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A NEW SYNTHESIS OF DIHYDRO-1,4-DITHIINS

C. H. Chen*

Research Laboratories, Eastman Kodak Company, Rochester, New York 14650

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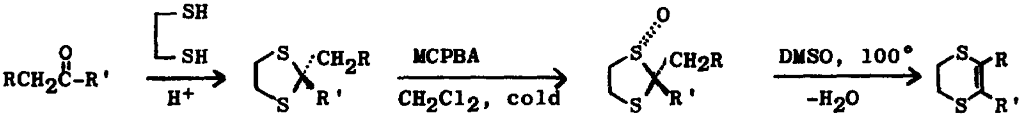
Surveying the literature, one finds that very few examples of monosulfoxides of 1,3-dithiolanes are known and that their chemistry is little explored. In connection with our interest in the syntheses of sulfur heterocycles, we wish to report a novel synthesis of dihydro-1,4-dithiins utilizing a facile thermal ring-expansion reaction of 1,3-dithiolane-1-oxides. The general synthetic scheme is represented as follows:

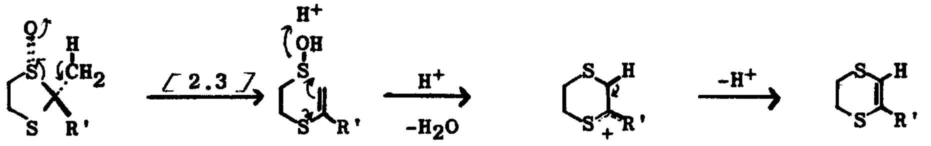


I

II

Monosulfoxides of 1,3-dithiolanes (Table I) are prepared by selective oxidation of ethylene dithioketals of the corresponding ketones with *m*-chloroperbenzoic acid (MCPBA) in cold CH_2Cl_2. The sulfoxides, upon heating (100°C) in an aprotic solvent (such as DMSO or DMF), are transformed smoothly by formal loss of H_2O to the corresponding dihydro-1,4-dithiins (Table II) in good yields. In view of the neutral and mild conditions employed in the ring expansion step, this method for preparing the dihydro-1,4-dithiin system from ketones is of considerable synthetic value, since the published procedures for the synthesis of II are limited,[1] particularly that from the corresponding ketones.[2]

A possible pathway for the formation of II from I is shown in the following scheme, involving a [2.3] sigmatropic rearrangement of the *cis*-2-methyl-1,3-dithiolane-1-oxide (I, R = H) to generate the sulfenic acid intermediate III,[3] presumably followed by self-catalyzed ring closure through the sulfur-stabilized carbonium ion IV. This proposed mechanism is supported by the following observations. (1) The rate of ring expansion is highly dependent on the



I (R = H) III IV II (R = H)

Table I. 1,3-Dithiolane-1-oxides[4] (I)

No.	R	R'	Mp(bp),°C	Yield, %[5]
Ia	H	Anisyl	99-101	83
Ib	H	p-Nitrophenyl	142-3	79
Ic	H	t-Bu	63.5-65.5	60
Id	H	Me	83-4/1 mm	84
Ie[6]	Ø	ØCH$_2$	132-3	80
If	n-C$_8$H$_{17}$	n-C$_9$H$_{19}$	---	80[7]

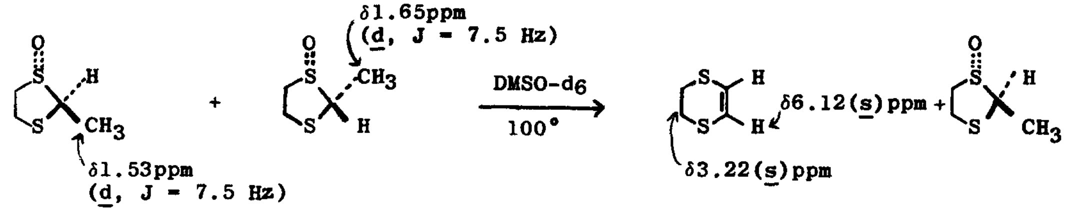
Table II. Dihydro-1,4-dithiins[4] (II)

No.	R	R'	Mp(bp),°C	Thermolysis conditions of the corresponding monosulfoxides	Yield, %
IIa	H	Anisyl	77-8	(Ia) DMSO, 100°/15 hr	81
IIb	H	p-Nitrophenyl	139-140	(Ib) DMSO, 100°/15 hr	50[8]
IIc	H	t-Bu	67-8/1.5 mm	(Ic) DMF, 100°/15 hr	80
IId	H	Me	80-2/27 mm	(Id) DMSO, 100°/65 hr	80
IIe	Ø	ØCH$_2$	97.5-98.5	(Ig) DMSO, 100°/6 hr	85
IIf	n-C$_8$H$_{17}$	n-C$_9$H$_{19}$	192-7°/0.7 mm	(If) DMSO, 100°/72 hr	83

polarity of the solvent media (e.g. $t_{1/2}^{100^\circ} \sim 1$ hr in DMSO, whereas $t_{1/2}^{100^\circ} \sim 3$ hr in nitrobenzene for Ia). (2) The reaction is catalyzed by acid. No II was detected (nmr) when the same reaction was conducted in pyridine. (3)

Qualitative nmr studies tend to support the intervention of a carbonium ion IV, which is, as expected, better stabilized by R' = p-methoxyphenyl (Ia) than by (R' = p-nitrophenyl) (Ib). Consequently, under identical conditions, Ia ($t_{1/2}^{100^\circ}$ ~3 hr) rearranged much faster than Ib ($t_{1/2}^{100^\circ} > 6$ hr) in nitrobenzene.

Studies of the lanthanide-shifted nmr spectra of Ia-c[9] has revealed essentially no trans-isomers (i.e. sulfoxide trans to methyl). Presumably, MCPBA oxidation takes place by approaching the 1,3-dithiolanes from the least-hindered site[10] to give predominantly the cis-methyl-sulfoxide configuration required for the initial [2.3] sigmatropic process. Further evidence is provided by the fact that when a mixture of cis and trans (ca. 3:7)[9] isomeric 2-methyl-1,3-dithiolane-1-oxide (V)[4] was heated at 100°C in DMSO-d_6 in an nmr tube for three weeks, all of the cis-sulfoxide V was found to have rearranged to dihydro-1,4-dithiin (VI).[11] The major trans-V isomer in the reaction mixture was unaffected. This result is consistent with the expectation that the unfavorable configuration of the sulfoxide V (trans) was generated predominantly during the MCPBA oxidation step of the corresponding 2-methyl-1,3-dithiolane. Furthermore, a six-electron [2.3] sigmatropic rearrangement[3] is forbidden in the transition state owing to the geometric restriction of the trans-configuration.



trans-V cis-V VI trans-V

This synthesis works best with symmetrical ketones because the intermediate sulfoxide I prepared by selective oxidation is isomerically homogeneous. In the case of unsymmetrical ones, this approach proves most valuable when the steric requirement of one group is distinctly larger than the other (such as compounds in Table I -- R' = Aryl, t-Bu and R = H) so that the amount of less-desired trans-isomers of the intermediate sulfoxide I formed can be kept to a minimum.

Acknowledgement

The author gratefully acknowledges the help of Dr. T. H. Regan of Eastman Kodak Company for obtaining the lanthanide-shifted nmr spectra.

References and Notes

1. For a summary of the state of art, *cf*. D. S. Breslow and H. Skolnik, "Multi-Sulfur and Sulfur and Oxygen Five- and Six-membered Heterocycles." Part 2, "The Chemistry of Heterocyclic Compounds," A. Weissberger, ed., Interscience Publishers, New York, 1966, pp. 1112-1137.
2. "Ring Expansion Reactions of 1,3-Dithiolanes to Dihydro-1,4-dithiins" using *N*-chlorocarbamate is described in a recent communication [H. Yoshino, Y. Kawazoi, and T. Taguchi, *Synthesis*, 713 (1974)].
3. D. N. Jones and D. A. Lewton, *J. Chem. Soc.*, *Chem. Commun.*, 457 (1974).
4. All new compounds give satisfactory combustion analytical (or exact mass) and spectroscopic data, which are in full agreement with the proposed structure. Melting points are uncorrected, nmr spectra were recorded on Varian T-60 and A-60 spectrometers using TMS as internal standard. High resolution mass spectra were recorded on an AEI MS-902 double focusing mass spectrometer.
5. Yields are based on the corresponding ketones.
6. *Lit.*, mp 134-135°; R. Kuhn and F. A. Neugebauer, *Chem. Ber.*, **94**, 2629 (1961).
7. Thermally unstable, purified by column chromatography over silica gel. Mol. wt. (*Calcd.* for $C_{21}H_{42}OS_2$: 374.2676) 374.2681.
8. Extensive tar formation was observed.
9. For details of determination of configuration of α-substituted cyclic sulfoxides by lanthanide-shifted nmr, *cf*., R. R. Fraser, T. Durst, M. R. McClory, R. Viau, and Y. Y. Wigfield, *Int. J. Sulfur Chem., Part A*, **1**, 133 (1971).
10. W. O. Siegl and C. R. Johnson, *J. Org. Chem.*, **35**, 3657 (1970).
11. L. Levine, U. S. Patent 3,439,051 (1967).