

Condensation of 1,2-Dithiols with α -Keto Aldehydes.
A Convenient Synthesis of 2-Methyl-1,3-dithiolane-2-carboxaldehydes (1)

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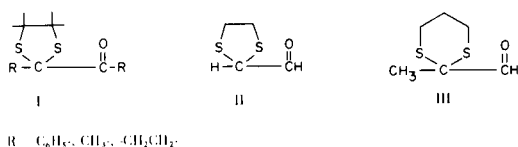
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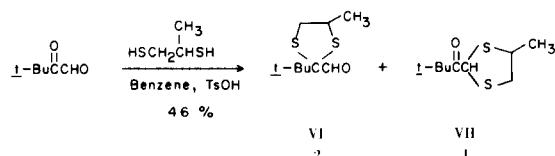
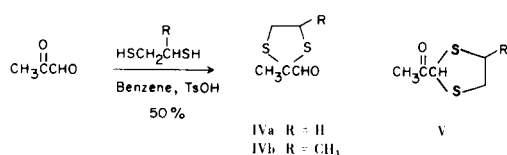
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Received January 14, 1971

The acid-catalyzed condensations of 1,2-dithiols with aromatic and aliphatic α -diketones are known to afford monocyclic mercaptols of structure I (3). Parham and co-workers (4) reported the isolation of 1,3-dithiolane-2-carboxaldehyde (II) (as the 2,4-dinitrophenylhydrazone) from the reaction of glyoxal and 1,2-ethanedithiol. Shahak and Bergmann have prepared mercaptal derivatives from a variety of dicarbonyl compounds and 1,2-dimethyl-4,5-di(mercaptomethyl)benzene (5). However, insofar as can be determined, there have been no studies of the analogous reactions of 1,2-dithiols with α -keto aldehydes. Corey and Seebach (6) have synthesized 2-methyl-*m*-dithiane-2-carboxaldehyde (III) and related ketones by acylation of the carbanion derived from 2-methyl-*m*-dithiane.

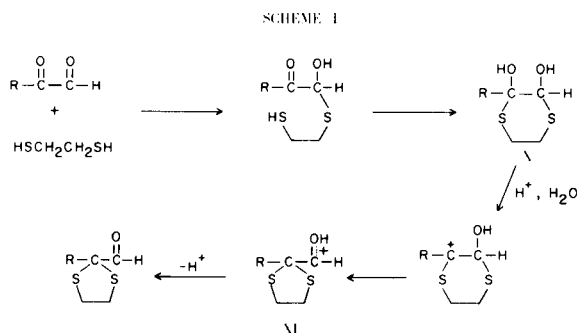


We now report that equimolar amounts of a 1,2-dithiol and aqueous pyruvaldehyde condense to afford novel 2-methyl-1,3-dithiolane-2-carboxaldehydes (IV) in moderate yields. Nmr spectra (see Experimental) clearly show the products to be aldehydes with no evidence of the isomeric 1,3-dithiolan-2-yl methyl ketones (V) being present. The condensation of 1,2-propanedithiol with *t*-butylglyoxal gave an approximately 2:1 mixture of the mercaptol aldehyde VI and mercaptal ketone VII, respectively, despite the high degree of steric hindrance associated with the ketone carbonyl group.

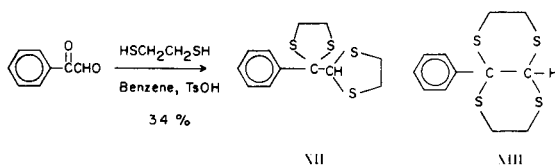


The selectivity observed for the two α -keto aldehydes was quite unexpected in light of prior literature which reports that α -keto aldehydes give α -keto acetals (VIII) when condensed with alcohols (7) and afford α -keto hemimercaptals (IX) when combined with thiols (8). In general, ketones are considered less reactive than aldehydes towards condensation with thiols and dithiols (5,9).

The mechanism illustrated in Scheme I is consistent with the results and is presented as a possible explanation of the apparent selectivity of 1,2-dithiols toward the ketone carbonyl of α -keto aldehydes. Addition is considered to occur successively to the aldehyde and ketone carbonyl groups to afford the intermediate glycol X, which can be protonated and lose water to generate the more stable carbonium ion. This is followed by ring contraction with subsequent loss of a proton from the carbonium-oxonium ion XI to give the product. The proposed rearrangement of glycol X may be aided by the increased ability of oxygen, relative to sulfur, to stabilize an adjacent carbonium ion, as suggested in the analogous acid-catalyzed rearrangement of 2,3-diacetoxy-1,4-dithiane to 1,3-dithiolane-2-methanediol diacetate (4). Another possibility which exists in the case of aqueous pyruvaldehyde is that the aldehyde carbonyl may be "blocked" as a hydrate thereby favoring dithiolane formation on the ketone function.



Extension of the condensation reaction to phenylglyoxal hydrate gave a solid derivative which contained no carbonyl group. The compound is tentatively assigned the structure XII on the basis of analytical and spectral evidence, and by analogy to the 2,2'-bi-1,3-dithiolane structure confirmed for the product from the reaction of glyoxal and two equivalents of 1,2-ethanedithiol (10). However, the isomeric structure XIII cannot be conclusively eliminated at this time.



EXPERIMENTAL

All melting points were determined in open capillary tubes on a Thomas-Hoover apparatus and are uncorrected. Infrared spectra were obtained on a Perkin-Elmer Model 127 recording spectrophotometer. The nmr spectra were recorded on a Varian A-60 spectrometer with tetramethylsilane as an internal reference (11). *t*-Butylglyoxal was prepared by the method of Fuson and coworkers (12).

2-Methyl-1,3-dithiolane-2-carboxaldehyde (IVa).

A stirred mixture of 40% aqueous pyruvaldehyde (360 g., 2.0 moles), 1,2-ethanedithiol (188 g., 2.0 moles), benzene (600 ml.) and *p*-toluenesulfonic acid hydrate (2.0 g.) was heated at reflux 4 hours, during which time water was separated in a Dean-Stark apparatus. The dark solution was successively washed with aqueous sodium bicarbonate and water, dried over magnesium sulfate and the solvent removed under reduced pressure. Vacuum distillation of the dark brown residue gave 151 g. (54%) of a light yellow liquid, b.p. 97-112° (20 mm), collected in three equal fractions, all of which possessed identical infrared spectra. The center cut, b.p. 105-108° (20 mm), was analyzed. Ir(neat) 1710 cm⁻¹ (C=O); nmr (deuteriochloroform) τ 0.87 (1H, s, -CHO), 6.58 (4H, s, -CH₂CH₂-), 8.24 (3H, s, -CH₃).

Anal. Calcd. for C₅H₈OS₂: C, 40.5; H, 5.4. Found: C, 40.7; H, 5.6.

The aldehyde IVa was converted in the usual manner into its oxime (m.p. 106-107°) and thiosemicarbazone (m.p. 168-170°) derivatives.

Anal. Calcd. for C₅H₉NOS₂ (oxime): C, 36.8; H, 5.6; N, 8.6. Found: C, 37.0; H, 5.5; N, 8.3.

Anal. Calcd. for C₆H₁₁N₃S₃ (thiosemicarbazone): C, 32.6; H, 5.0; N, 19.0. Found: C, 32.8; H, 4.9; N, 18.7.

2,4-Dimethyl-1,3-dithiolane-2-carboxaldehyde (IVb).

Condensation of 1,2-propanedithiol (43.3 g., 0.4 mole) with 40% pyruvaldehyde (72.1 g., 0.4 mole) as described for IVa afforded 31.7 g. (49%) of IVb as a light yellow liquid, b.p. 110-118° (20 mm); ir (neat) 1710 cm⁻¹ (C=O); nmr (deuteriochloroform) τ 0.84 and 0.88 (1H, two s, -CHO), 6.00 (1H, m, -CH₂CH-), 6.80 (2H, m, -CH₂CH-), 8.52 and 8.57 (3H, two d, J = 6.4 and 6.2 cps, respectively, -CHCH₃), 8.25 and 8.27 (3H, two s, -CH₃). The double peak positions are consistent with the presence of *cis-trans* isomers of IVb.

Anal. Calcd. for C₆H₁₀OS₂: C, 44.4; H, 6.2. Found: C, 44.5; H, 6.4.

The aldehyde IVb was converted in the usual manner into its oxime (m.p. 63-65°) and thiosemicarbazone (m.p. 155-157°) derivatives.

Anal. Calcd. for C₆H₁₁NOS₂ (oxime): C, 40.7; H, 6.3; N, 7.9. Found: C, 40.5; H, 6.3; N, 7.9.

Anal. Calcd. for C₇H₁₃N₃S₃ (thiosemicarbazone): C, 35.8; H, 5.6; N, 17.9. Found: C, 35.9; H, 5.6; N, 18.1.

2-*t*-Butyl-4-methyl-1,3-dithiolane-2-carboxaldehyde (VI) and *t*-Butyl 4-Methyl-1,3-dithiolan-2-yl Ketone (VII).

Condensation of 1,2-propanedithiol (7.5 g., 70 mmoles) with *t*-butylglyoxal (8.0 g., 70 mmoles) as described for IVa afforded 6.5 g. (46%) of a yellow liquid, b.p. 64-75° (1.5 mm). The following spectral and elemental analyses support an approximately 2:1 mixture of structural isomers VI and VII. Ir (neat) 1705 cm⁻¹ (C=O); nmr (deuteriochloroform) τ 0.67 (2/3H, s, -CHO), 4.75 (1/3H, s, -SCHS-), 6.1 and 6.9 (3H, two m, -CH₂CH-), 8.56 (3H, two overlapping d, -CHCH₃), 8.78 (9H, s, (CH₃)₃C-).

Anal. Calcd. for C₉H₁₆OS₂: C, 52.9; H, 7.9. Found: C, 52.7; H, 7.8.

Reaction of 1,2-Ethanedithiol with Phenylglyoxal Hydrate.

Condensation of 1,2-ethanedithiol (9.4 g., 0.1 mole) with phenylglyoxal hydrate (15.2 g., 0.1 mole) as described for IVa afforded an orange oil which slowly solidified on standing. Two recrystallizations from chloroform-hexane gave 4.8 g. (34%) of XII as pale yellow crystals, m.p. 109-112°; nmr (deuteriochloroform) τ 4.52 (1H, s, -SCHS-), 6.71 (4H, m, -CH₂CH₂-), 7.09 (4H, m, -CH₂CH₂-), 2.2 and 2.75 (5H, two m, C₆H₅-).

Anal. Calcd. for C₁₂H₁₄S₄: C, 50.3; H, 4.9. Found: C, 50.4; H, 4.9.

Acknowledgments.

The authors are indebted to Mr. G. J. Lillquist and members of the Analytical Research and Services Laboratory of the 3M Company for spectral analyses and microanalytical determinations.

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