Tetrahedron Vol. 28, pp. 2617 to 2626. Pergamon Press 1972. Printed in Great Britain

PROPERTIES AND REACTIONS OF 1,3-OXATHIANES V[1]

CONFORMATIONAL ANALYSIS AND CONFORMATIONAL ENERGIES OF AXIAL ALKYL GROUPS

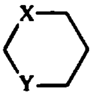
P. PASANEN and K. PIHLAJA

Department of Chemistry, University of Turku, 20500 Turku 50, Finland

(*Received in the UK* 11 *January* 1972; *Accepted for publication* 17 *January* 1972)

Abstract—Several epimeric alkyl-substituted 1,3-oxathianes have been chemically equilibrated. The equilibrations and some compilations yielded values for the conformational energies of axial methyl, ethyl and isopropyl groups on position 2, and values for the conformational energies of axial methyl groups on positions 4, 5 and 6. These results are discussed in comparison with the corresponding data for 1,3-dioxanes and 1,3-dithianes.

DURING THE LAST FEW YEARS increasing attention has been paid to saturated six-membered heterocycles containing heteroatoms at positions 1 and 3.



(1) X = Y = 0
(2) X = Y = S
(3) X = 0; Y = S

The ring conformation and conformational effects in 1,3-dioxanes (**1**) have been most widely explored[2] whereas only one extensive study has been reported on 1,3-dithianes (**2**).[3] 1,3-Oxathianes (**3**) are very interesting structural intermediates between **1** and **2** and hence their conformational properties seemed to be worthy of detailed investigation.

To date only a few reports[4] have been published on the conformational aspects of **3** and thus we began a systematic study of this series of compounds. In continuation of our investigation the present paper deals with different conformational interactions and ring conformations of 1,3-oxathianes (**3**) by the chemical equilibration of several epimeric stereoisomers.

RESULTS AND DISCUSSION

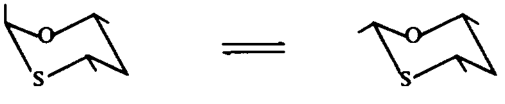
2,4,6-*Trimethyl*-1,3-*oxathianes*

The conformational energy of an axial Me group on position 2 is directly obtainable from the equilibration of *r*-2-*trans*-4-*trans*-6- and *r*-2-*cis*-4-*cis*-6-trimethyl-1,3-oxathianes* (Eq. 1) if we assume the entropy difference is equal to zero (Table 1). This assumption is very reasonable, since even in the equilibration of *r*-2-*cis*-4-*trans*-6- and *r*-2-*trans*-4-*cis*-6-trimethyl 1,3-oxathianes (Eq. 2) the entropy difference is almost negligible. Consequently, we can select the value $-\Delta G^\circ = H_{2a}{}^{i} = 3\cdot25$ kcal/mol to

* The substituent to which the orientation of the other substituents is compared has the notation *r*.

represent the conformational energy of an axial Me group on position 2 in 1,3-oxathianes (Tables 1 and 2).

If we compare the above value to the corresponding interactions in 1,3-dioxanes and 1,3-dithianes we observe that the value in 1,3-oxathianes is slightly greater than a half of the sum of the respective conformational energies in the former compounds 0·5 × 1·77 + 0·5 × 4·07 = 2·92 kcal/mol.[2a, 2q, 3a]



r-2-*trans*-4-*trans*-6 *r*-2-*cis*-4-*cis*-6 (1)

TABLE 1. EQUILIBRATIONS OF ISOMERIC 2,4- AND 2,6-DIALKYL- AND 2,4,6-TRIMETHYL-1,3-OXATHIANES AT 25°

Entry	Equilibrium
1	*trans*-2,4-diMe $\rightleftharpoons$ *cis*-2,4-diMe
2	*trans*-2,6-diMe $\rightleftharpoons$ *cis*-2,6-diMe
3	*r*-2-*trans*-4-*trans*-6-triMe $\rightleftharpoons$ *r*-2-*cis*-4-*cis*-6-triMe
4*	*r*-2-*cis*-4-*trans*-6-triMe $\rightleftharpoons$ *r*-2-*trans*-4-*cis*-6-triMe
5	*trans*-2-isoPr-4-Me $\rightleftharpoons$ *cis*-2-isoPr-4-Me
6	*trans*-2-Et-6-Me $\rightleftharpoons$ *cis*-2-Et-6-Me
7	*trans*-2-isoPr-6-Me $\rightleftharpoons$ *cis*-2-isoPr-6-Me

Entry	No. of Exp.	Equil. Time	*K*	−Δ*G*°, kcal/mol
1	11	25 days	18·08 ± 1·05[a]	1·715 ± 0·035[a]
1	5	36 days	18·06 ± 0·84	1·715 ± 0·028
2[b]	10	14 days	89·48 ± 9·82	2·663 ± 0·065
2[b]	6	28 days	89·08 ± 8·98	2·660 ± 0·060
3[b]	5	14 days	237·7 ± 30·1	3·24 ± 0·08
3[b]	5	28 days	244·0 ± 34·9	3·26 ± 0·08
4*	10	23 days	7·35 ± 0·32	1·182 ± 0·025
4*	10	41 days	7·048 ± 0·159	1·157 ± 0·013
4*[c]	10		6·219 ± 0·088	1·156 ± 0·009
4*[d]	8		5·609 ± 0·124	1·159 ± 0·015
5[b]	10	23 days	21·64 ± 0·42	1·822 ± 0·011
5[b]	10	40 days	21·28 ± 0·83	1·812 ± 0·023
6[b]	7		89·90 ± 7·47	2·665 ± 0·049
7[b]	6		104.2 ± 9·0	2·753 ± 0·051

* −Δ*H*° 1·145 ± 0·022 kcal/mol; Δ*S*° 0·04 ± 0·07 cal/mol degree.

[a] Standard deviations. [b] Measured using internal standard. [c] At 45°. [d] At 65°.

Somewhat enhanced *syn*-axial 2,4 and 2,6 interactions in 1,3-oxathianes are easily understood. The chair form is highly distorted as the result of the large difference in C—S (1·81 Å) and C—O (1·42 Å) bond distances.[4c] On the average, the puckering increases on both sides of the 1,3-oxathiane ring and leads to an increase in the

TABLE 2. CONFORMATIONAL ENERGIES OF SOME AXIAL ALKYL GROUPS ON POSITION 2 IN 1,3-DIOXANES, 1,3-OXATHIANES AND 1,3-DITHIANES

		Conformational energy, kcal/mol			
		Me	Et	i-Pr	Ref.
1,3-dioxane	25°	4·07			2a
	25°	3·98	4·04	4·17	2q
1,3-oxathiane	25°	3·25	3·25	3·55	This work
1,3-dithiane	69°	1·77	1·54	1·95	3a

TABLE 3. EQUILIBRATIONS OF ISOMERIC 2-ISOPROPYL-5-METHYL- AND 2,5,6-TRIMETHYL-1,3-OXATHIANES AT 25°

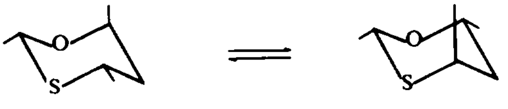
Entry	Equilibrium
5	*cis*-2-isoPr-5-Me ⇌ *trans*-2-isoPr-5-Me
6	*r*-2-*cis*-5-*trans*-6-triMe ⇌ *r*-2-*trans*-5-*cis*-6-triMe
7	*r*-2-*trans*-5-*trans*-6-triMe ⇌ *r*-2-*cis*-5-*cis*-6-triMe

Entry	No. of Exp.	Equil. Time	K	$-\Delta G°$, kcal/mol
5	7	28 days	3·13 ± 0·08[a]	0·676 ± 0·015[a]
6	5	14 days	176 ± 16[b]	3·06 ± 0·05[b]
6	6	30 days	130.3 ± 6·0[b]	2·90 ± 0·03
7	4		37·2 ± 2·1[b]	2·14 ± 0·03
7	7		34·5 ± 1·7	2·10 ± 0·03

[a] Standard deviations. [b] Measured using internal standard.

syn-axial 2,4 and 2,6 interactions in comparison with these interactions in 1,3-dithianes and 1,3-dioxanes.

The other two epimeric 2,4,6-trimethyl-1,3-oxathianes (Eq. 2) were equilibrated at three temperatures (Table 1) and the values of the



r-2-*cis*-4-*trans*-6 *r*-2-*trans*-4-*cis*-6 (2)

$-\Delta H° = 1{\cdot}15$ kcal/mol
$-\Delta S° = 0{\cdot}04$ cal/mol degree
$-\Delta G° = 1{\cdot}16$ kcal/mol

thermodynamic parameters were derived by the method of least squares from the plot of ln K vs. $1/T$ (Eq. 2 and Table 1). The entropy change is almost zero and the enthalpy change represents the difference between the conformational energies of axial Me groups on positions 4 and 6. Thus $H_{4a}{}^{i} = H_{6a}{}^{i} - 1{\cdot}15$ kcal/mol.

Gelan and Anteunis[4a] measured the free energy difference between the conformational isomers of *trans*-4,6-dimethyl-1,3-oxathiane (Eq. 3) with the aid of coupling constants. Their value $-\Delta G^\circ = 1{\cdot}1$ kcal/mol agrees closely with the above estimate. Nearly the same energy is also obtainable using the difference between the respective interactions in 1,3-dioxanes and 1,3-dithianes 2·92–1·69 = 1·23 kcal/mol.[2a, 2b, 3a]

(3)

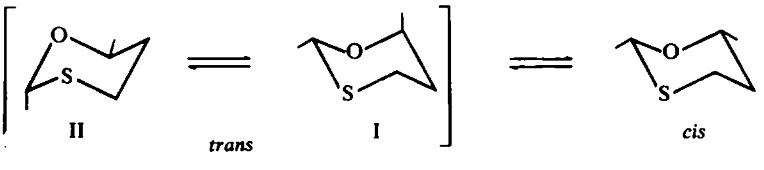
$-\Delta G^\circ = 1{\cdot}1$ kcal/mol[4a]

However, Anteunis[4b] argued later against the result based on the coupling constants[4a] and calculated using his "improved" chemical shift method the following thermodynamic parameters for the conformational equilibrium of *trans*-4,6-dimethyl-1,3-oxathiane (Eq. 3):

$$-\Delta H^\circ\ 0{\cdot}5\ \text{kcal/mol};\ \Delta S^\circ\ 3{\cdot}7\ \text{cal/mol degree};\ -\Delta G^\circ\ 1{\cdot}6\ \text{kcal/mol}$$

At present we are investigating a series of alkyl-substituted 1,3-oxathianes existing in non-chair conformations with the aid of chemical equilibration, ionization potentials,[4e] PMR spectra[4f] and ^{13}C-spectra[4g] and some of these results show that the excess entropy of a 1,3-oxathiane derivative existing in a twist conformation is around 3 cal/mol degree. Consequently, the entropy change 3·7 cal/mol degree for equilibrium (3) proposed by Anteunis[4b] suggests strongly (see also Eq. 2) that the more stable conformation (4*a*6*e*) should be in a flexible form. This is strictly speaking a paradox since now also the less stable conformation (4*e*6*a*) should inevitably be in another flexible form and consequently, the entropy difference should be very small. That is why we prefer the coupling constant method in this case[4a] and would like to suggest great care when using chemical shift values for conformational calculations.[1d, 5a–d, g]

2,6-*Dimethyl*-1,3-*oxathianes*



(4)

trans-2,6-Dimethyl-1,3-oxathiane has two nearly equally stable conformations—2*a*6*e* (II) and 2*e*6*a* (I) forms (Eq. 4). To evaluate the conformational energy of an axial Me group on position 6 let K_{obs} be the observed equilibrium constant, K_{II} the known (see above) equilibrium constant for II and K_{I} the desired equilibrium constant for I, taking the separate equilibria of I and II with the *cis* isomer into account.[6] Then $K_{\mathrm{obs}} = cis/trans$ and consequently, $1/K_{\mathrm{obs}} = trans/cis = (\mathrm{I} + \mathrm{II})/cis = \mathrm{I}/cis + \mathrm{II}/cis = 1/K_{\mathrm{I}} + 1/K_{\mathrm{II}}$

Thus

$$1/K_{\mathrm{I}} = 1/K_{\mathrm{obs}} - 1/K_{\mathrm{II}} \tag{5}$$

Using the value 3·25 kcal/mol for the conformational energy of the axial Me group in the 2*a*6*e* conformation we can derive the value $K_I = 141{\cdot}3$ (Eq. 5) which gives the value 2·93 kcal/mol for the conformational energy of the axial Me group on position 6. Again this result is quite near but somewhat higher than the value obtainable by comparison with the respective values in 1,3-dioxans and 1,3-dithianes;[2a, 3a]

$$0{\cdot}5\,H_{2a}{}^{i}(0,0) + H_{4a}{}^{i}(\mathrm{S,S}) - 0{\cdot}5\,H_{2a}{}^{i}(\mathrm{S,S}) = 2{\cdot}035 + 1{\cdot}69 - 0{\cdot}885 = 2{\cdot}84\ \mathrm{kcal/mol.} \tag{6}$$

If we now assume that the entropy difference between I and II (Eq. 4) is zero—a very reasonable assumption for a pair of conformations having the same ring conformation—we can easily calculate the composition of *trans*-2,6-dimethyl-1,3-oxathiane and its entropy of mixing. It is also highly probable that the *cis* and *trans* forms has nearly equal entropies except the mixing entropy of the *trans* isomer. Thus

$$\begin{aligned}\Delta S_{\mathrm{mix}} &= -\,(0{\cdot}63\,H_{\mathrm{I}} + 0{\cdot}37\,H_{\mathrm{II}})/T - \Delta G/T\\ &= -(0{\cdot}63 \times 2{\cdot}93 + 0{\cdot}37 \times 3{\cdot}25)/0{\cdot}298 + 2{\cdot}66/0{\cdot}298\\ &= -10{\cdot}23 + 8{\cdot}93 = -1{\cdot}30\ \mathrm{cal/mol.degree}\end{aligned} \tag{7}$$

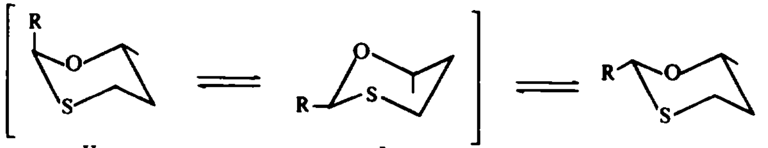
(see also Table 4).

We showed earlier that $H_{4a}{}^{i}$ was equal to $H_{6a}{}^{i} - 1{\cdot}15$ kcal/mol. Thus the conformational energy of an axial Me group on position 4 is 1·78 kcal/mol. Using the respective values in 1,3-dioxans and 1,3-dithians we get the value[2a, 3a] (*cf.* Eq. 5):

$$0{\cdot}5\,\mathrm{H}_{2a}{}^{i}(\mathrm{S,S}) + H_{4a}{}^{i}(0,0) - 0{\cdot}5\,\mathrm{H}_{2a}{}^{i}(0,0) = 0{\cdot}885 + 2{\cdot}92 - 2{\cdot}035 = 1{\cdot}77\ \mathrm{kcal/mol}$$

in good agreement with the above estimate.

2-*Ethyl-6-methyl-* and 2-*isopropyl-6-methyl-*1,3-*oxathianes*



IIa *trans* Ia R = Et or i-Pr cis

(4a)

Also in these compounds the *trans* isomer is a mixture of two conformations—Ia and IIa. In the case of 2-ethyl-6-methyl-1,3-oxathianes the experimental free energy difference is −2·66 kcal/mol. This value equals to the free energy difference between *cis*- and *trans*-2,6-dimethyl-1,3-oxathianes (Table 1). Consequently, if we accept again the value 2·93 kcal/mol for the interaction enthalpy of an axial Me group on position 6, the interaction enthalpy of IIa is equal to the conformational energy of an axial 2-Me group, 3·25 kcal/mol.

The experimental free energy difference between *cis*- and *trans*-2-isopropyl-6-methyl-1,3-oxathianes is −2·75 kcal/mol. Using the value 2·93 kcal/mol for $H_{6a}{}^{i}$ and the method discussed above (Eq. 5) we can get the value 3·55 kcal/mol for the excess interaction of an axial 2-isopropyl over that of an equatorial 2-isopropyl group.

Table 2 presents a short review for the conformational energies of axial alkyl groups on position 2 in 1,3-dioxanes, 1,3-dithianes and 1,3-oxathianes. Generally, the values for 1,3-oxathianes are 0·4–0·5 kcal/mol greater than half of the sum of the respective interactions in 1,3-dioxanes and 1,3-dithianes.

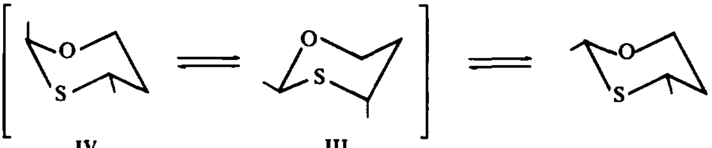
2-Isopropyl-4-methyl-1,3-oxathianes

trans *cis*

(8)

We evaluated above that the conformational enthalpy of an axial isopropyl group on position 2 was about 3·55 kcal/mol. Correspondingly, the value estimated for H_{4a}^{i} was 1·78 kcal/mol. Thus the predominating conformation of the *trans* isomer is that with an axial Me group on position 4. Consequently, we can expect the experimental free energy difference to be nearly equal to H_{4a}^{i} in this case. Really, the observed free energy difference between *cis*- and *trans*-2-isopropyl-4-methyl-1,3-oxathianes was −1·82 kcal/mol in excellent agreement with the estimation, −1·78 kcal/mol.

2,4-Dimethyl-1,3-oxathianes



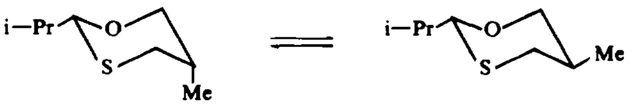
IV III
trans *cis*

(8a)

Again the *trans* isomer is a mixture of two conformations—2*a*4*e* (IV) and 2*e*4*a* (III) (Eq. 8). The energy difference between III and the *cis* isomer is again obtained using equation (5). $1/K_{III} = 1/K_{obs} - 1/K_{IV} = 0{\cdot}055340 - 0{\cdot}004147 = 0{\cdot}051193$. Thus $K_{III} = 19{\cdot}53$ and we get the value 1·76 kcal/mol for the conformational energy of an axial Me group on position 4 in good agreement with the two earlier estimates, 1·78 and 1·82 kcal/mol.

The proportion of the 2*a*4*e* form is only about 8% and the entropy of mixing for the *trans* isomer about 0·5 cal/mol·degree (Table 4).

2-Isopropyl-5-methyl-1,3-oxathianes

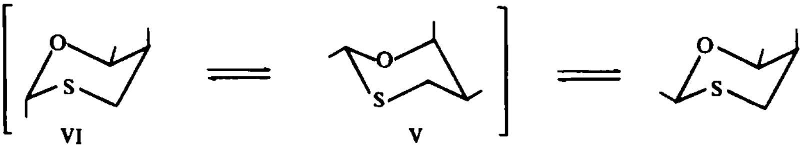


cis *trans*

(9)

This pair of epimers (Eq. 9) was chosen to determine the conformational energy of an axial Me group on position 5 since the isopropyl group biases the *cis* isomer in such a way that it exists essentially in the conformation with an axial Me group. Consequently, the experimental free energy difference, −0·68 kcal/mol, between the *trans* and *cis* forms of 2-isopropyl-5-methyl-1,3-oxathiane is a direct measure of the conformational energy—$H_{5a}{}^{i}$—of the axial Me group at position 5. Both the biased *cis* form and the *trans* form has an equatorial isopropyl group and consequently, the entropy due to the free rotation of the isopropyl groups is equal in both isomers. Again a nice agreement prevails between the experimental, −0·68 kcal/mol and the compiled value, −0·74 kcal/mol (see below).

2,5,6-*Trimethyl*-1,3-*oxathianes*



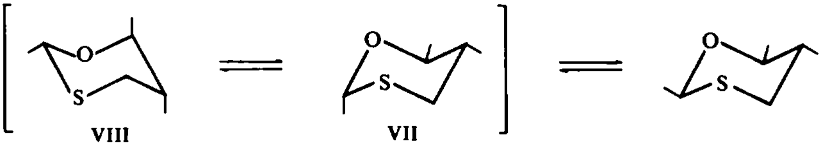
VI V (10)

r-2-*trans*-5-*trans*-6 *r*-2-*cis*-5-*cis*-6

If we assume that the butane *gauche* type interactions $H_{5a6e}{}^{i}$ and $H_{5e6a}{}^{i}$ are cancelled out the conformational energies of the conformers (V and VI) of *r*-2-*trans*-5-*trans*-6-trimethyl-1,3-oxathiane are 3·25 kcal/mol (VI) and 2·93 − $H_{5a}{}^{i}$ kcal/mol (V) greater than that of *r*-2-*cis*-5-*cis*-6-trimethyl-1,3-oxathiane. Using equation (5) we can write

$$1/K_{\mathrm{V}} = 1/K_{\mathrm{obs}} - 1/K_{\mathrm{VI}} = 0{\cdot}028986 - 0{\cdot}004147 = 0{\cdot}024839 \qquad (11)$$

Thus $K_{\mathrm{V}} = 40{\cdot}26$ and $-\Delta G^{\circ} = 2{\cdot}19$ kcal/mol for this equilibrium. Consequently, the value of $H_{5a}{}^{i}$ is 0·74 kcal/mol if we assume that entropy contributions other than the mixing entropy of the *trans* isomer have again minor roles. The result is very close to that of 0·68 kcal/mol obtained by a direct equilibration of epimeric 2-isopropyl-5-methyl-1,3-oxathianes (see Table 3).



VIII VII (12)

r-2-*cis*-5-*trans*-6 *r*-2-*trans*-5-*cis*-6

From the other pair of epimeric 2,5,6-trimethyl-1,3-oxathianes *r*-2-*cis*-5-*trans*-6-trimethyl-1,3-oxathiane is also a mixture of two conformations—2*e*5*a*6*a* (VIII) and 2*a*5*e*6*e* (VII). If we use the notation X^{i} for the total conformational energy of VIII (Eq. 12) in excess of that of *r*-2-*trans*-5-*cis*-6-trimethyl-1,3-oxathiane the excess conformational energy of VII is 3·25 kcal/mol. If we again use equation (5) we obtain

$$1/K_{\text{VIII}} = 0{\cdot}007675 - 0{\cdot}004147 = 0{\cdot}003528$$

Thus $K_{\text{VIII}} = 283{\cdot}4$ and the corresponding free energy difference $-\Delta G^\circ = 3{\cdot}35$ kcal/mol. Making the normal entropy assumption this value equals to X^i. In reality this value corresponds the sum

$$H_{6a}{}^{i}(\text{VIII}) + H_{5a}{}^{i}(\text{VIII}) - H_{5e6e}{}^{i}(\text{VII}).$$

On the basis of the previous discussion it is obvious that an axial Me group on position 6 tends to deform the ring to decrease the 2,6-*syn*-axial interaction. Similarly, the small value of the 5-axial Me interaction demonstrates appreciable flattening in the C_4–C_5–C_6 region. Both of these effects are competing in VIII. If we accept the value 0·36 kcal/mol available from a study of 1,3-dioxanes[2e] then for the gauche interaction $H_{5e6e}{}^{i}$ in VII and in the other epimer the sum of the *syn*-axial interactions of VIII equals to 3·35 + 0·36 or 3·71 kcal/mol. Correspondingly, the sum of $H_{6a}{}^{i}$ and $H_{5a}{}^{i}$ is 3·68 kcal/mol using the normal values $2{\cdot}93_3$ and $0{\cdot}74_4$ kcal/mol (Table 4). Consequently, both of the competing structural deformations in VIII are nearly equally strong and thus the real situation is very close to that in those derivatives with only a 5- or 6-axial Me group.

CONCLUSIONS

The above results and discussion led to the clarification of conformational energies of axial Me, Et and i-Pr groups on position 2 and to that of axial Me groups on the other positions of the 1,3-oxathiane ring. They also showed that 1,3-oxathianes generally exists in a chair form, which may be distorted so as to minimize the *syn*-axial interactions.

TABLE 4. CONFORMATIONAL ENERGIES AND EQUILIBRIA IN SOME METHYL-SUBSTITUTED 1,3-OXATHIANES WHICH CANNOT BE CONSIDERED CONFORMATIONALLY HOMOGENOUS (SEE ALSO TABLES 1 AND 3)

Compound	Conformational equilibrium	ΔS_{mix} cal/mol°K	$H_{2a}{}^{i}$	$H_{4a}{}^{i}$	$H_{5a}{}^{i}$	$H_{6a}{}^{i}$	$H_{\text{tot}}{}^{i}$
					kcal/mol		
trans-2,6-diMe	$2a6e \rightleftharpoons 2e6a$ 37% 63%	1·30	3·25	—	—	2·93	3·05[a]
trans-2,4-diMe	$2a4e \rightleftharpoons 2e4a$ 8% 92%	0·52	3·25	1·76	—	—	1·87[b]
r-2-*trans*-5-*trans*-6-triMe	$2a5a6e \rightleftharpoons 2e5e6a$ 14% 86%	0·81	3·25	—	0·74	2·93	2·34[c]
r-2-*cis*-5-*trans*-6-triMe	$2e5a6a \rightleftharpoons 2a5e6e$ 46% 54%	1·37	3·25	—	*	*	3·30[d]

* $H_{6a}{}^{i} + H_{5a}{}^{i} - H_{5e6e}{}^{i} = 3{\cdot}35$ kcal/mol in this case (see text also).

[a] $-\Delta G^\circ$ (obs) = 2·66 kcal/mol and $-\Delta G^\circ$ (calc) = 2·66 kcal/mol for the equilibrium between epimers (Eq. 4).

[b] $-\Delta G^\circ$ (obs) = 1·72 kcal/mol and $-\Delta G^\circ$ (calc) = 1·72 kcal/mol for the equilibrium between epimers (Eq. 8).

[c] $-\Delta G^\circ$ (obs) = $-\Delta G^\circ$ (calc) = 2·10 kcal/mol for the equilibrium between epimers (Eq. 10).

[d] $-\Delta G^\circ$ (obs) = $-\Delta G^\circ$ (calc) = 2·90 kcal/mol for the equilibrium between epimers (Eq. 12).

Inspection of models[5e] shows that the 2,6 and 2,4 *syn*-axial interactions in 1,3-oxathianes should increase in comparison with the values in 1,3-dioxanes and 1,3-dithianes. At the same time the 4,6 *syn*-axial interaction decreases since the groups on 4 and 6 positions tend to bend away from each other. If we compare the experimental findings in Table 5 to the above conclusions a general agreement is observable. As to the interaction of an axial 5-Me group it is understandable that its value in 1,3-oxathianes is smaller than in 1,3-dioxanes but the value for 1,3-dithianes cannot use as a reference because of a possible contribution from a twist conformation.[3a]

In order to obtain further support for the predominance of chair conformation in 1,3-oxathianes let us briefly discuss the chair-twist equilibrium. It is well known that 1,3-dioxan has a very high barrier for the chair-twist equilibrium about 8·5 kcal/mol[2a, 2o, 2p] and also an estimate is available for the barrier in 1,3-dithianes, namely about 3·4 kcal/mol.[3a] In the light of the conformational energies in these three series of compounds (Tables 2 and 5) it is also obvious that the enthalpy change for the chair-twist equilibrium in 1,3-oxathianes is about half of the sum of the barriers in 1,3-dioxans and 1,3-dithianes *i.e.* about 6 kcal/mol.[4e, 5e] Tables 2, 4 and 5 present a summaryof the results attained in this work.

TABLE 5. CONTRIBUTIONS OF THE 2,4-, 2,6-, 4,6-, 5,1- AND 5,3-*syn*-AXIAL INTERACTIONS TO THE CONFORMATIONAL ENERGIES OF AXIAL METHYL GROUPS IN 1,3-DIOXANES, 1,3-DITHIANES AND 1,3-OXATHIANES

Atom		Contributions of different *syn*-axial methyl-hydrogen interactions in kcal/mol					
1	3	2-H, 6-Me 2-Me, 6-H	2-H, 4-Me 2-Me, 4-H	4-H, 6-Me 4-Me, 6-H	5-Me, 1	5-Me, 3	Ref.
O	O	2·035	2·035	0·885	0·46	0·46	2*a*, 5*f*
S	S	0·885	0·885	0·805	0·52	0·52	3*a*
O	S	2·20	1·05	0·73	0·74*		

* The sum of both contributions 5-Me,1 and 5-Me,3.

EXPERIMENTAL

All of the studied compounds except 2-isopropyl-5-methyl-1,3-oxathiane were prepared earlier.[1a, 1c] 2-Isopropyl-5-methyl-1,3-oxathiane—a mixture of *cis* and *trans* forms—was prepared conventionally[1c] from 2-methyl-3-mercapto-1-propanol and isobutyraldehyde. B.p. 77–84° at 13 torrs and n_D^{20} 1·4707. The yield was 92%.

The equilibrations were carried out in sealed ampoules including 500 μl CCl_4, about 50 μl of the substrate in question and about 5 μl $BF_3 . Et_2O$ as catalyst acid. In one case equilibration at three temperatures was made to determine the enthalpy and entropy differences between the epimers.

Before analysis each sample was quenched by addition of methanolic NaOMe. In all cases the equilibria were established after two to six weeks. Equilibrium was considered as attained when the same and reproducible area ratios were obtained from both the initial *cis*-rich and *trans*-rich samples or from two separate samples from which the other was analyzed at least two weeks after the other.

If both stereoisomers in question were available the equilibration was started using samples including initially either the one or the other isomeric form. Two to four samples were equilibrated in each case. The equilibria were analyzed using Perkin-Elmer F11 gas chromatograph equipped with a 2 m × ⅛ in column containing 5% Carbowax 20 M on Chromosorb G (60/80 mesh). To separate the isomeric 2-isopropyl-5-methyl-1,3-oxathianes a 10 m × ⅛ in column containing 5% Carbowax 20 M and 0·5% KOH on Chromosorb G was used.

In the case of 2,5,6-trimethyl-1,3-oxathianes we were only able to separate the less stable configurations of both epimer pairs in a pure state by prep. GLC.[1c] This was due to the fact that the more stable isomers overlapped badly with each other under all available conditions.

Acknowledgements—One of the authors (K.P.) wishes to express his gratitude for the National Science Foundation for a fellowship.

REFERENCES

1. [a] Part I: K. Pihlaja and P. Pasanen, *Acta Chem. Scand.* **24**, 2257 (1971); [b] Part II: P. Pasanen and K. Pihlaja, *Org. Mass Spectrom.* **5**, 763 (1971); [c] Part III: P. Pasanen and K. Pihlaja, *Acta Chem. Scand.* **25**, 1908 (1971); [d] Part IV: P. Pasanen and K. Pihlaja, *Tetrahedron Letters* 4515 (1971)
2. [a] K. Pihlaja and S. Luoma, *Acta Chem. Scand.* **22**, 2401 (1968); [b] E. L. Eliel and M. C. Knoeber, Sr., *J. Am. Chem. Soc.* **90**, 3444 (1968); [c] F. G. Riddell and M. J. T. Robinson, *Tetrahedron* **23**, 3417 (1967); [d] K. Pihlaja and P. Äyräs, *Suomen Kemistilehti B* **42**, 65 (1969); [e] K. Pihlaja, *Ibid B* **42**, 74 (1969); [f] H. Friebolin, H. G. Schmid, S. Kabuss and W. Faisst, *Org. Magn. Res.* **1**, 67 (1969); [g] E. L. Eliel and C. A. Giza, *J. Org. Chem.* **33**, 3754 (1968); [h] G. M. Kellie and F. G. Riddell, *J. Chem. Soc.* (*B*) 1030 (1971); [i] M. Anteunis and G. Swaelens, *Org. Magn. Res.* **2**, 389 (1970); [j] J. Tocanne, *Bull. Soc. Chim. France* 750 (1970); [k] J. P. Maffrand and P. Maroni, *Tetrahedron Letters* 4201 (1969); [l] E. L. Eliel and M. K. Kaloustian, *Chem. Comm.* 290 (1970); [m] E. L. Eliel and D. I. Raileanu, *Ibid.* 291 (1970); [n] V. I. P. Jones and J. A. Ladd, *J. Chem. Soc.* (*B*) 567 (1971); [o] K. Pihlaja, G. M. Kellie and F. G. Riddell, *J. Chem. Soc.* (*B*), (in press); [p] K. Pihlaja and J. Jalonen, *Org. Mass Spectrom.* **6**, 1363 (1971); [q] E. L. Elliel and F. W. Nader, *J. Am. Chem. Soc.* **92**, 3050 (1970)
3. [a] E. L. Eliel and R. O. Hutchins, *Ibid.* **91**, 2703 (1969); [b] E. L. Eliel, *Acc. Chem. Res.* **3**, 1 (1970)
4. [a] J. Gelan and M. Anteunis, *Bull. Soc. Chim. Belges* **77**, 423 (1969); [b] M. Anteunis in *Conformational Analysis: Scope and Present Limitations*, Ed. G. Chiurdoglu, pp. 31–50, Academic Press, London, (1971); [c] H. R. Buys and N. de Wolf, *Tetrahedron Letters* 551 (1970); [d] See also references 1b and 1d; [e] J. Jalonen, P. Pasanen and K. Pihlaja, Part VI in this series of papers; [f] P. Pasanen, PhD thesis, to be published; [g] K. Pihlaja, unpublished results.
5. [a] K. Pihlaja and P. Äyräs, *Acta Chem. Scand.* **24**, 204, 531 (1970); [b] K. Pihlaja and P. Äyräs, *Suomen Kemistilehti* B **43**, 175 (1970); [c] K. Pihlaja, P. Pasanen, H. Nikander and A. Nikkilä, *Unpublished results*; [d] See footnote (32) in ref. 2q; [e] Dreiding models were used; [f] F. G. Riddell and G. M. Kellie, *Private Communication*; [g] F. R. Jensen, C. H. Bushweller and B. H. Beck, *J. Am. Chem. Soc.* **91**, 344 (1969)
6. E. L. Eliel and R. S. Ro, *J. Am. Chem. Soc.* **79**, 5992 (1957)