

The Reaction of Dihydroxyacetone with Ethanedithiol.

Synthesis and X-ray Crystal Structure of 1,4,7,10-Tetrathiaspiro[5.5]undecane

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Reaction of dihydroxyacetone with an excess of ethanedithiol in the presence of 10*M* hydrochloric acid gives 2,2-di(hydroxymethyl)-1,3-dithiacyclopentane (**1**) in low yield. When boron trifluoride etherate is used instead of hydrochloric acid, the same reactants give 1,4,7,10-tetrathiaspiro[5.5]undecane (**3**). The structure of the latter was established by X-ray crystallography. The crystals are monoclinic, space group $P2_1/n$, with $a = 6.31(1)$, $b = 21.57(2)$, $c = 7.61(1)\text{\AA}$, $\beta = 102.2(1)^\circ$ and $Z = 4$, $R = 0.038$ for 2289 reflections. The two 1,4-dithiane rings in **3** are significantly more puckered than normal cyclohexane rings. The uv spectrum of **3** is consistent with values reported for other sulphides and with the X-ray structure.

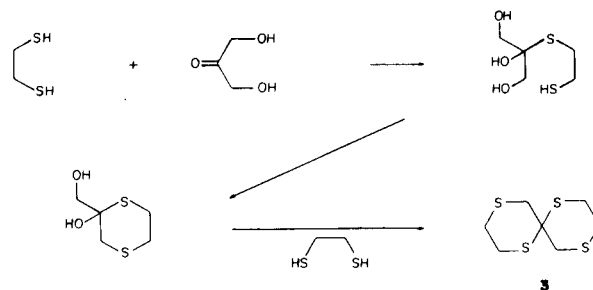
J. Heterocyclic Chem., **20**, 33 (1983).

In order to obtain some esters of dihydroxyacetone it was necessary to obtain a blocking group for the carbonyl function which could be removed under mild conditions. An obvious choice was to use ethanedithiol, which in the presence of a suitable acid catalyst would be expected to give 2,2-di(hydroxymethyl)-1,3-dithiacyclopentane, **1**.



Condensation of dihydroxyacetone with an excess of ethanedithiol in the presence of aqueous concentrated hydrochloric acid gave a crystalline compound whose elemental analysis, nmr, ir and mass spectra were consistent with it having the expected structure **1**. The yield of the compound was low (~20%), however, and attempts to increase this by changing the proportion of the reactants and the type of acid used as the catalyst, were not successful.

Thus, it was apparent that another reaction was taking place. For example, when dihydroxyacetone was treated with ethanedithiol (two molecular proportions) in the presence of boron trifluoride etherate (1), an exothermic reaction occurred to give a crystalline product in 40% yield. This was different from **1**, however; the nmr and ir spectra showed the absence of hydroxyl groups and the elemental analysis and mass spectrum indicated that the product has been formed by the reaction of two molecules of ethanedithiol with one molecule of dihydroxyacetone with the elimination of two molecules of water. There appear to be several possible reaction pathways. One is the initial formation of compound **1** followed by condensation with another molecule of ethanedithiol to give compound **2**. Another route is as follows:



Other possibilities are dehydration of the dihydroxyacetone to give either malondialdehyde or pyruvaldehyde followed by condensation of these with ethanedithiol to give compounds **4** and **5**, respectively.



The ¹H nmr spectrum of the product was not consistent with structures **4** and **5**. Moreover compound **4** is known (2) and is reported to have different physical properties from those of **3**. The ¹H nmr spectrum of our compound was consistent with structures **2** and **3** but did not distinguish between them. The structure was determined by X-ray crystallography, therefore, and shown to be 1,4,7,10-tetrathiaspiro[5.5]undecane (**3**).

A stereoscopic view of the molecule is shown in Figure 1, which also indicates the atomic numbering scheme.

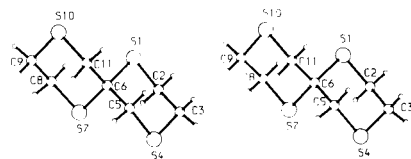


Figure 1. Stereoscopic view molecule (**3**)

Atomic coordinates are in Table 1 and molecular dimensions in Table 2. The two 1,4-dithiane rings are in the chair conformation with torsion angles in the range 55.4-68.1°, mean 61.5°, and are thus significantly more puckered than a normal cyclohexane ring with mean torsion angle 56° (3). This can be attributed to the effect of the smaller valence angles at sulphur (range 98.7-101.2°, mean 99.2°) and the longer C-S bond lengths (1.801-1.832 Å, mean 1.813 Å). The angles at carbon in **3**, excluding those at the spiro atom C(6), are generally larger than those in cyclohexane. Those at C(6) are all within 3° of the tetrahedral value. Bond angles and lengths are generally in good agreement with those found previously in structures containing 1,4-dithiane rings (4).

Table 1

Atomic Coordinates Expressed as Fractions of the Unit Cell Axes and Isotropic Temperature Factors (U)

	x	y	z	$U_{\text{eq}}/U_{\text{iso}}$ (Å ²) (a)
S(1)	0.45059(9)	-0.33279(2)	0.32116(7)	0.041
S(4)	0.73653(10)	-0.47255(3)	0.35502(8)	0.051
S(7)	0.60662(7)	-0.38313(2)	-0.00047(7)	0.037
S(10)	0.08546(8)	-0.32275(3)	-0.06778(9)	0.046
C(2)	0.7264(4)	-0.3475(1)	0.4400(3)	0.047
C(3)	0.7613(5)	-0.4119(1)	0.5221(3)	0.055
C(5)	0.4621(4)	-0.4578(1)	0.2378(3)	0.041
C(6)	0.4194(3)	-0.3937(1)	0.1500(2)	0.032
C(8)	0.5053(3)	-0.3120(1)	-0.1138(3)	0.039
C(9)	0.2738(4)	-0.3153(1)	-0.2144(3)	0.045
C(11)	0.1847(3)	-0.3941(1)	0.0462(3)	0.041
H(2A)	0.824(5)	-0.339(1)	0.356(4)	0.051
H(2B)	0.746(5)	-0.317(1)	0.532(4)	0.060
H(3A)	0.667(6)	-0.423(2)	0.597(5)	0.075
H(3B)	0.906(7)	-0.413(2)	0.605(6)	0.086
H(5A)	0.437(5)	-0.488(1)	0.140(4)	0.061
H(5B)	0.364(4)	-0.462(1)	0.320(3)	0.042
H(8A)	0.523(4)	-0.278(1)	-0.023(3)	0.039
H(8B)	0.605(4)	-0.301(1)	-0.200(4)	0.058
H(9A)	0.250(4)	-0.347(1)	-0.297(4)	0.051
H(9B)	0.247(5)	-0.277(2)	-0.282(4)	0.066
H(11A)	0.179(4)	-0.428(1)	-0.040(4)	0.047
H(11B)	0.083(5)	-0.403(1)	0.129(4)	0.058

(a) For the non-hydrogen atoms these are equivalent isotropic temperature factors derived from the refined anisotropic thermal parameters by $U_{\text{eq}} = \frac{1}{3}(U_{11} + U_{22} + U_{33} + 2U_{12}\cos\beta)$. Mean square amplitudes of vibration (U_{ij} are all normal (range 0.029 - 0.076 Å²).

The production of **3** in the reaction of ethanedithiol with dihydroxyacetone does not establish that the reaction pathway is as indicated above. The reaction might proceed *via* **1** and **2** which then rearranges to give **3**, which is more stable than **2**.

Compound **3** shows absorption maxima in the uv region at 208.5 nm (ϵ , 2770) and 230.8 nm (ϵ , 1130). It is of interest to compare these values with those obtained for other alkyl sulphides. Dimethyl and diethyl sulphide show

Table 2

Molecular Dimensions

(a) Bond Lengths (Å)

S(1)-C(2)	1.812(2)	C(2)-H(2A)	1.00(3)
C(3)-S(4)	1.809(3)	C(2)-H(2B)	0.96(3)
S(4)-C(5)	1.801(2)	C(3)-H(3A)	0.94(4)
C(6)-S(7)	1.826(2)	C(3)-H(3B)	0.99(3)
S(7)-C(8)	1.809(2)	C(5)-H(5A)	0.98(3)
		C(5)-H(5B)	0.97(2)
C(9)-S(10)	1.802(2)	C(8)-H(8A)	1.00(3)
S(10)-C(11)	1.813(2)	C(8)-H(8B)	1.03(3)
C(6)-S(1)	1.832(2)	C(9)-H(9A)	0.92(3)
C(2)-C(3)	1.519(3)	C(9)-H(9B)	0.98(3)
C(5)-C(6)	1.534(3)	C(11)-H(11A)	0.98(3)
C(8)-C(9)	1.501(3)	C(11)-H(11B)	1.01(3)
C(11)-C(6)	1.524(3)		

(b) Bond Angles (°)

C(6)-S(1)-C(2)	100.2(1)	S(7)-C(8)-C(9)	114.3(2)
C(3)-S(4)-C(5)	98.7(1)	C(8)-C(9)-S(10)	112.7(2)
C(6)-S(7)-C(8)	101.2(1)	S(10)-C(11)-C(6)	116.3(1)
C(9)-S(10)-C(11)	99.6(1)	C(11)-C(6)-S(7)	111.2(1)
S(1)-C(2)-C(3)	114.0(2)	S(1)-C(6)-S(7)	111.8(1)
C(2)-C(3)-S(4)	112.8(2)	S(1)-C(6)-C(11)	108.7(1)
S(4)-C(5)-C(6)	115.9(1)	C(5)-C(6)-S(7)	108.0(1)
C(5)-C(6)-S(1)	110.7(1)	C(5)-C(6)-C(11)	106.4(2)

(c) Selected Torsion Angles (°); e.s.d.'s 0.2-0.3°

S(1)-C(2)-C(3)-S(4)	68.1
C(2)-C(3)-S(4)-C(5)	-59.3
C(3)-S(4)-C(5)-C(6)	61.1
S(4)-C(5)-C(6)-S(1)	-67.1
C(5)-C(6)-S(1)-C(2)	57.1
C(6)-S(1)-C(2)-C(3)	-60.0
C(6)-S(7)-C(8)-C(9)	-59.4
S(7)-C(8)-C(9)-S(10)	67.9
C(8)-C(9)-S(10)-C(11)	-59.0
C(9)-S(10)-C(11)-C(6)	59.6
S(10)-C(11)-C(6)-S(7)	-64.3
C(11)-C(6)-S(7)-C(8)	55.4

maxima at 210 nm (ϵ , 1000 and 1600 respectively) (5). Considering each of the isolated sulphur atoms at positions 4 and 10 of **3** as separate dialkyl sulphides, a uv maximum at ~210 nm and an extinction coefficient of 2000-3000 might be expected. This agrees closely with the values observed. The situation with regard to the sulphur atoms at positions 1 and 7 is more complex. The uv absorption spectra of mercaptals have been thoroughly studied and the spectra of cyclic mercaptals have been interpreted in terms of d-orbital participation (6). Interaction between the two sulphur atoms of an S-C-S function is observed to shift the uv maximum to a longer wavelength. This is particularly marked in 5- and 6-membered cyclic mercaptals where the degree of overlap of the appropriate orbitals is large and shifts of maxima to 245-250 nm are observed. For sterically hindered acyclic mercaptals, the overlap is reduced and maxima are observed at 230-235 nm. In the case of the spiran **3** the X-ray data show that the appropri-

ate overlap of orbitals is low. Hence the observed maximum of 230.8 nm, similar to that of an acyclic mercaptal, is as expected.

EXPERIMENTAL

2,2-Di(hydroxymethyl)-1,3-dithiacyclopentane (1).

Ethanedithiol (3.26 ml, 40 mmoles) was added to dihydroxyacetone (1.44 g, 16 mmoles) with thorough mixing. Aqueous hydrochloric acid (2.8 ml, 22 mmoles) was added with vigorous stirring and the mixture kept at room temperature for 1 hour, water (25 ml) was then added and the solution extracted with ethyl acetate (3×30 ml). The combined extracts were dried (magnesium sulphate) and evaporated to a volume of about 20 ml. Upon cooling the solution to -15° colourless needles were formed. These were filtered off to give 2,2-di(hydroxymethyl)-1,3-dithiacyclopentane (0.6 g, 21% yield), mp $115-116^\circ$; nmr (deuteriodimethyl sulphoxide): 3.2 (s, $\text{CH}_2\text{-CH}_2$, 4H), 3.65 (d, collapses to singlet on adding deuterium oxide) hydroxymethylene, 4H), 5.12 (t, (disappears on addition of deuterium oxide) -OH, 2H); ir: 3000-3600, 2959, 1470, 1040 cm^{-1} ; ms: 166.0126 (M^+ , 0.4%), 134.9945 ($\text{C}_4\text{H}_7\text{OS}_2^+$, 100%).

Anal. Calcd. for $\text{C}_5\text{H}_{10}\text{O}_2\text{S}_2$: C, 36.1; H, 6.02; S, 38.6. Found: C, 35.8; H, 6.20; S, 38.7.

1,4,7,10-Tetrathiaspiro[5.5]undecane (3).

Ethanedithiol (0.42 ml, 5 mmoles) was added to 1,3-dihydroxyacetone (0.18 g, 2 mmoles) with thorough mixing. Boron trifluoride etherate (0.37 ml, 3 mmoles) was added and the mixture stirred vigorously. It became warm and set to a viscous paste. To this was added methanol (15 ml) with stirring, the solution cooled to 0° and filtered to give, after washing with methanol, a solid (120 mg, 40% yield). Crystallization of this from chloroform-carbon tetrachloride gave 1,4,7,10-tetrathiaspiro[5.5]undecane, mp $101-102^\circ$; uv: λ max 208.5 nm (ϵ , 2770), 230.8 nm (ϵ , 1130); λ min 222.5 nm (ϵ , 1000) in ethanol; ^1H nmr (deuteriochloroform): 2.6-3.4 (multiplet); ms 223.9821 (M^+ , 34%).

Anal. Calcd. for $\text{C}_7\text{H}_{12}\text{S}_4$: C, 37.5; H, 5.39; S, 57.1. Found: C, 37.4; H, 5.4; S, 57.4.

X-Ray Analysis.

The crystal used had approximate dimensions $0.4 \times 0.3 \times 0.3$ mm.

After preliminary examination by photographic methods, final unit cell dimensions and the intensity data were measured on a Stoe two-circle automatic diffractometer with graphite monochromated Mo-K α radiation, using ψ -scans, scan speed $0.6^\circ \text{ min}^{-1}$ and 30 s stationary background measurements at each of the scan. Of 2744 reflections scanned within the range $0.1 < \sin\theta/\lambda < 0.65 \text{ \AA}^{-1}$, 2289 having intensities, $I, > 2.5\sigma(I)$ were used in the analysis.

The structure was solved by direct methods with SHELX (7). Hydrogen atoms were located from a subsequent difference Fourier synthesis. Least-squares refinement of positional parameters for all the atoms, anisotropic thermal parameters for the heavier atoms and isotropic temperature factors for H converged to $R = 0.038$, $R_w = 0.044$. The weighting scheme was $w = 1/[\sigma^2(F) + 0.001F^2]$ where $\sigma(F)$ is the standard deviation in the observed amplitudes based on counting statistics.

Crystal Data.

Monoclinic, $a = 6.31(1)$, $b = 21.57(2)$, $c = 7.61(1) \text{ \AA}$, $\beta = 102.2(1)^\circ$, $Z = 4$, $D_c = 1.47 \text{ g cm}^{-3}$.

Systematic absences: $0k0$, k odd; $h0l$, $h + l$ odd; space group $P2_1/n$, Absorption coefficient for Mo-K α radiation, $\mu = 0.77 \text{ mm}^{-1}$.

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