[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

THE PREPARATION AND RELATIVE REACTIVITIES OF MANY-MEMBERED CYCLIC DISULFIDES

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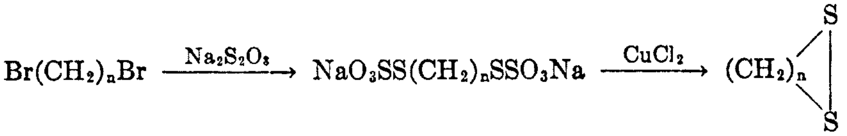
It has recently been shown that cyclic 1,2-disulfides (I) can be opened catalytically to rubbery disulfide polymers without any substantial volume change (1). The resulting interest in rings of this type has led to the present search for an improved synthetic method.

Davis and Fettes have shown that steam-distillation of a polymeric disulfide latex results in the slow removal of the cyclic monomer (2). This is the only method previously reported by which a series of cyclic disulfides of many ring members might be successfully prepared. In the present work, attempts to cyclize polymethylene Bunte salts (II) by oxidation with iodine or hydrogen peroxide in aqueous or aqueous-alcoholic solution failed in every case (3, 4). The only products that were obtained were polymeric disulfides. This result was not changed by decreasing the concentration of the reactant (Bunte salt). It was discovered, however, that these salts react with aqueous cupric chloride to produce molecular complexes (from II when n = 2, 3, 4 or 5) or clear aqueous solutions (from II when n = 6, 7, 8, 9 or 10), from which the desired cyclic disulfides can be isolated by steam-distillation. The constitution of the yellow or orange molecular complexes could not be determined, nor is the nature of the reaction involved clearly understood. It is significant that ferric and stannic chlorides are as effective in producing dibenzyl disulfide from sodium benzylthiosulfate as is cupric chloride. Zinc chloride is approximately 50% as effective. These observations would indicate that oxidation is not a necessary part of the reaction. The action of the metal cation may consist in an electrophilic attack on the bivalent sulfur atom, thereby weakening the vulnerable sulfur-sulfur bond.



II I

The cyclic disulfides prepared are listed in Table I together with analytical data and an indication of their relative reactivities in the sense of ring opening and polymer formation. The relative yields are roughly comparable to those generally obtained from other cyclization reactions (5). It is presumed that this comparison will remain valid, and that the yields will increase as ring size is increased beyond twelve atoms. The increase in yield which results upon replacement of a methylene group by an oxygen atom is clearly visible in the case of 1,4,5-oxadithiepane and, again, is in conformity with investigations on other ring systems (5). 1,3-Dioxa-6,7-dithionane is somewhat soluble in water and this may account for the lower yield of this substance.

TABLE I

ANALYTICAL DATA AND RELATIVE REACTIVITIES OF CYCLIC DISULFIDES, R—S—S

NO ATOMS IN RING	R	YIELD, %	REACTIVITY (1 = least reactive)	B.P., °C.	MOLECULAR WEIGHT		S	
					Calc'd	Found	Calc'd	Found[a]
4	$-(CH_2)_2-$	trace	6	-	-	–[b]	-	–[b]
5	$-(CH_2)_3-$	60	5+	-	106	150.5[c]	60.4	60.0
6	$-(CH_2)_4-$	22	5	*Ca.* 60 at 5 mm.	120	130	53.4	52.9
7	$-(CH_2)_5-$	13	1	57–60 at 5 mm.	134	136.5	47.8	47.4
8	$-(CH_2)_6-$	4	5	-	148	153	-	–[d]
9	$-(CH_2)_7-$	2	1	*Ca.* 70 at 5 mm.	162	169	39.5	38.8
10	$-(CH_2)_8-$	3	5	-	176	168	36.4	36.7[e]
11	$-(CH_2)_9-$	0.2	1	-	-	–[f]	-	–[f]
12	$-(CH_2)_{10}-$	2-3	5+	-	-	–[g]	31.4	31.5
7	$-(CH_2)_2\diagdown$ $\rangle O$ $-(CH_2)_2\diagup$	50	4	55–56 at 3 mm.	136	133	47.1	46.4
9	$-(CH_2)_2-O\diagdown$ $\rangle CH_2$ $-(CH_2)_2-O\diagup$	1.0	1	*Ca.* 70 at 5 mm.	-	–[h]	38.6	38.3

[a] Sulfur analyses were done by the method of Cheyney, *Ind. Eng. Chem., Anal. Ed.*, **13**, 238 (1941), except where otherwise noted. [b] Less than 1 mg. of polymeric material was obtained from 0.2 moles of reactant. [c] Trimethylene disulfide could not be isolated as the monomeric oil. Its molecular weight was determined by passing the uncondensed steam mixture through benzene. The monomeric material is stable in benzene solution. The freezing-point of an aliquot of the benzene solution was determined and the solute weighed after evaporation to the polymeric residue. [d] Hexamethylene disulfide polymerized to a sticky rubber on standing. This material could not be further purified, and the commercial analysis proved unsatisfactory. [e] This analysis was done commercially. [f] The trace of oil obtained was too small to be readily purified. The commercial analysis proved unsatisfactory. [g] Decamethylene disulfide polymerized almost spontaneously. [h] The trace of oil obtained was too small for a molecular weight determination.

The chemical reactivity of these cyclic disulfides can be estimated by the readiness with which their rings are opened to form linear polymers. All the rings listed in Table I polymerize within a few hours in contact with a trace of aluminum chloride (1). The five- and twelve-membered rings are obtained as oils which immediately become viscous and polymeric when the solvent is removed. The six-, eight- and ten-membered rings and the cyclic ether disulfide are stable if they are separated directly from the distillate; if they are extracted from the distillate with ether they polymerize slowly on standing when the solvent has been removed. The seven-, nine-, and eleven-membered rings and the 1,3-dioxa-6,7-dithionane are stable indefinitely even after treatment with ether. The action of ether is presumed to be due to the presence of peroxides.

The ease with which the five- and six-membered rings are opened is unexpected. These rings should resemble cyclopentane and cyclohexane in structure, for the C—S—S angle is very nearly tetrahedral, 107 ± 3° (6). The S—S bond distance, 2.05 Å, is considerably larger than the C—C distance, but construction of the disulfide models indicates that this is not sufficient to induce much strain into the ring. It is believed that the relative reactivities of the cyclic disulfides may be taken as evidence for restricted rotation about the S—S bond.

Quantum-mechanical calculations have shown that in the hydrogen peroxide molecule the O—O bond presents its valencies at an azimuthal angle of about 100°, and that a very real energy barrier must be surpassed to permit rotation from this angle (7). It appears that rotation to an azimuthal angle of 180° (*trans-*) requires an activation of about 4000 calories and that rotation to the *cis*-form requires about 12,000 calories (8). It seems very reasonable for one to assume that a similar situation exists with the hydrogen persulfide molecule. Dipole moment measurements have been made on many molecules containing a S—S single bond (9), but this technique cannot distinguish between a freely rotating S—S bond and one restricted at an azimuthal angle of nearly 90°. Electron diffraction studies of hydrogen persulfide and dimethyl disulfide were unable to present any evidence for or against restricted rotation (6). Similar studies on sulfur monochloride indicate that an azimuthal angle of 97° may exist in this case (10).

If the assumption of restricted rotation about a S—S single bond may be accepted, the relative reactivities observed for the cyclic disulfides are more easily explained. On this basis the five-membered ring must be highly strained. Its formation requires rotation of the bond to an azimuthal angle of nearly 0° and this is the most unstable position in which this bond could be held. The largest azimuthal angle possible for the six-membered ring disulfide is about 70° as shown by molecular models. The strain involved in this ring must therefore be small. Larger rings do not require any large deviation from an angle of about 100° and so should be quite strainless. The alternation in reactivity found in this range may be due to a compression of the domain required for the methylene groups, an idea which is frequently used to explain the instability of rings of eight to twelve members of various types (11). A study of the models of cyclic disulfides indicates that a fixed azimuthal angle of 100° for the S—S bond may result in a very slight increase in the domain available for the methylene groups in the nine- and eleven-membered rings relative to that available in the eight-, ten-, and twelve-membered rings.

EXPERIMENTAL

Preparation of Bunte salts. Solutions of 125 grams (0.5 mole) of sodium thiosulfate pentahydrate in 250 cc. of water and 0.2 mole of the polymethylene dihalide in 250 cc. of alcohol were mixed and the mixture refluxed on the water-bath until it became homogeneous. The alcohol was then removed by low-temperature distillation. The cyclization reaction could be run directly on the aqueous-alcoholic solution, the alcohol being removed from the steam distillate; however, it was found to be more convenient to remove it from the Bunte salt solution.

Preparation of cyclic disulfides. In a 5-liter flask was placed 255 grams (1.5 moles) of cupric chloride dihydrate in 500 cc. of water. Steam which had been preheated to 150° was passed through this solution and the Bunte salt solution (0.2 to 0.4 molar) was added dropwise over a period of about two hours. Distillation was stopped when the condensate became clear. Any subnatant oil was separated from the distillate which was then extracted with ether. The extracts were combined, dried over calcium chloride, and the solvent removed. The products were then distilled under reduced pressure in those cases in which they were sufficiently plentiful and sufficiently stable. The presence of the disulfide bond and the absence of mercaptan and thiocarbonyl groups in the product were demonstrated in each case by tests with Grote's solution (12).

Although the method just outlined gives the largest yields of those disulfides having more than seven ring members, it is apparently inferior for the smaller rings. These were best prepared by the direct solution of solid cupric chloride in the hot (80°) Bunte salt solution. After standing for several hours, preferably overnight, a voluminous precipitate of a molecular complex separated. The solution was then steam-distilled, and the distillate worked up as before.

SUMMARY

A new method for the synthesis of cyclic disulfides is described. The relative reactivity of the rings is discussed, and an explanation is offered to account for the ease of opening of the five- and six-membered disulfide rings.

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