Tetrahedron Letters, Vol.27, No.4, pp 441-444, 1986 0040-4039/86 $3.00 + .00
Printed in Great Britain

HIGH YIELD PREPARATION OF CYCLIC DISULFIDES USING ALKYLTIN THIOLATES[1]

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Abstract: Cyclic disulfides with ring sizes ranging from 5 to 10 are formed by iodination or bromination of alkyltin thiolates without the need of high dilution.

There have been a number of recent reports on tin-directed cyclization reactions[2]. These mild, template-driven ring closure procedures show good yields of monomer formation. The following is a report of a tin-mediated synthesis of cyclic disulfides in good yield without the necessity of employing high dilution[3] or titrimetric[3b,4] techniques.

The cyclic disulfides (4a-4f) were prepared by oxidative cyclization with bromine or iodine from the corresponding bis(tri-n-butyltin)dithiolates[5] (3a-3f); these were all prepared by the same general procedure (Scheme1).

The synthesis of bis(tri-n-butyltin)-1,4-butanedithiolate (3b) and subsequently 1,2-dithiane (4b) is presented. To 10mmol of 1,4-butanedithiol and 22mmol of triethylamine in 75 ml of CCl_4 is added 20mmol of tri-n-butyltin chloride; the reaction mixture was allowed to stir for 3 hours. The triethylamine hydrochloride salt is collected and the filtrate washed with 5% acetic acid, dried ($MgSO_4$) and evaporated *in vacuo* affording only 3b as a very viscous liquid.

To a 0.05M solution of 3b (used without further purification) in CH_2Cl_2 at 0°C is added at a constant rate of 2 ml/ minute, a 0.20M solution of either I_2 or Br_2 in CH_2Cl_2. These oxidation reactions along with the workup are carried out in subdued light with Al-foiled glassware to avoid polymerization.[3b] Typically, the total addition time is 5 to 10 minutes. The reaction mixture is allowed to stir for 5 minutes before being washed with 5% sodium thiosulfate, dried ($MgSO_4$) and evaporated. After purification on 200 g of aluminum oxide, the

TABLE 1

	Disulfide (4)	% YIELDS[a]		lit. % yields	mp/refractive index	
		I_2	Br_2		this work	lit.
a	1,2-dithiolane	92	88	70-84[b], 90[c]		
b	1,2-dithiane	96	95	93-95[b] 96[c],95[d]	30-31	31-31.5[d],29[e]
c	1,2-dithiepane	74	76	80[d], 82[c], 13[f]	1.5681	1.569[b],1.570[d]
d	1,2-dithiacyclooctane	37	36	30[d], 86[c], 4[f]	1.567	1.5698[d]
e	1,2-dithiacyclononane	42	39	45[d],74[g], 2[f]	1.5627	1.5642[d],1.5623[g]
f	1,2-dithiacyclodecane	61	59	50[d], 3[f]	1.5407	1.5461[d]

Table 1:a) yields of cyclic disulfides from the dithiols. All yields are isolated except entry 4a. The yield of 4a was determined by UV (λ max 330 nm e=142)[8]; attempts to isolate 4a result in polymerization. Other entries have physical properties which match published data ; their MS, NMR and Raman spectra are consistent with the indicated structure; b) ref 3b; c) ref 9, this reference does not have experimental, physical or spectroscopic data; d) ref 2b, long addition time of oxidant ($FeCl_3$) ranged from 2 to 9 days; e) ref 10; f) ref 2c; solution concentration was 0.2 to 0.4 M and addition of oxidant took 2 hours; g) ref 3a, titrimetric addition, final concentration is 0.04M and addition time was 4 hours.

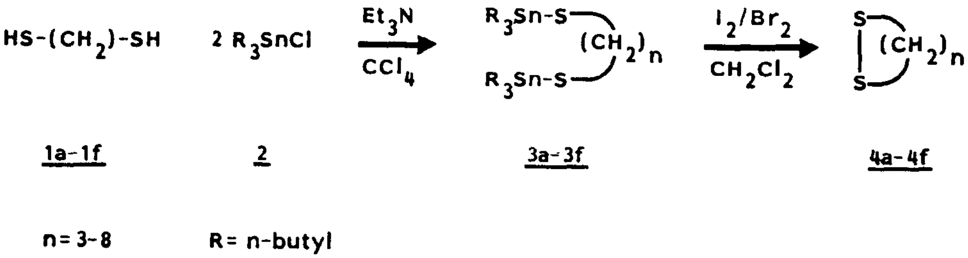
TABLE 2

Disulfide (4): (ring size)	a(5)	b(6)	c(7)	d(8)	e(9)	f(10)
ratio of yields: (with Sn / without Sn)	1.8/1	1.1/1	2.7/1	12/1	10/1	11/1

disulfide <u>4b</u> (mp 30-31^{o}C) is obtained with a yield of 95% or better. Alternatively, once the oxidation is complete, excess KF can be added to the reaction mixture and this mixture refluxed so as to form insoluble tri-alkyltin fluoride[6]. Purification of the disulfides can then be achieved with a lesser amount of aluminum oxide, however the isolated yields of the disulfides <u>4</u> is lower.

This method permits a rapid synthesis of cyclic disulfides in good to excellent yields, and appears to indicate some kind of "template effect"[2,7] inasmuch as dithiol oxidation under identical conditions (concentration of reactants and addition time of oxidant) shows lower yields of monomer formation (Table 2).

Scheme 1



Acknowledgements:

We thank the National Research Council of Canada and the Ministère de l'Education du Québec for financial support.

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(Received in USA 27 August 1986)