

Conformational Analysis. Part XI.¹ Chemical Equilibration of Diastereoisomeric Alkyl-1,3-dithians. Conformational Preferences of Alkyl Substituents and the Chair–Boat Energy Difference. A Revision of the Chair–Boat Energy Difference of Cyclohexane

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Acid-catalysed equilibration of diastereoisomeric 2-alkyl-4-methyl-1,3-dithians led to the following equatorial–axial free energy differences (in kJ mol⁻¹): 2-Me, 8.02; 4- or 6-Me, 6.49; 2-Prⁱ, 9.70. For 5-alkyl groups the conformational energies were also re-estimated. The enthalpy and entropy differences, 12.21 ± 0.04 kJ mol⁻¹ and -20.10 ± 0.11 J mol⁻¹ K⁻¹, for the equilibrium between the chair form of the *r*-2-*t*-butyl-2,4-dimethyl derivative and the twist form of the *r*-2-*t*-butyl-2,4-dimethyl derivative were also determined by a study of the epimer equilibrium at several temperatures. These data together with some earlier findings were used to derive the following thermodynamic parameters for the chair–twist interconversion of the 1,3-dithian ring: ΔH°_{CT} 16.7 ± 1.0 kJ mol⁻¹, ΔS°_{CT} 19.0 ± 2.0 J mol⁻¹ K⁻¹, ΔG°_{CT} (298 K) 11.0 ± 1.6 kJ mol⁻¹. Known equilibrium data for the diastereoisomeric 1,3-di-*t*-butylcyclohexanes, together with the observation that the *trans*-chair form is thermodynamically more stable by 1.55 ± 0.84 kJ mol⁻¹ than the *trans*-twist form, were used to re-estimate the conformational enthalpy of an axial *t*-butyl group, -23.7 ± 0.9 kJ mol⁻¹, and the chair–twist energy parameters, ΔH°_{CT} 25.2 ± 0.9 kJ mol⁻¹ and ΔS°_{CT} 13.4 ± 1.5 J mol⁻¹ K⁻¹ for cyclohexane.

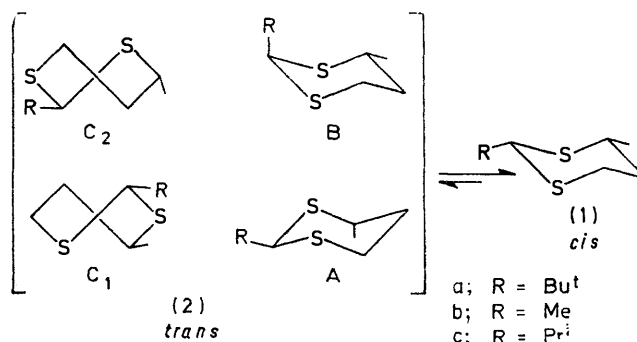
SEVERAL recent reports have dealt with the chair–twist equilibrium of 1,3-dioxans² and of 1,3-oxathians³ but only one with that of 1,3-dithians.⁴ The chair–twist enthalpy and entropy differences, 14.3 kJ mol⁻¹ and 22.3 J mol⁻¹ K⁻¹, respectively, determined for 2,5-di-*t*-butyl-1,3-dithian⁴ suggest that the chair form is favoured in free energy by *ca.* 7.6 kJ mol⁻¹ only, an energy difference very close to the values estimated for the conformational preferences of the equatorial methyl groups at positions 2 and 4 (7.4 and 7.1 kJ mol⁻¹, respectively⁴). In other words, *trans*-2,4-dimethyl-1,3-dithian (2b) should contain an appreciable amount of the twist conformation. However, disregarding the above conclusions, the other conformational energies

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¹ Part X, K. Pihlaja and P. Pasanen, *J. Org. Chem.*, 1974, in the press.

² (a) K. Pihlaja, *Acta Chem. Scand.*, 1968, **22**, 716; (b) K. Pihlaja and S. Luoma, *ibid.*, p. 2401; (c) K. Pihlaja and J. Jalonen, *Org. Mass Spectrometry*, 1971, **5**, 1361; (d) M. Anteunis and G. Swaelens, *Org. Magnetic Resonance*, 1970, **2**, 389; (e) P. Dirinck and M. Anteunis, *Canad. J. Chem.*, 1972, **50**, 412; (f) E. L. Eliel, *Pure Appl. Chem.*, 1971, **25**, 509; 1971, Supplement, **7**, 219; (g) E. L. Eliel and F. W. Naber, *J. Amer. Chem. Soc.*, 1970, **92**, 3050; (h) R. M. Clay, G. M. Kellie, and F. G. Riddell, *ibid.*, 1973, **95**, 4632; (i) K. Pihlaja, G. M. Kellie, and F. G. Riddell, *J.C.S. Perkin II*, 1972, 252; (j) K. Pihlaja and E. Taskinen, 'Thermochemical Applications to Heterocyclic Chemistry,' in 'Physical Methods in Heterocyclic Chemistry,' ed. A. R. Katritzky, Academic Press, New York, 1974, vol. IV

reported by Eliel and Hutchins⁴ for the 1,3-dithian series seemed reasonable in the light of a recent study of alkyl-substituted 1,3-oxathians and their conformational



SCHEME 1

energies.^{3a} Accordingly, it is inevitable to assume that the chair–twist free energy difference should exceed 11 kJ mol⁻¹ at least in other than 2,5-dialkyl-substituted 1,3-dithians to make the conformational preferences of alkyl groups based on 'biased' 1,3-dithian models⁴ at all acceptable. The only reliable way to test this

³ (a) P. Pasanen and K. Pihlaja, *Tetrahedron*, 1972, **28**, 2617; (b) J. Jalonen, P. Pasanen, and K. Pihlaja, *Org. Mass Spectrometry*, 1973, **7**, 949; (c) ref. 2j.

⁴ E. L. Eliel and R. O. Hutchins, *J. Amer. Chem. Soc.*, 1969, **91**, 2703.

prediction was to perform a study of the temperature dependence of the acid-catalysed equilibria of 2-alkyl-4-methyl-1,3-dithians (Scheme 1). In addition, the equilibrium between *r*-2-*t*-butyl-2,4- and *r*-2-*t*-butyl-2,4-dimethyl-1,3-dithians, the former of which is likely to adopt a twist conformation to avoid the interactions present in the chair form, *viz.* the axial orientation of the *t*-butyl group or the 2,4-*syn*-axial arrangement of the methyl groups, was investigated at several temperatures.

RESULTS

The equilibria were established at 3–8 temperatures. The respective equilibrium constants are shown in Table 1 and the values of ΔH^0 and ΔS^0 obtained from them by the method of least squares in Table 2.

DISCUSSION

The dithians used in the present study were prepared conventionally⁴ by acid-catalysed condensation of butane-1,3-dithiol with appropriate aldehydes or ketones. Epimeric 2-*t*-butyl-2,4-dimethyl-1,3-dithians were separated by preparative g.l.c. (see Experimental section). Equilibration of the isomers was carried out in carbon tetrachloride or ether solutions using catalytic amounts of $\text{BF}_3 \cdot \text{Et}_2\text{O}$. Equilibrated samples were analysed by g.l.c. to obtain equilibrium constants (at different temperatures) from which enthalpy and entropy differences between isomers were calculated (Tables 1 and 2).

TABLE 1

Equilibration of 2-alkyl-4-methyl- and 2-*t*-butyl-2,4-dimethyl-1,3-dithians at different temperatures (Schemes 1 and 2) together with some comparable data (Scheme 3)

2-R ¹	2-R ²	4-R	6-R	T/K	K ^a	−ΔG ⁰ / J mol ^{−1}
Me	H	Me	H	333·15	6·622 ± 0·114 ^{b,c}	5236·3
Me	H	Me	H	336·15	6·413 ± 0·132	5193·8
Me	H	Me	H	354·15	5·683 ± 0·166	5116·1
Me	H	Me	H	355·15	5·672 ± 0·059	5124·8
Me	H	Me	H	356·15 ^d	5·637 ± 0·133	5120·9
Me	H	Me	H	356·15 ^d	5·677 ± 0·085	5141·9
Me	H	Me	H	357·15	5·575 ± 0·248	5102·5
Me	H	Me	H	358·15	5·548 ± 0·153	5102·3
Me	H	Me	H	408·15	4·146 ± 0·139	4826·1
Pr ⁱ	H	Me	H	333·15	7·974 ± 0·139 ^{b,c}	5750·9
Pr ⁱ	H	Me	H	356·15	6·705 ± 0·147	5634·7
Pr ⁱ	H	Me	H	373·15	5·996 ± 0·280	5556·9
Pr ⁱ	H	Me	H	403·15	5·085 ± 0·109	5451·3
Bu ^t	H	Me	H	333·15	10·345 ± 0·161 ^{b,c}	6472·0
Bu ^t	H	Me	H	356·15	8·850 ± 0·271	6456·6
Bu ^t	H	Me	H	373·15	7·990 ± 0·171	6447·7
Bu ^t	H	Me	H	388·15	7·361 ± 0·250	6442·2
Bu ^t	Me	Me	H	338·15	7·353 ± 0·155 ^{b,e,f}	
Bu ^t	Me	Me	H	358·15	5·884 ± 0·181	
Bu ^t	Me	Me	H	378·15	4·829 ± 0·216	
Bu ^t	H	Me	Me	342·15	55·15 ^g	
Me	H	Me	Me	342·15	13·55 ^g	
Pr ⁱ	H	Me	Me	342·15	17·71 ^g	

^a Area ratio. ^b Standard deviation. ^c $K = \text{cis}/\text{trans}$. Solvent CCl_4 . Response ratio assumed to be unity. ^d Two sets of parallel determinations. ^e $K = r\text{-}2\text{-Bu}^t\text{-}2,4\text{-Me}_2/r\text{-}2\text{-Bu}^t\text{-}2,4\text{-Me}_2$. ^f Corrected with response ratio (r.r. = 1·057 ± 0·018 = cis/trans). ^g $K = \text{syn-}2\text{-cis-}4,6/\text{anti-}2\text{-cis-}4,6$. Solvent CHCl_3 (ref. 4).

The equilibrium constants were not corrected for the response ratio (r.r.) of the respective isomers with the exception of 2-*t*-butyl-2,4-dimethyl-1,3-dithians (r.r. =

$[\text{trans-}2,4\text{-Me}_2]/[\text{cis-}2,4\text{-Me}_2] = 1\cdot057 \pm 0\cdot018$) since in other cases the response ratios do not differ significantly from unity.⁴

2-t-Butyl-4-methyl-1,3-dithians.—In accord with an earlier report⁴ the predominant conformation of (2a) is

TABLE 2

Thermodynamic parameters for some conformational and epimer equilibria in 1,3-dithian series

Equilibrium	−ΔH ⁰ /kJ mol ^{−1}	−ΔS ⁰ /J mol ^{−1} K ^{−1}
2,4-Me ₂ (<i>trans</i> ⇌ <i>cis</i>)	7·011 ± 0·095 ^a	5·330 ± 0·264 ^a
2-Pr ⁱ -4-Me (<i>trans</i> ⇌ <i>cis</i>)	7·163 ± 0·105	4·270 ± 0·285
2-Bu ^t -4-Me (<i>trans</i> ⇌ <i>cis</i>)	6·653 ± 0·018	0·547 ± 0·048
2-Bu ^t -2,4-Me ₂ ^b	12·21 ± 0·04	20·10 ± 0·11
2,5-Bu ^t ₂ (<i>cis</i> ⇌ <i>trans</i>)	14·32 ± 0·05	22·30 ± 0·05
<i>cis</i> -2-Bu ^t -5-Pr ⁱ (<i>twist</i> ⇌ <i>chair</i>) ^c	9·92 ± 0·38	20·04 ± 2·01

^a Statistical errors of the least squares plots. ^b $r\text{-}2\text{-Bu}^t\text{-}2,4\text{-Me}_2$ (*chair*) ⇌ $r\text{-}2\text{-Bu}^t\text{-}2,4\text{-Me}_2$ (*twist*); see text. ^c Ref. 4.

A (Scheme 1) in which the 4-methyl group is axial. The other chair form B has the 2-*t*-butyl group axially orientated and hence its contribution may be neglected. The twist conformations²ⁱ (Scheme 1) in which both alkyl groups are pseudoequatorial (C_1) or one (Bu^t) pseudoequatorial and the other (Me) isoclinical (C_2) may still have a minor contribution. However, the experimentally found entropy difference (Table 2), $-0\cdot55 \pm 0\cdot05$ J mol^{−1} K^{−1}, between the *cis*- and *trans*-isomers is so small that within experimental error the observed free energy difference, $-\Delta G^0$ (298 K) = 6·49 kJ mol^{−1}, is equal to the conformational energy of the axial 4-methyl group.*

2,4-Dimethyl-1,3-dithians.—On the basis of the above discussion* the only conceivable *trans*-conformations (2) in this case are A and B. Since^{3a} equation (1) holds,

$$1/K_{\text{obs}} = \frac{[A]}{[\text{cis}]} + \frac{[B]}{[\text{cis}]} = 1/K_A + 1/K_B \quad (1)$$

and taking into account that $\Delta S^0(A - \text{cis})$ ca. 0 and $-\Delta G^0(4ax\text{-Me})$ is 6·49 kJ mol^{−1} (see above), then $1/K_B = 0\cdot11223 - 0\cdot07294 = 0\cdot03929$ at 298 K. In other words, $-\Delta G^0(2ax\text{-Me})$ in the 1,3-dithian is 8·02 kJ mol^{−1}. The excess of entropy (ΔS_{mix}) of this isomer should then be 5·38 J mol^{−1} K^{−1} in excellent agreement with the experimentally determined entropy difference, $5\cdot33 \pm 0\cdot26$ J mol^{−1} K^{−1} (Tables 1 and 2).

Eliel and Hutchins⁴ obtained a value of 7·41 kJ mol^{−1} for the equatorial-axial free energy difference of the 2-methyl group at 342 K by equilibrating *anti*- and *syn*-2,4,6-trimethyl-1,3-dithians. This estimate is, however, in close agreement with ours, if, as pointed out later, the contribution of twist conformations to the *anti*-isomer is taken into account.

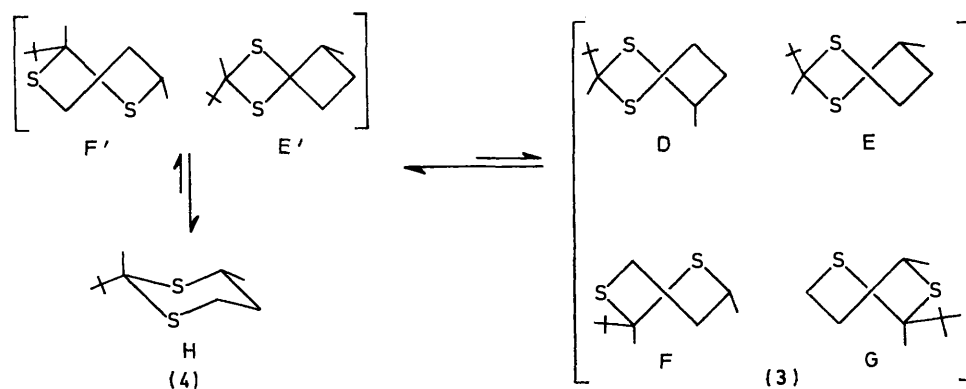
* If the values $\Delta H^0_{\text{CT}} = 14\cdot3$ kJ mol^{−1} and $\Delta S^0_{\text{CT}} = 22\cdot3$ J mol^{−1} K^{−1} obtain in this case, the *trans*-isomer should include at least ca. 40% of the twist form C: ΔG^0_{CT} ca. $14\cdot3 - 6\cdot5 - (0\cdot3 \times 22\cdot3) = 1\cdot1$ kJ mol^{−1} at 298 K and then $-\Delta S^0(\text{cis-trans})$ should be ca. $0\cdot4 \times 22\cdot3 + R(0\cdot4 \ln 0\cdot4 + 0\cdot6 \ln 0\cdot6) = 14\cdot5$ J mol^{−1} K^{−1}. The experimental results (ΔH^0_{obs} and ΔS^0_{obs} , see Table 2) inevitably rule this possibility out and point out clearly that the proportion of A (Scheme 1) is >99%.

2-Isopropyl-4-methyl-1,3-dithians.—The equilibrium (Scheme 1) may be treated as in the preceding case. Hence $1/K_B = 0.09292 - 0.07294 = 0.01998$ at 298 K and $-\Delta G^0(2ax-Pr^i)$ in (2B) is 9.70 kJ mol^{-1} . Again our estimate is greater than that (8.16 kJ mol^{-1}) of Eliel and Hutchins⁴ for the reason mentioned before.

The excess of entropy (ΔS_{mix}) of (2c) at 298 K should then be $4.33 \text{ J mol}^{-1} \text{ K}^{-1}$, again in fair agreement with the experimental entropy difference, $4.27 \pm 0.28 \text{ J mol}^{-1} \text{ K}^{-1}$.

2-t-Butyl-2,4-dimethyl-1,3-dithians.—In order to investigate the chair-twist equilibrium in other than 2,5-dialkyl derivatives⁴ *r*-2-t-butyl-2,*t*-4- and *r*-2-t-butyl-2,*c*-4-dimethyl-1,3-dithians were chosen as models.

The *trans*-2-Bu^t,4-Me form (3) exists solely in the twist forms D—G (Scheme 2) to avoid the interactions



SCHEME 2

present in the possible chair forms. The *cis*-form (4) exists mainly though not solely in the chair form H in which the 2-methyl group is axial. The *cis*-isomer (4) also has, however, two conceivable twist forms E' and F', which are similar in energy to those of the *trans*-2-Bu^t,4-Me derivative (E and F). D' would have an extra interaction between the 2-t-butyl and 4-methyl groups and G' would have both methyl groups pseudoaxial and hence their contribution may be neglected. Of the two basic types of twisted boat conformation for a 1,3-dithian ring the 1,4- or 3,6-twist (e.g. F, G, and F') should have somewhat smaller torsion strain effects²ⁱ and hence it is likely to be thermochemically more stable than the 2,5-twist (e.g. D, E, and E'). This effect may, however, be counterbalanced by the non-bonded interactions due to the substituents. This is probably the case in the conceivable twist forms of 2-t-butyl-2,4-dimethyl-1,3-dithians. For instance, both F and G have a pseudoaxial 2-methyl group whereas E is practically free from extra interactions and D has a pseudoaxial 4-methyl group only. Consequently, it may be assumed that all the twist forms (D—F, E', and F') are roughly equally stable, despite the fact that D is slightly more crowded than E owing to the pseudoaxial 4-methyl-sulphur interaction, which, however, is likely to be relatively small.¹

Consequently, both the twist families have equal

enthalpies, but the entropy favours the *trans*-2-Bu^t,4-Me twist form by *ca.* $R \ln 2$.

Taking into account that equation (2) holds we can

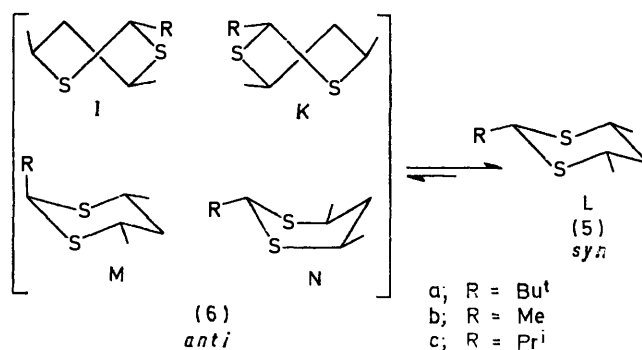
$$K_{\text{obs}} = \frac{[H] + [E' + F']}{[D + E + F + G]} = K_H + 0.500 \quad (2)$$

correct the observed equilibrium constants (Table 1) to refer to the (4H) \rightleftharpoons (3) equilibrium and then estimate $\Delta H^0[(4H) - (3)] = 12.21 \pm 0.04 \text{ kJ mol}^{-1}$ and the chair-twist entropy difference $\Delta S^0_{\text{CT}}[(4H) - (3)] = 20.10 \pm 0.11 \text{ J mol}^{-1} \text{ K}^{-1}$ (Table 2).

The conformational enthalpy of an axial 2-methyl group is likely to be very close to the conformational free energy and hence the chair-twist enthalpy difference $\Delta H^0_{\text{CT}} = 12.21 + 8.02 = 20.23 \text{ kJ mol}^{-1}$ for 2-t-butyl-2,4-dimethyl-1,3-dithians. The value of ΔS^0_{CT} , 20.1

$\text{J mol}^{-1} \text{ K}^{-1}$, is comparable with the values (20.0—22.3 $\text{J mol}^{-1} \text{ K}^{-1}$) reported by Eliel and Hutchins⁴ for some 2,5-dialkyl-1,3-dithians whereas the enthalpy difference is appreciably higher in the present case.

2-Alkyl-4,6-dimethyl-1,3-dithians.—Let us next consider the equilibration⁴ of *anti*- and *syn*-2-alkyl-*cis*-4,6-dimethyl-1,3-dithians at 342 K. The *anti*-isomers (6)



SCHEME 3

have two conceivable (1,4 and 3,6) twist conformations I and K²ⁱ which are practically free from extra non-bonded interactions due to the substituents. They are shown in Scheme 3 together with the chair form M having the 2-alkyl group axially orientated and with the

boat form N, which has been stated to be the only conceivable conformation when $R = \text{Bu}^t$.^{4,*}

Evidently (6a) exists preponderantly in the twist forms I and K and its excess of entropy is approximately equal to that of twist γ -2-t-butyl-2,4-methyl-1,3-dithian (4E' and F'), *i.e.* $20.1 - 5.8 = 14.3 \text{ J mol}^{-1} \text{ K}^{-1}$. Thus $\Delta H_{\text{OT}}^0 = \Delta G_{\text{OT}}^0(342 \text{ K}) + 0.342 (14.3 \pm 2.0) = 11.4 + 4.9 = 16.3 \pm 0.7 \text{ kJ mol}^{-1}$ which actually represents the chair-twist enthalpy difference between the 1,4- or 3,6-twist and a chair form of the 1,3-dithian ring.

Consequently, the total non-bonded interaction due to the substituents in the twist forms of 2-t-butyl-2,4-dimethyl-1,3-dithians amounts to $20.2 - 16.3 = 3.9 \text{ kJ mol}^{-1}$. We estimated earlier¹ that for the 1,3-oxathian series the extra non-bonded interaction due to a pseudoaxial 2-methyl group is *ca.* 4.3 kJ mol^{-1} .

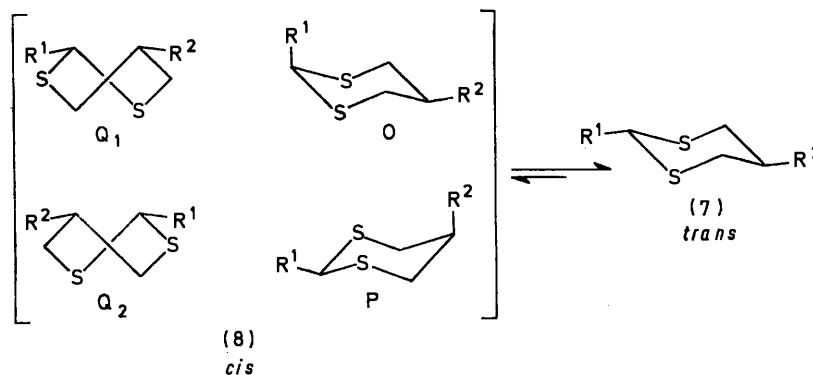
As for the free energy differences⁴ at 342 K between (5) and (6) when $R = \text{Me}$ or Pr^i in comparison with that between (5) and (6) when $R = \text{Bu}^t$ it is easily seen that in the former cases also the *anti*-isomers include appreciable amounts (15–25%) of the twist forms (Scheme 3). Presumably ΔG_{OT}^0 does not greatly differ in any of the three cases and hence for 2-methyl⁴ ($K_{\text{obs}} = 13.55$) we obtain $1/K_{\text{M}} = 1/K_{\text{obs}} - 0.01813 = 0.05567$ and $-\Delta G^0(2ax\text{-Me}) = 8.2 \text{ kJ mol}^{-1}$ at 342 K. This is not far from the value derived before (Table 3). Similarly, for the 2-isopropyl derivative⁴ at 342 K ($K_{\text{obs}} = 17.71$) $K_{\text{M}} = 26.1$ or $-\Delta G^0(2ax\text{-Pr}^i) = 9.3 \text{ kJ mol}^{-1}$ again close to the result, 9.70 kJ mol^{-1} , based on the equilibration of 2-isopropyl-4-methyl-1,3-dithians.

consequence of the less crowded environment of the pseudoequatorial 5-t-butyl (or 5-isopropyl) group in Q_1 and Q_2 in comparison with that of the equatorial 5-t-butyl (or 5-isopropyl) group in the *trans*-isomer (7) rather than a real drop in the excess of enthalpy of the twist family.

If this postulate is valid, the same chair-twist parameters should apply to *cis*-2-isopropyl-5-t-butyl-1,3-dithians (Scheme 4). The amount of P may be neglected. Hence⁴ $1/K_{\text{O}} = 0.06549 - 0.04526 = 0.02023$ at 298 K and $-\Delta G^0(2ax\text{-Pr}^i)$ is 9.67 kJ mol^{-1} in good agreement with both the previous estimates (Table 3). For *cis*-2-t-butyl-5-isopropyl-1,3-dithian, Eliel and Hutchins⁴ estimated (O being neglected) $\Delta H^0(Q - P) = 9.92 \pm 0.38 \text{ kJ mol}^{-1}$ and $\Delta S_{\text{OT}}^0 = 20.04 \pm 2.01 \text{ J mol}^{-1} \text{ K}^{-1}$. Consequently $K_{\text{P}}(342 \text{ K}) = 1.341K_{\text{obs}} = 4.70$.⁴ Thus $-\Delta G^0(5ax\text{-Pr}^i) = 4.40 \text{ kJ mol}^{-1}$. $\Delta G^0[(8) - (7)]$ at 342 K was found⁴ to be 3.57 kJ mol^{-1} giving $\Delta S^0[(8) - (7)] = 9.80 \text{ J mol}^{-1} \text{ K}^{-1}$ and $\Delta H^0[(8) - (7)] = 6.92 \text{ kJ mol}^{-1}$.

Further $\Delta H_{\text{OT}}^0 = \Delta H^0[(8) - (7)] + X_{\text{P}}\Delta H^0(Q - P) = 14.32 \text{ kJ mol}^{-1}$ as for 2,5-di-t-butyl-1,3-dithians. It is interesting that $\Delta G^0(5ax\text{-Pr}^i) \approx \Delta H^0(5ax\text{-Pr}^i)$ which demonstrates that the effect of the various rotameric conformations of the isopropyl group have really been cancelled out in the above treatment (*cf.* footnote 39 of ref. 4). Also the 2,5-twist forms (both 5-alkyl groups being isoclinal) may in these cases contribute to the twist nature of the *cis*-isomers.

Let us now consider 2,5-di-isopropyl-1,3-dithians



SCHEME 4

2,5-Dialkyl-1,3-dithians.—Eliel and Hutchins⁴ found that in the case of 2,5-di-t-butyl-1,3-dithians ΔH_{OT}^0 is only $14.32 \text{ kJ mol}^{-1}$ and $\Delta S_{\text{OT}}^0 = 22.30 \text{ J mol}^{-1} \text{ K}^{-1}$. Inspection of molecular models reveals, however, that the decrease in ΔH_{OT}^0 (*ca.* 2 kJ mol^{-1}) is likely to be a

* At first sight one could argue that the n.m.r. spectra and especially the $J_{4,5}$ values⁴ of (6a) are in agreement only with M or N. M is, however, ruled out by the interaction of the axial 2-t-butyl group and N by the availability of the much more stable twist forms I and K. Moreover, inspection of molecular models (Dreiding and 'Orbit Molecular Building Systems' models were used) reveals that there is no reason to believe that the conditions met in the C(4)—(6) region of I and K may not be responsible for the observed magnitude of $J_{4,5}$. For instance, many alkyl-1,3-dioxans with non-chair conformations²⁴ have similar $J_{4,5}$ values to those observed in *anti*-2-alkyl-*cis*-4,6-dimethyl-1,3-dithians.⁴

(Scheme 4; $R^1 = R^2 = \text{Pr}^i$).⁴ In this case $1/K_{\text{O}} = 1/K_{\text{obs}} - 1/K_{\text{P}}$ and $K_{\text{O}} = 14.1$ at 342 K. $1/K_{\text{obs}}$ (0.3168) was the value reported by Eliel and Hutchins⁴ and $1/K_{\text{O}}$ (0.0334) and $1/K_{\text{P}}$ (0.2127) were determined above. Thus (ΔS_{OT}^0 *ca.* $20 \text{ J mol}^{-1} \text{ K}^{-1}$) $\Delta H_{\text{OT}}^0 = 7.54 + 0.342 \cdot 20.0 = 14.4 \text{ kJ mol}^{-1}$ in fair agreement with the other 5-Bu^t or 5-Prⁱ derivatives. It is worth emphasizing that in this case the change of $J_{4,5}$ with temperature⁴ is not a very reliable indication for the conformational status of the *cis*-isomer because of the appreciable amount of O (Scheme 4) present (3–12%).

As for the *cis*-2-t-butyl-5-methyl- and *cis*-2-t-butyl-5-ethyl-1,3-dithians the twist forms clearly contribute less than in the case of 5-Prⁱ and 5-Bu^t derivatives.

Using equation (3) (O may be neglected, *cf.* Scheme 4)

$$K = \frac{[P]}{[Q]} = \frac{14.60 - (J_{AX} + J_{BX})_{obs}}{(J_{AX} + J_{BX})_{obs} - 6.20} \quad (3)$$

derived by Eliel and Hutchins⁴ ($J_{obs} 7.4 \pm 0.1$ for 5-Me and 6.6 ± 0.1 Hz for 5-Et at 314 K⁴) and the value 20.0 ± 2.0 J mol⁻¹ K⁻¹ for $\Delta S^0(Q - P)$, we obtain $\Delta H^0(Q - P) = 11.36 \pm 0.88$ for the *cis*-2-Bu^t-5-Me and 14.10 ± 1.32 kJ mol⁻¹ for the *cis*-2-Bu^t-5-Et derivative. Further $[P]/[Q]$ at 342 K is 4.89 ± 0.52 (5-Me) and 12.82 ± 3.38 (5-Et). Hence $K_{Me} = [trans]/[P] = (1.204 \pm 0.022)K_{obs} = 5.56 \pm 0.10$ and $K_{Et} = (1.078 \pm 0.021)K_{obs} = 3.35 \pm 0.07$. The values of K_{obs} are those determined by Eliel and Hutchins⁴ at 342 K. Thus $-\Delta G^0(5ax-Me) = 4.88 \pm 0.05$ and $-\Delta G^0(5ax-Et) = 3.44 \pm 0.06$ kJ mol⁻¹. These estimates are likely to be close to the corresponding conformational enthalpies and hence $\Delta H^0_{CT} = \Delta H^0[Q - (7)] = 16.2 \pm 0.9$ kJ mol⁻¹ for 2-t-butyl-5-methyl-1,3-dithians and $\Delta H^0_{CT} = \Delta H^0[Q - (7)] = 17.5 \pm 1.4$ kJ mol⁻¹ for 2-t-butyl-5-ethyl-1,3-dithians. Hence the extra interactions supposed to be present in the *trans*-isomers (7) are real when R² = Prⁱ or Bu^t, but do not occur as expected when R² = Et or Me.* Eliel and Hutchins⁴ carried out calculations using the equations given by Hendrickson⁵ and the numerical findings suggested that the distance between the closest methyl hydrogen of an axial 2-methyl group and the axial 4-hydrogen in 1,3-dithian ring is somewhat shorter than the corresponding distance in cyclohexane. In fact, axial-equatorial free energy differences for 2-Me and 2-Prⁱ were found to be somewhat greater than for the corresponding substituents in cyclohexane whereas that for 4-Me is somewhat less than in cyclohexane (Table 3).

It is also of interest to compare conformational energies in cyclohexanes, 1,3-dioxans, and 1,3-oxathians with those in 1,3-dithians and this has been done in Table 3. The conformational energies of 5-alkyl groups are worth paying further attention. The $-\Delta G^0$ values for 5-methyl, -ethyl, and -isopropyl in 1,3-dioxans and 1,3-dithians are substantially lower than the corresponding values in cyclohexane as expected,^{2,4,6} but the dithian values in turn are appreciably higher than the dioxan values. This is likely to be due to the different geometry of the rings. In the 1,3-dioxan ring (bond lengths, C-O 1.41 and C-C 1.54 Å) C(2) is in a 'superchair' position whereas the C(4)-(6) region is more or less flattened.² In 1,3-dithian⁴ (bond lengths, C-S 1.81 and C-C 1.54 Å) the situation is inverted C(5) now being in a 'superchair' position. In fact, inspection of molecular models reveals that an axial 5-t-butyl group interacts much more strongly with the heteroatoms and also with an equatorial 2-t-butyl group in the 1,3-dithian than in the 1,3-dioxan ring. Consequently, the twist form, which is energetically much closer to the chair form in the 1,3-dithian series, than is

* In the case of 2,5-dialkyl-substituted 1,3-dithians, the substitution pattern makes the *trans*-twist family clearly less favoured than the *cis*-twist family. Hence the contribution of the former can be neglected.

the case in the 1,3-dioxan series,² becomes the predominant conformation of *cis*-2,5-di-t-butyl-1,3-dithian. In Table 4 a different comparison has been carried out. It is seen that the 2,4- and 2,6-*syn*-axial Me-H interactions in 1,3-oxathians are slightly increased in comparison with the values in 1,3-dioxans and 1,3-dithians as predicted by molecular models. The 4,6-*syn*-axial Me-H interaction is just halfway between the values in

TABLE 3

The equatorial-axial preferences of alkyl groups in some six-membered heterocycles and cyclohexane

Substituent	Conformational energy $-\Delta G^0/kJ mol^{-1}$			
	1,3-Dithian	1,3-Oxathian	1,3-Dioxan	Cyclohexane
2-Me	8.02 ^a 8.2 ^b	13.6 ^c	16.65 ^d 17.0 ^e	7.1 ^f
2-Pr ⁱ	9.70 ^a 9.3 ^b 9.67 ^g	14.85 ^c	17.45 ^d	9.0 ^f
4-Me	6.49 ^a 7.07 ^f	7.5 ^c	12.2 ^{d,e} 11.4 ± 2.2 ^e	7.1 ^f
5-Me	4.88 ^g	2.7 ^c	4.04 ^{d,h}	7.1 ^f
5-Et	(3.44 ^g)		2.8-3.0 ^d	7.3 ^f
5-Pr ⁱ	4.40 ^g		4.1 ^d	9.0 ^f
5-Bu ^t			5.7-6.1 ^d	23.7 ⁱ
6-Me	6.49 ^a 7.07 ^f	12.3 ^c	12.2 ^{d,e} 11.4 ± 2.2 ^e	7.1 ^f

^a From the equilibration of 2-alkyl-4-methyl-1,3-dithians. ^b Corrected values based on the equilibration of 2-alkyl-4,6-dimethyl-1,3-dithians in ref. 4. ^c Ref. 3a. ^d Ref. 2g and E. L. Eliel and Sr. M. Knoeber, *J. Amer. Chem. Soc.*, 1968, **90**, 3444. ^e Ref. 2b. ^f *Cf.* Ref. 4. ^g Corrected values based on the equilibration of 2,5-dialkyl-1,3-dithians in ref. 4. The 5-Et value in parentheses is less reliable. ^h Ref. 2h. ⁱ See text.

TABLE 4

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 cyclohexanes, 1,3-dioxans, 1,3-dithians, and 1,3-oxathians^a (kJ mol⁻¹)

Atom	2-H, 6-Me	2-H, 4-Me	4-H, 6-Me	5-Me, 1	5-Me, 3
I 3	2-Me, 6-H	2-Me, 4-H	4-Me, 6-H		
C C	3.55	3.55	3.55	3.55	3.55
O O	8.5	8.5	3.7	2.0	2.0
S S	4.0	4.0	2.5	2.4	2.4
O S	9.2	4.4	3.1		3.0 ^b

^a For references see Table 3. ^b 5-Me, 1 + 5-Me, 3.

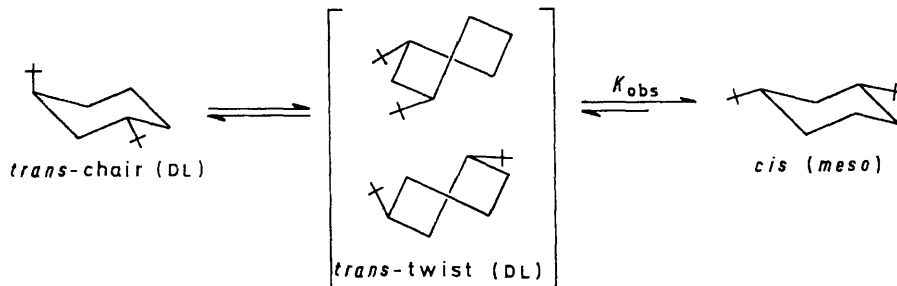
1,3-dioxans and 1,3-dithians as expected. It is also noteworthy that the 5-methyl interaction in 1,3-oxathians is even lower than in 1,3-dioxans. Obviously more data are needed on 5-alkyl interactions in 1,3-oxathians.

Before a comparison of the thermodynamic parameters of chair-twist interconversion in the above compounds (Table 5) a revision of the chair-boat energy difference in cyclohexane seems to be necessary. Allinger and Freiberg^{6a} studied the equilibrium between *cis*- and *trans*-1,3-di-t-butylcyclohexanes and from their results the following values may be obtained by least squares analysis: $-\Delta H^0 = 24.89 \pm 0.25$ kJ mol⁻¹ and $-\Delta S^0 = 20.55 \pm 0.45$ J mol⁻¹ K⁻¹. The *trans*-isomer was stated to exist predominantly in the twist form

⁵ J. B. Hendrickson, *J. Amer. Chem. Soc.*, 1962, **84**, 3355.

⁶ (a) N. L. Allinger and L. A. Freiberg, *J. Amer. Chem. Soc.*, 1960, **82**, 2393; (b) N. L. Allinger, J. A. Hirsch, M. A. Miller, I. J. Tyminski, and F. A. Van-Catledge, *ibid.*, 1968, **90**, 1199.

(Scheme 5). Later Allinger *et al.*,⁶⁶ however, calculated that the conformational energy of an axial t-butyl group at 298 K should be 22.64 kJ mol⁻¹ and estimated, using the i.r. spectrum of the *trans*-isomer, that the enthalpy difference between the chair and twist families is only *ca.* 1.55 ± 0.84 kJ mol⁻¹. Comparison of



SCHEME 5

$\Delta H^0_{\text{obs}}(\text{trans} \rightleftharpoons \text{cis})$ and $\Delta G^0_{\text{calc}}(2\text{ax-Bu}^t)$ readily shows that the *trans*-chair form is favoured by enthalpy (1.55 kJ mol⁻¹) but the *trans*-twist by entropy. Furthermore the observed entropy difference = 20.55 J mol⁻¹ K⁻¹ [= -Rln2 - R($x_{\text{twist}} \ln x_{\text{twist}} + x_{\text{chair}} \ln x_{\text{chair}}$) + $x_{\text{twist}} \Delta S^0_{\text{CT}}$] and after some 'iterations' at 555 K a constant value of 13.34 J mol⁻¹ K⁻¹ was obtained for ΔS^0_{CT} .

Thus ΔS^0_{calc} between *trans*-twist and *trans*-chair forms is also 13.34 J mol⁻¹ K⁻¹ and we are able to calculate $K_C = [\text{cis}]/[\text{trans-chair}]$ and $K_T = [\text{cis}]/[\text{trans-twist}]$ at different temperatures since $K' = [\text{trans-chair}]/[\text{trans-twist}]$ with $K_T = (1 + K')K_{\text{obs}}$ and $K_C = K_T/K'$.

Consequently, the conformational enthalpy of an axial t-butyl group in cyclohexane is 23.7 ± 0.9 kJ mol⁻¹ and the thermodynamic parameters for the chair-twist equilibrium are ΔH^0_{CT} 25.2 ± 0.9 kJ mol⁻¹ and ΔS^0_{CT} 13.4 ± 1.5 J mol⁻¹ K⁻¹ (*cf.* Table 5). Both estimates are in fair agreement with the calculated values 22.64 kJ mol⁻¹ (axial Bu^t) and 20.3–27.6 (twist-boat).⁶⁶ On the basis of the data in Table 5 it is evident that a 1,3-dioxan ring (especially alkyl-substituted) has a relatively biased twist conformation (1,4; 2,5 or 3,6 depending on the substitution) since the pseudoaxial interactions tend to be high due to the relatively small intramolecular distances.² Consequently, the excess of entropy of the twist form is generally low.² In contrast, the 1,3-dithian ring (even alkyl-substituted) may attain several twist forms and pseudorotate easily through the different conceivable twist conformations. Accordingly, ΔH^0_{CT} is appreciably lower and ΔS^0_{CT} higher than in the other six-membered rings in question (Table 5). This is also in agreement with the relatively large ring 'size.' The 1,3-oxathian ring is an intermediate between the symmetric analogues. Alkyl-substituted derivatives are likely to attain¹ several twist conformations which, however, are moderately 'biased' and hence ΔS^0_{CT} is mainly due to mixing of these different twist forms.¹

Conclusions.—The following main conclusions with respect to the conformational analysis of 1,3-dithians has been reached.

(1) Alkyl substituents (Me, Prⁱ) in the 2-position have conformational energies similar to, but in general clearly larger than, those of corresponding groups in cyclohexane. The values are also consistent with those of similar groups in 1,3-dioxan and 1,3-oxathian.

(2) Alkyl groups in the 5-position have conformational

energies greater than those in 1,3-dioxan and 1,3-oxathian, but still considerably smaller than corresponding energies in cyclohexane. These findings have been used to explain the fact that *cis*-2,5-di-t-butyl-1,3-dithian exists preponderantly in a twist form.

TABLE 5

Chair-boat interconversion in cyclohexane, 1,3-dioxan, 1,3-oxathian, and 1,3-dithian

	$\Delta G^0_{\text{CT}}(298 \text{ K})/$ kJ mol ⁻¹	$\Delta H^0_{\text{CT}}/$ kJ mol ⁻¹	$\Delta S^0_{\text{CT}}/$ J mol ⁻¹ K ⁻¹	Ref.
Cyclohexane ^a	21.2 ± 1.4	25.2 ± 0.9	13.4 ± 1.5	6
1,3-Dioxan ^{b-d}	33.5 ± 2.0	35.8 ± 2.3	≤ 9.1	2 ⁿ
	30.9	33.2	7.7	2 ^j
1,3-Oxathian ^{e,j}	23 ± 2	25.2	~9.1	1
1,3-Dithian	7.7 ± 0.1	14.3 ± 0.1	22.3 ± 0.1	4 ^g
	8.4 ± 1.0	14.3 ± 0.4	20.0 ± 2.0	4 ^h
	14.2 ± 0.3	20.2 ± 0.3	20.1 ± 0.1	<i>i</i>
	12.0 ± 1.3	16.3 ± 0.7	14.3 ± 2.0	<i>j</i>
	10.2 ± 1.5	16.2 ± 0.9	20.0 ± 2.0	<i>k</i>
	11.5 ± 2.0	17.5 ± 1.4	20.0 ± 2.0	<i>l</i>
	11.0 ± 1.6	16.7 ± 1.0	19.0 ± 2.0	<i>m</i>

^a See text. ^b $\Delta H^0_{\text{CT}}(\text{g})$ 35.6 ± 2.1 kJ mol⁻¹ (ref. 2c). ^c Ref. 2 ^j reports $\Delta H^0_{\text{CT}}(\text{l})$ 33.2 kJ mol⁻¹ and $\Delta H^0_{\text{CT}}(\text{g})$ 31.9 kJ mol⁻¹ based on enthalpies of combustion. ^d Values ranging from 26 to 30 kJ mol⁻¹ have been proposed to ΔH^0_{CT} on the basis of the dependence of geminal [C(2)] and vicinal coupling constants on temperature (*cf.* ref. 2e). ^e $\Delta H^0_{\text{CT}}(\text{g})$ 25.0 ± 4.0 kJ mol⁻¹ (refs. 1 and 3b). ^f See also ref. 2 ^j. ^g 2,5-Di-t-butyl-1,3-dithians (ref. 4). See text. ^h *cis*-2-t-Butyl-5-isopropyl-1,3-dithian (ref. 4). See text. ⁱ 2-t-Butyl-2,4-dimethyl-1,3-dithians. The twist form includes at least an extra non-bonded interaction due to a pseudoaxial 2-methyl group (*ca.* 3.9 kJ mol⁻¹). See text. ^j 2-Alkyl-4,6-dimethyl-1,3-dithians (ref. 4). See text. ^{k,l} 2-t-Butyl-5-methyl- and 2-t-butyl-5-ethyl-1,3-dithians, respectively. See text. ^m Averaged most probable values to the chair-twist equilibrium of the unsubstituted 1,3-dithian ring. $\Delta(\Delta S_{\text{mix}})_{\text{CT}}$ *ca.* 9.1 ± 1.0 J mol⁻¹ K⁻¹ = Rln6 - Rln2. $\Delta(\Delta S_{\text{rot}})_{\text{CT}}$ *ca.* 8.6 ± 1.0 J mol⁻¹ K⁻¹ = 20.1 - Rln4. Hence, $\Delta S^0_{\text{CT}} = 19.0 ± 2.0$ J mol⁻¹ K⁻¹. ⁿ $\Delta H^0 = 24.4 ± 0.1$ kJ mol⁻¹ between *cis*- and *trans*-2,4,4,6-tetramethyl-1,3-dioxans, of which the latter exists in a twist form (*cf.* ref. 2h). $\Delta H^0(4\text{ax} - \text{Me}) = 11.4 ± 2.2$ kJ mol⁻¹ based on enthalpies of formation of several 1,3-dioxans (*cf.* ref. 2b).

(3) ΔH^0_{CT} For the chair-twist interconversion in 1,3-dithian (16.7 kJ mol⁻¹) is considerably smaller than the corresponding value in cyclohexane (25.2 kJ mol⁻¹), 1,3-dioxan (33–36 kJ mol⁻¹), or 1,3-oxathian (25.2 kJ mol⁻¹). Moreover, in the case of 2,5-dialkyl-1,3-dithians (5-R = Prⁱ or Bu^t) the environment of the

5-alkyl group is less crowded in the *cis*-twist form than in the *trans*-chair form leading to a further drop in ΔH^0_{OT} (14.3 kJ mol^{-1}).

(4) *r*-2-*t*-Butyl-2,*t*-4-dimethyl-1,3-dithian exists entirely in the twist form and also the corresponding *trans*-isomer includes *ca.* 5% of the twist family at 298 K. Correspondingly, *anti*-2-*t*-butyl-*cis*-4,6-dimethyl-1,3-dithian may also exist in similar twist conformations and hence the relatively small free energy difference between *anti*- and *syn*-isomers indicates again the high excess of entropy of the twist form.

(5) The conformational energies reported earlier⁴ as corrected with respect to the twist contributions are in close agreement with the present findings and thus give further support for the present approach.

EXPERIMENTAL

Preparative g.l.c. separations were carried out on a Perkin-Elmer F21 instrument using a 3/8 in \times 4.5 m stainless steel column containing 5% Carbowax 20M on Chromosorb G (60–80 mesh). The equilibrium mixtures were analysed using Perkin-Elmer F11 gas-liquid chromatograph equipped with a 2 m \times 18 in column containing 5% Carbowax 20M on Chromosorb G (60–80 mesh) or a 4 m \times 1/8 in column containing 20% XE-60 on Chromosorb A.

Preparation of Materials.—Butane-1,3-dithiol and all the 1,3-dithians were prepared according to known methods.⁴ Physical constants were: butane-1,3-dithiol, b.p. $80\text{--}82^\circ$ at 25 mmHg, n_D^{25} 1.5190, yield 50% (lit.,⁴ b.p. $64\text{--}67^\circ$ at 10 mmHg, n_D^{20} 1.5208); 2,4-dimethyl-1,3-dithian,⁴ b.p. 100° at 20 mmHg, n_D^{20} 1.5409, d^{20} 1.0718 (for a *ca.* 80:20 mixture of the *cis*- and *trans*-forms), yield 80%; 2-isopropyl-4-methyl-1,3-dithian,⁴ b.p. $113\text{--}114^\circ$ at 14 mmHg, n_D^{20} 1.5262, d^{20} 1.0310 (for a mixture of *cis*- and *trans*-forms), yield 87%; 2-*t*-butyl-4-methyl-1,3-dithian,⁴ b.p. $120\text{--}121^\circ$ at 15 mmHg, m.p. 42° (for a 80:20 mixture of *cis*- and *trans*-forms), yield 83%; and 2-*t*-butyl-2,4-dimethyl-1,3-dithian,⁴ b.p. $140\text{--}141^\circ$ at 20 mmHg, yield 90% (for a

mixture of diastereoisomers), n_D^{20} 1.5276, d^{20} 1.0201 (*trans*-2-Bu^t-4-Me form), m.p. $35.5\text{--}36.0^\circ$ (*cis*-2-Bu^t-4-Me form). The isomers were separated by preparative g.l.c. and their identification was by n.m.r. spectra (Perkin-Elmer R10 60 MHz), mass spectra (Perkin-Elmer M270), and chemical equilibration (Tables 1 and 2).

Equilibration Procedure.—For each pair of diastereoisomeric 1,3-dithians, several samples were prepared by dissolving 50 μ l of the appropriate mixture in 450 μ l of carbon tetrachloride or diethyl ether (pro analysis), adding 3 μ l of boron trifluoride-ether, and sealing parts of prepared solution into small glass vials. The samples were kept in a constant temperature bath at a given temperature. Before analysis each sample was quenched by addition of methanolic sodium methoxide. The equilibria were considered reached when the same and reproducible area ratios were obtained from both the initially *cis*-rich and *trans*-rich samples or from two separate samples analysed with at least two weeks time interval.

The area response ratio was obtained by g.l.c. analysis of an isomer mixture having a known (*ca.* 1:1) weight composition in the case of 2-*t*-butyl-2,4-dimethyl-1,3-dithians. Otherwise the response ratio was assumed to be unity.⁴ The equilibration of 2-*t*-butyl-2,4-dimethyl-1,3-dithians was accomplished in ether solution since this compound tended to decompose when using carbon tetrachloride. For comparison the equilibration of 2,4-dimethyl-1,3-dithians was also attempted in ether solution but within experimental error the equilibrium constants did not differ from those obtained using carbon tetrachloride as solvent. The equilibria were usually established after a few days (higher temperatures) or several weeks (lower temperatures).

Support of this work by the Royal Society, the S.R.C., the Finnish Academy of Sciences, and the Finnish Academy, the Division of Sciences is acknowledged. I thank Mr. A. Nikkila for help in experimental measurements and Dr. F. G. Riddell for discussions.

[4/061 Received, 14th January, 1974]