The authors are thankful to UGC and CSIR, New Delhi for financial assistance.

References

1. P. K. SRIVASTAVA and L. FIELD, *J. Org. Chem.*, 1972, 37, 4196.
2. P. K. SRIVASTAVA and L. FIELD, *J. Med. Chem.*, 1975, 18, 798.
3. A. ZWEIG and A. K. HOFFMANN, *J. Org. Chem.*, 1965, 30, 3997.
4. H. J. BARBER and S. SMILES, *J. Chem. Soc.*, 1928, 1141.
5. R. W. RAWSON, D. A. MCGINTY *et al*, *J. Pharmacol. Exptl. Therap.*, 1965, 93, 240.