Conformational Analysis

XIX† Properties and Reactions of 1,3-Oxathianes VIII§ A ^{1}H NMR Conformational Study of Methyl-Substituted Derivatives

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The addition of thioacetic acid to unsaturated alcohols or acids was utilized to obtain mercaptoalkanols which were condensed with suitable carbonyl compounds to prepare 24 methyl-substituted 1,3-oxathianes. The ^{1}H NMR spectra of the 1,3-oxathiane products were recorded at 60, 100 and/or 300 MHz and fully analysed. The results are best explained by a chair form which is completely staggered in the C-4—C-5—C-6 moiety (ψ_{45} or $\psi_{56} = 60 \pm 1°$). 1,3-Oxathianes having *syn*-axial 2,4- (and/or 2,6-) methyl-methyl interactions exist appreciably, if not exclusively, in twist forms. The vicinal coupling constants lead to the conformational free energies of axial methyl groups at C-4, $\Delta G° = 7.4 \pm 0.4$ kJ mol^{-1}, and at C-5, $\Delta G° = 3.7 \pm 0.3$ kJ mol^{-1}, in good agreement with previous estimates. They also show that both *r*-4,*cis*-5,*trans*-6- and *r*-4,*trans*-5,*trans*-6-trimethyl-1,3-oxathianes greatly favour the chair form where the methyl group at C-4 is axial. The chair-twist energy parameters are reestimated at $\Delta H°_{CT}$ 27.0 kJ mol^{-1}, $\Delta S°_{CT}$ 11.6 J mol^{-1}K^{-1}, and $\Delta G°_{CT}(298)$ 23.5 kJ mol^{-1} for a 2,5-twist form.

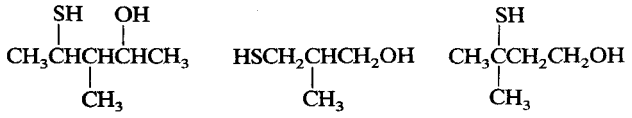
INTRODUCTION

In the past ^{1}H NMR spectra of many saturated 1,3-diheterocyclanes have been analysed as being first order.[3–7] In some cases this is a good approximation,[3,4,7] but fairly often the parameters obtained by an incomplete analysis lead to a severe structural misinterpretation.[5] ¶ To obtain a better insight into the conformational behaviour of 1,3-oxathianes and the influence of the assumed first-order character[6a,6c] of the ^{1}H NMR spectra, a number of methyl-substituted 1,3-oxathianes were prepared and their ^{1}H NMR spectra fully analysed with the aid of the LAOCOON III program. The chair-twist equilibrium in these compounds will also be discussed in the light of present and some earlier results.[8,9]

RESULTS AND DISCUSSION

Preparation of mercaptoalkanols

The known restrictions of substitution reactions by sulphur-containing nucleophiles in the syntheses of mercaptoalkanols from halogen compounds[10] or oxetanes[10,11] prompted us to examine the addition reaction of thioacetic acid to unsaturated alcohols as a step toward alkylated 1,3-oxathianes.[10b] This reaction, catalyzed by free radicals, was employed in the production of two intermediates, 3-methyl-4-mercapto-2-pentanol (**1**) (previously unknown) and 2-methyl-3-mercapto-1-propanol (**2**). A useful extension of this procedure is the acid-catalyzed addition of thioacetic acid to 3-methyl-2-butenoic acid which afforded 3-methyl-3-mercapto-1-butanol[12] (**3**) in two simple steps, consisting of the addition stage effected by internal acid catalysis and subsequent hydrogenolysis[12] with $LiAlH_4$. In the latter case advantage was taken of two older investigations dealing with the addition of sulphur compounds to unsaturated acids[13] and the hydrogenolysis of thioesters.[14]



1 **2** **3**

As the direction of the addition is easily controlled by the choice of proper catalytic conditions, the method provides a general approach to different mercaptoalkanols with the specific nature of the mercapto group required. The free radical modification can be profitably applied to the synthesis of primary and secondary mercaptans, whereas the ionic mechanism is best suited to preparing tertiary mercaptans.

1,3-Oxathianes

The geminal coupling constants (Table 1) are of the expected order of magnitude and are in general agreement with earlier results.[12,16,17] Only $J(55)$ changes significantly with increasing substitution, although the change does not reflect a difference in the ring conformation since the values for **20** (a chair) and **21** (a

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† For Part XVIII, see Ref. 1.
§ For Part VII, see Ref. 2.
¶ (a) In Ref. 5 the X parts of some ABX spectra are considered to give correct values for $J(AX)$ and $J(BX)$ despite the fact that $\Delta_{AB} \ll J(AB)$ as pointed out in Ref. 4; (b) In Ref. 6b the second order ^{1}H NMR spectra of some methyl-substituted 2-oxo-1,3,2-dioxathianes are erroneously analysed, as pointed out in Ref. 7.

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Table 1. Chemical shifts (ppm) and geminal and CH_3—H coupling constants (Hz) for the studied 1,3-oxathianes[h]

	Compound	δ 2e	2a	4e	4a	5e	5a	6e	6a	J 2e2a	4e4a	5e5a	6e6a
4[a]	2-Me	1.43	4.68	2.69	3.00	1.65	1.92	4.09	3.57	6.0	−13.38	−14.25	−11.75
5[a]	4-Me[b]	~4.72	~4.72	1.23	3.02	1.76	1.68	4.04	3.47	—[e]	6.5	-14.08_5	−11.94
6[c]	5-Me[b]	4.62	4.56	2.65	2.45	0.75	1.91	3.80	3.07	−11.2	−13.15	7.0	−11.61
7[a]	6-Me	4.79	4.86	2.74	3.01	1.78	1.65	1.19	3.52	−11.2	−13.88	−13.79	6.0
8[d]	*c*-2,4-Me_2	1.46_5	4.46	1.22	3.09	1.71	1.59	4.18	3.56	6.2	6.8	−13.89	−12.07
9[c]	*t*-2,5-Me_2	1.38	4.66	2.60	2.56	0.81	1.94	3.89	3.05	6.2	−13.40	6.8	−11.62
10[d]	*c*-2,6-Me_2	1.48	4.90	2.74	3.03	1.74	1.54	1.22	3.59	6.2	−13.42	−13.77	6.3
11[f]	4,4-Me_2	4.70	4.70	1.35	1.35	1.66	1.66	3.76	3.76	—[e]		—[e]	—[e]
12[f]	6,6-Me_2	4.77	4.77	2.78	2.78	1.70	1.70	1.20	1.20	—[e]	—[e]	—[e]	
13[c]	2,4,4-Me_3	1.35	4.82_5	1.22	1.43	1.34	1.80	3.92	3.68	6.1		−13.80	−12.09
14[c]	2,2,5-Me_3[b]	1.41	1.51	2.57	2.54	0.86	1.67	3.61	3.31		−13.43	6.8	−12.10
15[d]	2,6,6-Me_3	1.41_5	5.13	2.57	3.15	1.64	1.72	1.25	1.25	6.1	−13.66	−13.81	
16[c]	*r*-4,*t*-5,*c*-6-Me_3	4.64	4.76	1.22	2.66	0.90	—[e]	1.19	3.07	−11.1	6.7	6.5	6.2
17[c]	*r*-4,*c*-5,*c*-6-Me_3	4.67	4.72	1.17	3.17	~1.43	0.92	1.09	3.44	−10.7	7.1	6.6	6.4_5
18[f]	*r*-4,*t*-5,*t*-6-Me_3[b]	4.58	4.86	2.76	1.56	~1.34	1.05	1.11	3.91	−11.2	7.1	6.8	6.6
19[f]	*r*-4,*c*-5,*t*-6-Me_3[b]	4.63	4.94	2.88	1.38	0.87	1.94	1.14	3.51	−11.1	7.2	6.7	6.2
20[a]	2,2,*c*-4,6-Me_4	1.51	1.62	1.13	3.12	1.74	1.08	1.13	3.79		6.8	−12.90	6.2
21[c]	2,2,*t*-4,6-Me_4[g]	1.48_5	1.51	3.07	1.32	1.68	1.31	1.12	3.98		7.1	−13.02	6.3
22[f]	2,2,4,4-Me_4[b,g]	1.53	1.53	1.35	1.35	1.58	1.58	3.88	3.88			—[e]	—[e]
23[f]	2,2,6,6-Me_4[g]	1.53	1.53	2.80	2.80	1.68	1.68	1.23	1.23		—[e]	—[e]	
24[c]	2,2,*r*-4,*t*-5,*c*-6-Me_5	1.42	1.60	1.15	2.78	—[e]	—[e]	1.14	3.46		6.6	—[e]	6.1
25[f]	2,2,*r*-4,*c*-5,*c*-6-Me_5	1.45	1.60	1.14	3.33	—[e]	0.85	1.07	3.91		7.0	—[e]	6.4
26[c]	2,2,*r*-4,*t*-5,*t*-6-Me_5[g]	1.47	1.49	2.66	1.37	—[e]	0.97	1.04	4.16		7.1	6.5	6.5
27[f]	2,2,*r*-4,*c*-5,*t*-6-Me_5[g]	1.43	1.52	3.26	1.16	0.80	—[e]	1.13	3.43		7.4	—[e]	6.2

[a] JEOL Minimar-100, $CDCl_3$.
[b] Not conformationally homogeneous.
[c] Varian HA-100, CCl_4.
[d] Varian HR-300, $CDCl_3$.
[e] Not determined.
[f] Perkin Elmer R-10, CCl_4.
[g] Twist forms.
[h] Geminal coupling constants are negative.

2,5-twist) are equal within the combined error limits. The somewhat less negative value of $J(44)$ for **6** (Fig. 1) may indicate that its value becomes more positive in the axial chair conformation (**6b**) as a consequence of the outward bending of the methyl group. Otherwise the conclusions[6a,6c] presented earlier agree with the present ones.

Comparison of the individual values of the vicinal coupling constants (Table 2) with those presented earlier[6a] shows that the values obtained with the first-order analysis may be in error by as much as 2Hz, which, at least, makes them useless in estimating torsional angles by the Lambert-Buys method,[15,18] which allows the evaluation of the torsional angle for the C-4—C-5 (ψ_{45}) and/or for the C-5—C-6 fragment (ψ_{56}) of many of the compounds studied in this work (**4**, **5**, **7**, **8**, **10–13**, **15**, **22** and **23**). Furthermore, the vicinal coupling constants for **21** (Fig. 1) may be applied to estimate the average torsional angle for the C-4—C-5—C-6 moiety.[18b,19] A summary of these estimates is shown in Table 3. Both ψ_{45} and ψ_{56} are in all cases (except ψ_{av} for **21**) within $60\pm1°$ and do not differ significantly from each other. It has been pointed out earlier[18c] that $\psi_{45}=\psi_{56}=55°$ for 1,3-dioxanes, in agreement with the flattening in this part of the molecule. Similarly, $\psi_{45}=\psi_{56}=63°$ for 1,3-dithianes[18c] since a C—S bond is longer than a C—C bond and hence C-5 is now at a super-chair position.[20] It is interesting that, despite the three different bond lengths[6a] (C—O 141, C—C 154, and C—S 182 pm), the C-4—C-5—C-6 moiety may attain a fully staggered shape in 1,3-oxathianes. In contrast to the previous conclusion based on inaccurate ^1H NMR parameters,[6a] substitution has practically no influence on the magnitude of ψ_{45} and/or ψ_{56}. The discussion considering the spectrum of **15**, in particular, is misleading in Ref. 6a. The torsional angles in **21–23** (Fig. 1) deserve further attention since these derivatives are twist forms due to the *syn*-axial 2,4- or 2,6-Me,Me-interactions in their respective chair conformations.[6c,8,9]

As reported previously[6a,8] 2,2,*trans*-4,6-tetramethyl-1,3-oxathiane (**21**) exists predominantly in a 2,5-twist conformation where the methyl groups at position 2 are isoclinal and at positions 4 and 6 pseudoequatorial. The average torsional angle is only 54°, which is 6° less than in **22** (mainly a 1,4-twist) or in **23** (a 3,6-twist), in good agreement with the respective angle ($R=1.2$, $\psi=48°$, $\Delta=55°-48°=7°$) *in* 2,2,*trans*-4,6-tetramethyl-1,3-dioxane which also exists in a 2,5-twist form.[4] Our report[4] on methyl-substituted 1,3-dioxanes also demonstrated that compounds with geminal substituents at both positions 2 and 4 attained preponderantly 1,4-twist conformations, where both methyls at position 4 are isoclinal and one methyl group at position 2 has a hindered pseudoaxial orientation (cf. **22b**, Fig. 1). In 1,4-twist forms the C-5—C-6 fragment is quite normally staggered, as indicated by the magnitude of the vicinal coupling constants.[4,5] Although the AA'XX' spectra of **22** and **23** give the values of $J(trans)$ and $J(cis)$ only for the C-5—C-6 and C-4—C-5 fragments, respectively, their values are very

Table 2. Vicinal and long range (LR) coupling constants (Hz)

	J									
1,3-Oxathiane	4e5e	4e5a	4a5e	4a5a	5e6e	5e6a	5a6e	5a6a	LR	$\pm\Delta J \leq$
4	3.66	3.68	3.07	12.41	2.20	1.99	4.15	12.75	1.97[a]	0.03
5[b]			2.82_5	11.04	2.84	2.44	3.68	12.15		0.02
6[b]		3.37		9.92			3.64	9.52	1.46[a]; 1.36[c]	0.05
7	3.82_5	3.72	2.82	13.00		2.06		11.23		0.04
8			2.69	11.55	2.26	2.00	4.05	12.57		0.01
9		3.80		11.40			3.85	10.95	2.0[a]	0.05
10	3.50	3.69	2.82	12.75		2.04		11.22		0.02
11[b]					7.7[d]	3.2[e]	3.2[e]	7.7[d]		0.1
12[b]	8.5[d]	3.4[e]	3.4[e]	8.5[d]						0.1
13					2.34_5	1.97	4.39	12.93		0.02
14		4.23		9.49			4.11	9.71	0.90[a]	0.05
15	3.79_5	3.98_5	2.81	13.11						0.02
16				9.5				9.3		0.1
17			2.7			2.0			0.5[f]	0.1
18[b]	3.2					2.1				0.1
19[b]		3.8						8.85		0.1
20			2.76	11.94		2.05		11.32		0.01
21[g]	7.94	5.74				4.79		9.46_5		0.02
22[b,g]					7.5[d]	3.0[e]	3.0[e]	7.5[d]		0.1
23[g]	8.4[d]	3.3[e]	3.3[e]	8.4[d]						0.1
24				9.5				8.9		0.1
25			2.5			1.8				0.1
26[g]	6.1					3.6				0.1
27[g]		5.25						8.2		0.1

[a] 4e6e.
[b] A conformational mixture.
[c] 2e4e.
[d] $\frac{1}{2}[J(aa)+J(ee)]$.
[e] $\frac{1}{2}[J(ae)+J(ea)]$.
[f] 2e5e.
[g] Twist forms.

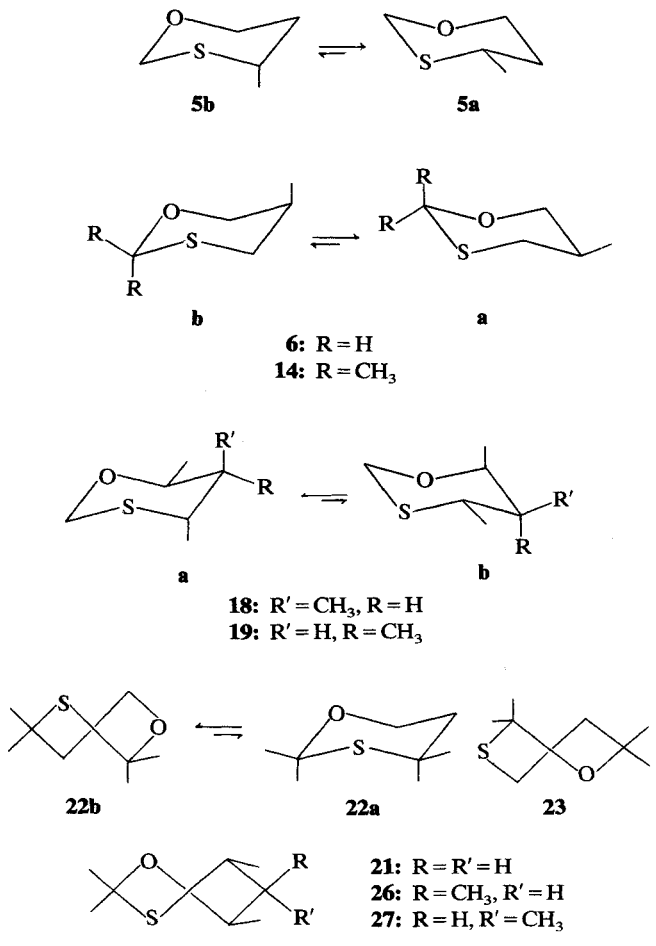


Figure 1. Conformational equilibria and twist conformations in the studied 1,3-oxathianes.

similar to those in 1,3-oxathianes with chair conformations (Table 3). Accordingly, the above postulate[4] in regard to the non-chair conformations of 1,3-dioxanes also seems to succeed in explaining the non-chair conformations of 1,3-oxathianes. The torsional angles ($\psi_{45} = \psi_{56} = 60°$) for **22** and **23** can only be explained if their prevailing conformations are 1,4- (**22b**) and 3,6-twist (**23**) forms.

2,2,4,4-Tetramethyl-1,3-oxathiane (**22**) may include chair form **22a**[9,20–22] in which the magnitude of the different interactions is approximately the following: 2,4-transannular Me,Me[8] $\simeq 19.2$ kJ mol^{-1}; 2,6-transannular Me,H[20,21] $\simeq 9.2$ kJ mol^{-1}; 4,6-transannular Me,H[20,21] $\simeq 3.1$ kJ mol^{-1}. The sum of these interactions, 31.5 kJ mol^{-1}, is clearly higher than the excess free energy of a 1,4-twist form which is at least less than 28 kJ mol^{-1} if we assume that the interaction due to the pseudoaxial methyl group in **22b** is of the order of 5 kJ mol^{-1}. In the case of **23** the chair form would include the following interactions:[20,21] 2,6-transannular Me,Me which now should be about 2.6 times that in cyclohexanes $\simeq$ 40.1 kJ mol^{-1}; 2,4-transannular Me,H $\simeq 4.4$ kJ mol^{-1} and 4,6-transannular Me,H $\simeq 3.1$ kJ mol^{-1}. The sum of these interactions, 47.6 kJ mol^{-1}, is at least 20 kJ mol^{-1} higher than the excess free energy of the respective 3,6-twist form (Fig. 1) which is again less than 28 kJ mol^{-1} if the interaction[9] due to the pseudoaxial methyl group is of the order of 5 kJ mol^{-1}. Compounds **26** and **27** also have non-chair forms and exist principally in 2,5-twists (Fig. 1), in agreement with the observed coupling constants which resemble those in **21** and 2,2,*r*-4,*cis*-5,*trans*-6-pentamethyl-1,3-dioxane[4] (Table 2). For **21**, **26** and

Table 3. Torsional angles on the S-side (ψ_{45}) and on the O-side (ψ_{56}) in the studied 1,3-oxathianes

	Compound	Side	J(trans)	J(cis)	R	ψ^a
4	2-Me	S	8.04	3.38	2.38	59.3
		O	7.48	3.07	2.44	59.7
5	4-Me	O	7.50	3.06	2.45	59.7
7	6-Me	S	8.41	3.27	2.57	60.4
8	*c*-2,4-Me_2	O	7.42	3.03	2.45	59.7
10	*c*-2,6-Me_2	S	8.13	3.26	2.49	60.0
11	4,4-Me_2	O	7.7	3.2	2.4	59.4
12	6,6-Me_2	S	8.5	3.4	2.5	60.0
13	2,4,4-Me_3	O	7.64	3.18	2.40	59.4
15	2,6,6-Me_3	S	8.45	3.40	2.49	59.9
21	2,2,*t*-4,6-Me_4	O,S	8.70	5.26	1.65	53.8[b]
22	2,2,4,4-Me_4	O	7.5	3.0	2.5	60.0
23	2,2,6,6-Me_4	S	8.4	3.3	2.55	60.3

[a] For compounds with a chair or a 1,4- or 3,6-twist conformation $\psi_{45} \sim \psi_{56} = 60 \pm 1°$.
[b] Average torsional angle for the C-4—C-5—C-6 moiety of a 2,5-twist form.

27 the 2,5-twists are at least 8 kJ mol^{-1} more stable than the respective chair forms, and hence the amounts of the latter do not exceed 5%.

In the light of the preceding discussion on the various twist forms it seems desirable to simplify our previous treatment of the chair-twist equilibrium of **28** and **29** (Fig. 2),[9] since we now believe that the equilibrium between *r*-2-*tert*-butyl-2, *trans*-6- (**28**) and *r*-2-*tert*-butyl-2, *cis*-6-dimethyl-1,3-oxathianes (**29**) is satisfactorily explained by taking into account only the conformations shown in Fig. 2.

Since **29b** is as stable as **28**, $K_T = [\mathbf{29a}]/[\mathbf{28}] = K_{obs} - 1$. Consequently, K_T has the values 80.2, 56.0, and 40.2 at 280.15, 298.15, and 318.15 K, respectively;[9] from which $-\Delta H° = 13.4 \pm 0.2$ kJ mol^{-1} and $-\Delta S° = 11.6 \pm 0.7$ J mol^{-1}K^{-1}. The chair-(2,5-twist) enthalpy difference, $\Delta H°_{CT}$, is hence 13.4 + 13.6 = 27.0 kJ mol^{-1} where the correction, 13.6 kJ mol^{-1}, is due to the conformational energy of the axial methyl group at position 2 in **29a**.[20,21] $\Delta S°_{CT}$ is equal to the experimental entropy difference, 11.6 J mol^{-1}K^{-1} and $\Delta G°_{CT}$ then becomes equal to 23.5 kJ mol^{-1} at 298 K. The present estimates do not differ appreciably from our original results,[9] although the latter were derived by a complex approach. Moreover, the agreement between $\Delta H°_{CT}$ in the gaseous state, 25 ± 2 kJ mol^{-1}, from appearance potential measurements[8,22] and the liquid state value, 27 ± 1 kJ mol^{-1}, is still very good.[8,9,22]

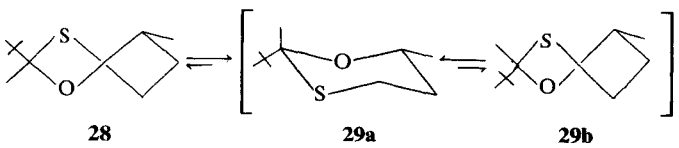
The derivatives which are mixtures of non-equivalent interconverting chair forms (**5**, **6**, **14**, **18** and **19** in Fig. 1) are finally considered. For 5-methyl-1,3-oxathiane (**6**) we can estimate the conformational equilibrium constant from the equation

$$K = \frac{\Sigma J_{obs} - \Sigma J(\mathbf{6b})}{\Sigma J(\mathbf{6a}) - \Sigma J_{obs}} \quad (1)$$

where $\Sigma J_{obs} = 26.45$ Hz (Table 2), $\Sigma J(\mathbf{6a}) = \Sigma J(\mathbf{14a}) = 30.0$ Hz (from **9**), and $\Sigma J(\mathbf{6b}) = \Sigma J(\mathbf{14b}) = 10.7$ Hz consists of the following individual coupling constants: J(4e5e) 3.7 (average for **4**, **7**, **10** and **15**); J(5e6e) 2.3 (average for **4**, **8** and **13**); J(4a5e) 2.7 (**8** and **17**), and J(5e6a) 2.0 Hz (all anancomeric chair forms). Thus K will be 4.4 ± 0.6 and $-\Delta G°$(5a−Me) at 298 K becomes equal to 3.7 ± 0.3 kJ mol^{-1}. Similarly, for **14** $\Sigma J_{obs} = 27.54$ Hz, $K = 6.8 \pm 1.3$ and $-\Delta G°(298)$ between **14a** and **14b** equals 4.8 ± 0.7 kJ mol^{-1}. Due to the axial methyl group at position 2 of **14** the model values for **14a** and **14b** may differ somewhat from those of **6a** and **6b**, although this difference is likely to be small in their sums. It is also easy to understand that the conformational energy difference between **14b** and **14a** is greater than the conformational energy of a single axial methyl group in **6b** (Fig. 1) since **14b** is unable to minimize simultaneously the conformational interactions due to the two axial methyl groups.[21] The present value, 3.7 kJ mol^{-1}, for $-\Delta G°$ (5a−Me) is somewhat larger than the value of 2.85 kJ mol^{-1} determined earlier by equilibrating epimeric 2-isopropyl-5-methyl-1,3-oxathianes.[21] This is, however, in line with the observations in the 1,3-dioxane series[23,24] which showed that the conformational energy of the axial methyl group at position 5 decreases if the 2 position carries an isopropyl substituent. At any rate, *cis*-2-alkyl-5-methyl-1,3-oxathianes exist almost exclusively in the 2e5a form (>98%), in contrast to the opinion of Bogatskii *et al.*[25]

In the case of **5**, the conformational equilibrium greatly favours the equatorial chair form (**5a**), since $-\Delta G°$ (4a−Me) has been determined to be 7.5 kJ mol^{-1} from the chemical equilibration of suitable model compounds.[20,21,24] Hence the denominator in Eqn (2) becomes very small and a more accurate value for the conformational equilibrium constant is now obtained using the values of the vicinal coupling constants separately. Furthermore, only J(ee) and J(aa) in **5b** and **5a** can be estimated accurately enough to determine $K = 20 \pm 3$ from the corresponding averaged coupling constants (Table 3) using J(4e5e) 3.15 (from *r*-2,*trans*-4,*cis*-6-trimethyl-1,3-oxathiane in Ref. 6a), J(4a5a) 11.55 (from **8**). J(5e6e) 2.35 (from **13**) and J(5a6a) 12.57 Hz (from **8**). This, in turn, leads to $-\Delta G°$(4a−Me) = 7.4 ± 0.4 kJ mol^{-1}, in excellent agreement with the equilibration results.[20,21,24]

In the case of compounds **18** and **19** the values of the vicinal coupling constants indicate that the contribution of the 6-axial conformations is minor and probably less than 10%. Taking into account the different interactions[21,24,26] in the possible chair forms, both **18a** and **19a** are favoured by at least about 5 kJ mol^{-1}, a result which is similar to the conclusion drawn from the vicinal coupling constants.



28 29a 29b

Figure 2. The chair-twist equilibrium of **28** and **29**.

EXPERIMENTAL

^{1}H NMR spectra (cf. Table 1) were recorded on one of the following instruments: Perkin Elmer R10

(60 MHz, 10% v/v solution in CCl_4, 306 K) Jeol[27] Minimar-100 (100 MHz, 10% v/v solution in $CDCl_3$, 298 K), Varian[28] HA-100 (100 MHz, 10% v/v solution in CCl_4, 298 K), and Varian[29] HR-300 (300 MHz, 5% v/v solution in $CDCl_3$, 293 K). Tetramethylsilane (1%) was the internal standard in all cases. Spectral analyses were carried out using an iterative LAOCOON III program on an Elliott 4130 computer (at the University of Stirling, Scotland[30] unless otherwise stated). In these cases (see also preceding Discussion) the analyses were confirmed by comparison of the observed spectra with those generated by a LAOCOON PLOT program.

Of the studied 1,3-oxathianes (Tables 1 and 2) **4**, **5**, **7**, **8**, **10** and **15** were obtained from previous work[10a,b] whereas **6**, **9**, **13**, **14** and **16–27** were synthesized for the present study. The ^1H NMR spectra of the first-mentioned compounds and **20** and **21** have been analysed earlier on a first-order basis,[6a] but the present results obtained by an iterative LAOCOON III analysis indicate that the assumed first-order[6a] analysis is valid for **20** and **21** only. The spectra of **6**, **9** and **14** were, however, analysed with the aid of two ABX-type subspectra and those of **16–19** and **24–27** as AMX spectra, treating the additional couplings due to the methyl groups on a first-order basis. Finally, the AA'XX' analysis of the spectra of **11**, **12**, **22** and **23** gave *J*(*trans*) and *J*(*cis*) only for their C-5—C-6 or C-4—C-5 fragments.[15]

Compounds

3-Methyl-4-mercapto-2-pentanol was prepared from thioacetic acid (0.1 mol) and 3-methyl-3-penten-2-ol (0.057 mol). The addition reaction was initiated by a few drops of ascaridole and brought to completion by stirring magnetically and heating at 80 °C overnight. 3-Methyl-4-acetylmercapto-2-pentanol was collected at 125–155 °C (8 Torr), n_D^{20} 1.4818. This material was decomposed by 2% HCl in methanol to a mixture (4.2 g, 55%) of the four diastereoisomeric 3-methyl-4-mercapto-2-pentanols, b.p. 100–112 °C (18 Torr), n_D^{20} 1.4804. Anal. Calcd. for $C_6H_{14}OS$: C 53.68, H 10.51. Found: C 53.42; H 10.70.

3-Methyl-3-penten-2-ol was prepared from 3-methyl-2,4-pentanediol (Fluka AG) through the cyclic carbonate.[11c] The catalytic pyrolysis of the carbonate obtained from 11.8 g (0.1 mol) of the diol gave 5.8 g (57%) of 3-methyl-3-penten-2-ol, b.p. 110–140 °C (760 Torr). Product analysis exhibited no trace of oxetane formation.

2-Methyl-3-mercapto-1-propanol was prepared from thioacetic acid (0.2 mol) and 2-methyl-2-propen-1-ol (0.1 mol) from Fluka AG using ascaridole as catalyst. The addition product was collected at 90–120 °C (8 Torr), n_D^{20} 1.4878. Methanolysis furnished 7.0 g (66%) of 2-methyl-3-mercapto-1-propanol, b.p. 73–76 °C (8 Torr), n_D^{20} 1.4877; lit.[33] b.p. 88–89 °C (16 Torr).

3-Methyl-3-mercapto-1-butanol was prepared from thioacetic acid and 3,3-dimethylacrylic acid (Fluka AG). A mixture consisting of 0.1 moles of the two reagents was refluxed under a nitrogen atmosphere at 120 °C for 4 days. The unreacted thioacetic acid was removed by vacuum distillation and the unchanged 3,3-dimethylacrylic acid, c. 50%, by fractional crystallization. The addition product was a viscous colourless liquid and was subjected to hydrogenolysis as follows. A solution of 8.8 g (0.05 mol) of the substrate in 300 ml of ether was slowly added to a magnetically stirred suspension of 5.7 g of $LiAlH_4$ in 500 ml of ether. The excess $LiAlH_4$ was destroyed with water and the mixture was poured into ice cold 20% H_2SO_4. After the usual work up, the yield of 3-methyl-3-mercapto-1-butanol [b.p. 85–90 °C (17 Torr), n_D^{20} 1.4725, lit.[12] b.p. 84 °C (12 Torr)] was 4.0 g (59%).

2-Methyl-4-mercapto-2-butanol was synthesized as described previously.[10b]

4-Mercapto-2-pentanol was available from earlier studies.[6c,10a,b]

The *1,3-oxathianes* were prepared conventionally[10a,10b] by condensation of the above mercaptoalkanols and the appropriate aldehydes or ketones with the exception of 2,2,6,6-tetramethyl-1,3-oxathiane which was prepared by refluxing 0.1 mol of 2-methyl-4-mercapto-2-butanol and 0.11 mol of 2,2-dimethoxypropane in the presence of a trace of Dowex 50. Methanol was removed by slow distillation through a Vigreux column. The residue was then purified by filtration and fractional distillation at reduced pressure.

The physical constants of the 1,3-oxathianes prepared in this work are shown in Table 4. Stereoisomeric 1,3-oxathianes were separated on a preparative Perkin-Elmer F21 gas chromatograph when necessary. Effective resolution of isomeric forms was achieved by subsequent use of two types of columns containing 10% XE-60 on Chromosorb G (60/80 mesh) and 10% QF-1 on Chromosorb W (6/80 mesh). The configurational assignments were straightforward with the aid of ^1H and ^{13}C NMR spectra.[31]

Table 4. Physical constants for the 1,3-oxathianes prepared in this work

Compound	B.p., °C (Torr)	n_D^{20}	Yield, %
6 5-Me	48–52 (8)	1.4938	19
9 2,5-Me_2[a]	49–51 (8)	1.4812	90
11 4,4-Me_2	68–80 (20)	1.4860	53
12 6,6-Me_2	51–54 (5)	1.4918	43
13 2,4,4-Me_3	67–73 (19)	1.4747[b]	42
14 2,2,5-Me_3	52–53 (6)	1.4797	
16 *r*-4,*trans*-5,*cis*-6-Me_3	86–93[c] (23)	1.4847	66[c]
17 *r*-4,*cis*-5,*cis*-6-Me_3		1.4873	
18 *r*-4,*trans*-5,*trans*-6-Me_3		1.4918	
19 *r*-4,*cis*-5,*trans*-6-Me_3		1.4934	
20 2,2,*cis*-4,6-Me_4	51–54[c] (8)	1.4704	79[c]
21 2,2,*trans*-4,6-Me_4		1.4676	
22 2,2,4,4-Me_4	73–77 (15)	1.4743	32
23 2,2,6,6-Me_4	60–63 (6)	M.p. 33–36 °C	28
24 2,2,*r*-4,*trans*-5,*cis*-6-Me_5	62–70[c] (7)	1.4752	72[c]
25 2,2,*r*-4,*cis*-5,*cis*-6-Me_5		1.4744	
26 2,2,*r*-4,*trans*-5,*trans*-6-Me_5		1.4713	
27 2,2,*r*-4,*cis*-5,*trans*-6-Me_5		1.4704	

[a] An approximately 85 : 15 mixture of *trans* and *cis* isomers.
[b] At 25 °C.
[c] For mixtures of diastereoisomers.

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