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ONE-STEP SYNTHESIS OF DITHIOHEMIACETALS

A NEW CLASS OF COMPOUNDS

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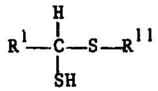
The compound 1-methylthioethanethiol (I) was recently isolated from the head-space of beef broth at this laboratory. The only compounds reported in the literature that can be regarded as falling into this class of dithiohemiacetals are II$^{1,2)}$ and III$^{3)}$.

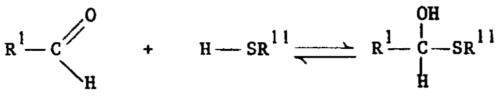


$$R^1-\overset{\displaystyle H}{\underset{\displaystyle SH}{C}}-S-R^{11}$$

	I	II	III	IV	V	VI	VII	VIII
R^1	CH_3	H	H	CH_3	C_2H_5	C_2H_5	$(CH_3)_3C$	$CH_3.CO$
R^{11}	CH_3	CH_3	C_2H_5	C_2H_5	CH_3	C_2H_5	C_2H_5	C_2H_5

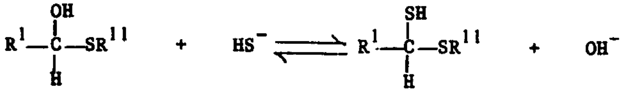
Peer et al.$^{4)}$ prepared the homologues IV, V, and VI by methods which unambiguously established the structures; compounds I-VI were characterized by ir, nmr, and mass spectrometry. In all syntheses the intermediate 1-alkylthio-1-chloroalkanes had to be isolated after the first reaction step. The halogen atom was subsequently replaced by a mercapto moiety, for example by treatment with sodium hydrogen sulfide, or via an isothiouronium salt or xanthate.

The results of an investigation into the natural precursors of I prompted us to attempt a one-step synthesis starting with an aldehyde (R^1CHO), a thiol ($R^{11}SH$), and hydrogen sulfide. This reaction follows a two-step mechanism. The first step is an equilibrium with the monothiohemiacetal subject to specific base and general acid catalysis$^{5)}$.



$$R^1-C\overset{\displaystyle O}{\underset{\displaystyle H}{\lessgtr}} + H-SR^{11} \rightleftharpoons R^1-\overset{\displaystyle OH}{\underset{\displaystyle H}{C}}-SR^{11}$$

The second step involves nucleophilic substitution of the OH group by SH^-. Since the pK_a of SH-H is about three units lower than that of RS-H, SH^- ions are present in far higher concentration than the (potentially) competing SR^- ions if the pH is brought to 5.



$$R^1-\overset{OH}{\underset{H}{C}}-SR^{11} + HS^- \rightleftharpoons R^1-\overset{SH}{\underset{H}{C}}-SR^{11} + OH^-$$

The preferred solvent for this ionic reaction is water. Alkanethiols are not very soluble in water, however, and we considered that addition of a solvent immiscible with water would prevent escape of the volatile thiol and, more important, remove the product from the aqueous phase as it was formed, shifting the equilibria to the product side.

Equimolar amounts of sodium sulfide and the appropriate aldehyde and thiol were dissolved in a two-layer system comprising dichloromethane and an aqueous acetate buffer (pH 5). The reaction mixture was allowed to stand for three days at room temperature. The dithiohemiacetal was isolated from the dichloromethane and purified by distillation under reduced pressure. The yields of I, IV, and V were 38%, 31%, and 26% respectively. The attempted synthesis of VII in water/dichloromethane failed.

In order to ascertain that the two-layer system gives, as expected, better results than a mono-layer system, VI was prepared from propionaldehyde, ethanethiol, and sodium sulfide in the manner described above, except that methanol was substituted for the dichloromethane. The yield of VI was only 1.5%.

We also attempted the synthesis of VIII by the two-layer method, starting from pyruvaldehyde, ethanethiol, and sodium sulfide. The product was worked up, and subjected to glc on an apolar column: a single peak was observed. Upon rechromatography on Carbowax the material comprising this peak was further separated into two compounds, the first of which was identified by ir and mass spectrometry as diethyl trisulfide. The major product was identified as 1-ethyldithio-2-propanone, which may be viewed as a rearrangement isomer of VIII.

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REFERENCES

1. F. Fehèr, K. Vogelbruch, *Chem. Ber.* 91, 996 (1958).
2. M.R. Altamura, T. Hasselstrom, L. Long Jr., *J. Org. Chem.* 28, 2938 (1963).
3. H. Böhme, H. Fischer, R. Frank, *Liebigs Ann.* 563, 54 (1949).
4. H.G. Peer, A. van der Heijden, S.B. Tjan, and T.L. van Orden, submitted to *Rec. Trav. Chim. Pays Bas*.
5. G.E. Lienhard, W.P. Jencks, *J. Amer. Chem. Soc.* 88, 3982 (1966).