THE STEREOCHEMISTRY OF HETEROCYCLES

IV. 2-Substituted 5-Alkyl-1,3-Dithianes*

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Fifteen previously unreported 2-alkyl- and 5-alkyl-2,2-dimethyl-1,3-dithianes have been synthesized by the condensation of 2-alkylpropane-1,3-dithiols with acetaldehyde, isobutylraldehyde, and acetone, and their structures have been confirmed by their IR spectra. The existence of stereoisomers in a number of the thioacetals has been shown by GLC and TLC. Some of the stereoisomeric 2,5-diakyl-1,3-dithianes have been separated by fractionation in an efficient column into the individual isomers, the purity of which was confirmed by TLC, GLC, and IR spectroscopy.

In view of the increasing interest in the stereochemistry of the hetero analogs of cyclohexane and the preparation of new physiologically active substances, the number of papers devoted to 1,3-dithianes has increased [1,3]. In recent years, some stereochemical questions have been studied in relation to the 2-substituted 1,3-dithianes and the substituted 5-hydroxy- and 5-acetoxy-1,3-dithianes [2,3].

Continuing our investigations on the problems of the stereochemistry of hetero analogs of cyclohexane [4], we have synthesized a number of cyclic thioacetals of the type of 2,5-dialkyl-1,3-dithianes and thioketals of the type of 2,2,5-trialkyl-1,3-dithianes which have not previously been reported in the literature. The starting materials for these syntheses were 2-alkylpropane-1,3-diols [5], which were converted into 2-alkyl-1,3-dibromopropanes [6] (I–III, Table 1); the latter were converted by reaction with thiourea in an alkaline medium into 2-alkylpropane-1,3-dithiols [7]. The 2-alkylpropane-1,3-dithiols (IV–IX, Table 2) were condensed with acetaldehyde, butyraldehyde, and acetone in the presence of catalysts [8,9], giving 1,3-dithianes (X–XXIV, Table 3).

Table 1. 2-Alkyl-1,3-dibromopropanes (I–III)

Compound	R	Bp, °C (pressure, mm)	d_4^{20}	n_D^{20}	MR_D		Empirical formula	Br, %		Yield, %
					found	calculated		found	calculated	
I	CH_3	65 (15)	1,7832	1,5080	36,09	35,97	$C_4H_8Br_2$	74,2	74,0	60
II	C_2H_5	93 (28)	1,6808	1,5070	40,78	40,72	$C_5H_{10}Br_2$	69,5	69,6	93
III	C_4H_9	88 (4)	1,5136	1,4985	49,97	50,02	$C_7H_{14}Br_2$	61,8	62,0	74

The IR spectra of compounds X–XXIV (Fig. 1) have strong absorption bands in the 1294–1279, 1194–1182, 1068–1055, 979–964 and 886–872 cm^{-1} regions which, according to literature data [1], can be ascribed to the characteristic bands of 1,3-dithiane systems.

The 2,5-dialkyl-1,3-dithianes synthesized must be mixtures of geometric isomers. The gas-liquid chromatography of substances XVI and XXI clearly showed the presence in the samples of two stereoisomers in a ratio of 40 : 60. A study of the thin-layer chromatograms of the 2,5-dialkyl-1,3-dithianes led to similar results. We separated some of the mixtures into individual isomers. This was performed in total-condensation columns with 40 theoretical plates. The percentages of the individual stereoisomers were, according to GLC, 92–99%; thin-layer chromatography led to similar results (Table 4). The results given represent the first case of the separation of 2,5-dialkyl-1,3-dithianes into cis-trans isomers.

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*For part III, see [11].

The IR spectra of the individual isomers differ from one another mainly in the 940–500 cm^{-1} region, which can also be used to check the course of the separation and its completeness. Thus, absorption bands in the IR spectrum (Fig. 2) at 914 and 680 cm^{-1} are characteristic for the low-boiling isomer, while bands at 926 and 711 cm^{-1} are present in the spectrum of the high-boiling isomer. The presence of a comparatively weak band at 926 cm^{-1} in the spectrum of the low-boiling isomer (far less intense than in the mixture of isomers) apparently shows the presence of a small amount (about 8%) of the high-boiling isomer, which was confirmed by the GLC method.

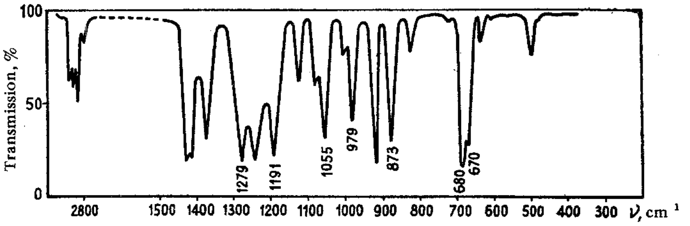


Fig. 1. IR spectrum of 2-methyl-1,3-dithiane (X) (film of the pure substance between KBr plates, IKS-14A spectrometer).

The results obtained do not give information on whether the individual isomers belong to the cis- or the trans-series. Further investigations will be devoted to elucidating the configuration of the isomers of the thioacetals and to a consideration of the stereochemical features of the thioketals of the 1,3-dithiane series. We may note that in the series considered (Table 4) there is some deviation from the Auwers-Skita rule, which shows the impossibility of applying it without substantial changes. However, the fact that the high-boiling isomer is solid under ordinary conditions permits the quite definite assumption that it, and consequently the other high-boiling isomers, are more stable than the low-boiling isomers.

Table 2. 2-Alkylpropane-1,3-dithiols (IV–IX).

Compound,	R	Bp, °C (pressure, mm)	d_4^{20}	n_D^{20}	MR_D		Empirical formula	S. %		Yield, %
					found	calculated		found	calculated	
IV	CH_3	81—82 (25)	1,0327	1,5250	36,18	36,10	$C_4H_{10}S_2$	52,2	52,4	70
V	C_2H_5	87 (28)	1,0275	1,5290	40,43	40,76	$C_{15}H_{12}S_2$	47,0	47,1	75
VI	C_3H_7	88 (8)	0,9985	1,5090	44,85	45,39	$C_6H_{14}S_2$	42,6	42,2	75
VII	i-C_3H_7	76 (5)	1,0087	1,5151	45,45	45,39	$C_6H_{14}S_2$	42,7	42,2	87
VIII	C_4H_9	96—97 (6)	0,9871	1,5085	49,67	50,06	$C_7H_{16}S_2$	38,8	39,1	84
IX	C_6H_{13}	99 (1)	0,9658	1,4978	58,88	59,23	$C_9H_{20}S_2$	32,6	33,0	81

EXPERIMENTAL

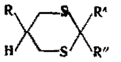
The 2-alkyl-1,3-dibromopropanes (I–III, Table 1) were synthesized as described previously [6].

The 2-alkylpropane-1,3-dithiols (IV–IX, Table 2) were obtained by a published method [7]. A mixture of 0.43 mole of a 2-alkyl-1,3-dibromopropane and 0.91 mole of thiourea in 50 ml of ethanol was boiled for 6 hr, cooled, treated with 300 ml of 5 N NaOH solution, and again heated in a constant flow of nitrogen for 2 hr, after which it was cooled and acidified with 2 N HCl to pH 2. The oily yellow layer of dithiol was separated off and the aqueous layer was extracted with ether; after drying with magnesium sulfate, the ether was distilled off and the dithiols were isolated by fractionation in vacuum. The IR spectra of the diothiols IV–IX exhibit the absorption bands of ν_{SH} at 2558–2550 cm^{-1} and of $\delta_{C—S}$ at 710 cm^{-1}.

The 2-substituted 5-alkyl-1,3-dithianes (X–XXIV, Table 3) were obtained by the condensation of the dithiols IV–IX with acetaldehyde, butyraldehyde, or acetone in the presence of acid catalysts (KU-1 or KU-2 ion-exchange resin in the H-form) in benzene solution by analogy with literature methods [8–10]. The separation of the stereoisomeric 1,3-dithianes was carried out by fractionation in the total-condensation columns with 40 theoretical plates (glass packing) in a similar manner to the separation of the isomers of XVI. Some 35 g of the mixture of isomers was distilled in a 24-hr column with a reflux number of 50. Thirteen fractions were collected, of which fractions 3–5 and 10–11, respectively, had similar constants. The properties of the isomers are given in Table 4.

Gas-liquid chromatograms of the mixtures of stereoisomers (XVI, XVIII, and XXI) and also those of the individual isomers after separation were recorded on a "Tsvet" chromatograph with a column 2 m long, SE-30 silicone elastomer as the liquid phase, and hydrogen as the carrier gas at a column temperature of 180° C in the case

Table 3


X-XXIV

Compound	R	R′	R″	Bp, °C (pressure, mm)	d_4^{20}	n_D^{20}	MR_D		Empirical formula	S. %		Yield, %
							found	calculated		found	calculated	
X	H	CH_3	H	56—59 (2)	1,1217	1,5595	38,60	39,09	$C_5H_{10}S_2$	47,4	47,8	81
XI	CH_3	CH_3	H	87 (12)	1,0701	1,5439	43,65	43,72	$C_6H_{12}S_2$	43,6	43,7	66
XII	i-C_3H_7	H	H	92 (3)	1,0705	1,5403	47,57	48,38	$C_7H_{14}S_2$	39,0	39,5	69
XIII	C_2H_5	CH_3	H	82—90 (5)	1,0563	1,5392	48,02	48,38	$C_7H_{14}S_2$	39,7	39,5	85
XIV	CH_3	CH_3	CH_3	75 (4)	1,0476	1,5315	47,94	48,38	$C_7H_{14}S_2$	39,3	39,5	61
XV	C_3H_7	CH_3	H	92—95 (3)	1,0285	1,5308	52,91	52,98	$C_8H_{16}S_2$	36,2	36,4	70
XVI	i-C_3H_7	CH_3	H	78—82 (1)	1,0465	1,5330	52,20	52,78	$C_8H_{16}S_2$	36,0	36,4	76
XVII	C_2H_5	CH_3	CH_3	55 (2)	1,0311	1,5270	52,54	52,98	$C_8H_{16}S_2$	36,2	36,4	78
XVIII	C_2H_5	i-C_3H_7	H	92—94 (2)	1,0221	1,5265	57,22	57,68	$C_8H_{16}S_2$	33,8	33,7	81
XIX	C_4H_9	CH_3	H	109—113 (4)	1,0184	1,5258	57,36	57,68	$C_9H_{18}S_2$	33,4	33,7	80
XX	i-C_3H_7	CH_3	CH_3	81 (1)	1,0227	1,5245	56,45	56,95	$C_9H_{18}S_2$	33,4	33,7	76
XXI	i-C_3H_7	i-C_3H_7	H	95—99 (3)	1,0186	1,5243	62,58	62,38	$C_{10}H_{20}S_2$	30,9	31,3	71
XXII	C_4H_9	CH_3	CH_3	99 (3)	0,9978	1,5178	62,10	62,38	$C_{10}H_{20}S_2$	31,0	31,3	80
XXIII	C_6H_{13}	H	H	132 (2)	1,0026	1,5230	62,15	62,38	$C_{10}H_{20}S_2$	31,1	31,3	65
XXIV	C_6H_{13}	CH_3	H	126 (4)	0,9865	1,5098	66,61	66,05	$C_{11}H_{22}S_2$	29,7	29,4	76

Table 4. Properties of the Isomers of the 2,5-Dialkyl-1,3-dithianes

Compound	Isomer	Bp, °C (pressure, mm)	d_4^{20}	n_D^{20}	MR_D		R_f*	Ratio of the isomer
					found	calculated		
XVI	a	69 (1)	1,0425	1,5348	52,44	52,18	0,68	40
	б	72 (1)	1,0395	1,5330	52,57	52,78	0,62	60
XVIII	a	76 (0,5)	1,0227	1,5279	57,68	57,68	0,62	40
	б	79 (0,5)	1,0194	1,5266	57,40	57,68	0,55	60
XXI	a	98 (2)	1,0165	1,5262	61,50	62,02	0,61	40
	б	Т. пл. 41					0,51	60

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*Chromatography was carried out in a thin nonfixed layer of Al_2O_3 of activity grade II in hexane.

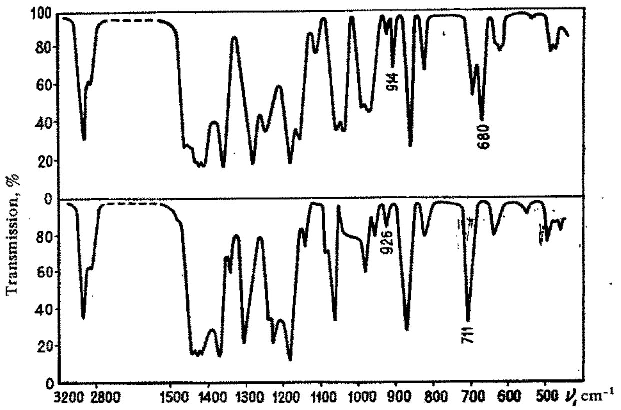

Fig. 2. IR spectra of 5-isopropyl-2-methyl-1,3-dithiane (XVI): top) low-boiling isomer; bottom) high-boiling isomer.

of compounds XVI and XVIII and 123° C in the case of compound XXI.

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