Hindered Internal Rotation in 3,4-Di-isopropyl-Δ^4-thiazoline-2-thione from Temperature-dependent Nuclear Magnetic Resonance Spectra of Five Different Groups of Protons: a Methodological Study

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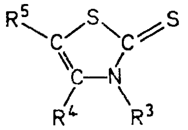
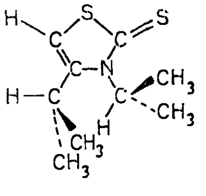
The internal rotation of the isopropyl groups in 3,4-di-isopropyl-Δ^4-thiazoline-2-thione has been studied by complete *n.m.r.* bandshape analysis of the five possible groups of protons in the molecule. The agreement among the derived sets of thermodynamic activation parameters is quite satisfactory, leading to the following average values: $\Delta G^{\ddagger}_{298.2\ \mathrm{K}}$ 65.4 kJ mol^{-1} (15.64 kcal mol^{-1}), $\Delta H^{\ddagger}$ 59.8 ± 0.6 kJ mol^{-1} (14.3 ± 0.1 kcal mol^{-1}), and $\Delta S^{\ddagger}$ −18 ± 2 J mol^{-1} K^{-1} (−4.4 ± 0.4 cal mol^{-1} K^{-1}). The effect of different methods of evaluation of the relaxation parameter, T_2, on the resulting activation parameters and the relevance of the small negative entropy value for the interpretation of the nature of the rotational process are discussed.

In connection with work on the ' gear effect ' in a series of alkyl-substituted Δ^4-thiazolinethiones (I),[1] it was of interest to have available a carefully determined set of thermodynamic activation parameters, derived from complete n.m.r. bandshape analysis, for the internal rotation of the intermeshing groups R^3 and R^4. The previously reported [1a] activation parameters for the compounds in this series showed suspiciously large variations, particularly in the entropy term, $\Delta S^{\ddagger}$, and since this term was considered especially interesting for these molecules it was desirable to obtain as reliable a value as possible for at least one of the compounds in the series. The compound for which $R^3 = R^4 = Pr^i$ and $R^5 = H$, was chosen as the most suitable member of the series for such a study, in view of its convenient rotamer ratio in deuteriochloroform solution [*ca.* 1 : 1; rotamers (IIa + b) and (IIc) [1a]], and the variety of signals on which a total bandshape analysis could in principle be performed. Thus, activation parameters for the same process can be determined from the temperature dependence of the bandshape of the 3- and 4-isopropyl methyl and methine protons, as well as from that of 5-H. The non-exchanging chemical shift parameters for the various sets of signals ranged from 3 to 150 Hz, making this system quite suitable for a thorough study, since the bandshapes of the various signals are most sensitive to changes in rate constant in different temperature regions.

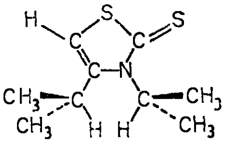


(I)

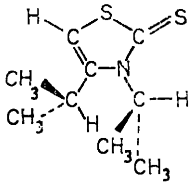
Previous work in which several sets of coalescing signals due to the same rate process were utilized for bandshape analysis is scarce in the literature. The work of Love *et al.*[2] on methyl *N*-acetylsarcosinate, that of Nilsson *et al.*[3] on substituted 1,3,5-trineopentylbenzenes, and that of Howells and Warren [4] on phosphine oxides may suffice as examples. It should also be mentioned in this connection that Marquardt [5] has suggested the use of ' coalescence temperature approximations ' † for the various sets of collapsing signals in order to obtain values of the exchange rate at different temperatures, from which activation parameters could then be extracted by use of the usual Eyring equation.[6] This method is probably not very useful for proton signals (see, however, ref. 4), but may find some use in ^{13}C n.m.r.



(IIa)



(IIb)



(IIIc)

The work presented in this paper may be primarily regarded as an n.m.r. methodological study, the results

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† As pointed out by one of the referees, Marquardt [5] suggests the use of the shift difference between lines 2 and 3 of the AB quartet in the formula for the rate constant at coalescence, when the correct parameter would be the chemical shift difference between nuclei A and B.

[1] (*a*) C. Roussel, Thesis, Université de Provence, Marseille, 1973; (*b*) C. Roussel, M. Chanon, and J. Metzger, *Tetrahedron Letters*, 1971, 1861; (*c*) C. Roussel, M. Chanon, and J. Metzger, *ibid.*, 1972, 3843; (*d*) C. Roussel, M. Chanon, and J. Metzger, *FEBS Letters*, 1973, **29**, 253; (*e*) A. Lidén, C. Roussel, M. Chanon, J. Metzger, and J. Sandström, *Tetrahedron Letters*, 1974, 3629. (*f*) C. Roussel, A. Lidén, M. Chanon, J. Metzger, and J. Sandström, to be published.

[2] A. L. Love, T. D. Alger, and R. K. Olsen, *J. Phys. Chem.*, 1972, **76**, 853.

[3] (*a*) B. Nilsson, R. E. Carter, K.-I. Dahlqvist, and J. Mårton, *Org. Magnetic Resonance*, 1972, **4**, 95; (*b*) B. Nilsson, P. Martinson, K. Olsson, and R. E. Carter, *J. Amer. Chem. Soc.*, 1973, **95**, 5615.

[4] D. Howells and S. Warren, *Tetrahedron Letters*, 1973, 675.

[5] F.-H. Marquardt, *J. Chem. Soc.* (*B*), 1971, 366.

[6] S. Glasstone, K. J. Laidler, and H. Eyring, ' Theory of Rate Processes,' McGraw-Hill, New York, 1941, pp. 195ff.

of which can add to our knowledge about the practical limits of the precision attainable in the determination of activation parameters, in particular the entropy of activation, by means of n.m.r. bandshape analysis. Critical methodological evaluations of the n.m.r. total bandshape technique * have been reported by several groups,[7-12] and it has become increasingly evident that extraordinary care is required to achieve reliable results. This is especially true with respect to the determination of the relaxation time and non-exchanging shift parameters (T_2 and $\Delta\nu_\infty$) as functions of temperature, a point which has been previously stressed.[7-13]

EXPERIMENTAL

Sample Preparation.—The synthesis of 3,4-di-isopropyl-Δ^4-thiazoline-2-thione has been described elsewhere.[14] The sample used in connection with the n.m.r. bandshape analysis was prepared directly in a 10 mm n.m.r. tube as a 0.5M solution in deuteriochloroform, with the addition of a small amount of tetramethylsilane. A sample in [$^2H_6$]-acetone solution, used for decoupling and nuclear Overhauser experiments, was prepared in a 5 mm n.m.r. tube. The samples were carefully degassed and sealed off under vacuum.

TABLE 1

Chemical shifts and coupling constants for the various protons in rotamers (IIa + b) and (IIc)

Group	$\delta_{(IIa+b)}$	$\delta_{(IIc)}$	δ_{avg}	$J_{(IIa+b)}$/Hz	$J_{(IIc)}$/Hz	J_{avg}/Hz
CDCl$_3$ Solution	−20°		+120°		−20°	+120°
=CH	6.28	6.35	6.13	0.95 *†	‡	
N–CH	4.57	6.11	5.30	7.0	7.3	7.15
C–CH	2.86	3.37	3.05	6.8	6.7	6.75
N–CCH$_3$	1.91	1.55	1.68	6.9	7.3	7.1
C–CCH$_3$	1.30	1.33	1.28	6.8	6.7	6.75
CD$_3$COCD$_3$ Solution						
=CH	6.62	6.78		0.95 *†	0.3 *†	
N–CH	4.73	5.04		7.0	7.3	
C–CH	3.04	3.47		6.8	6.6	
N–CCH$_3$	1.86	1.51		7.0	7.3	
C–CCH$_3$	1.29	1.35		6.8	6.6	

* Long-range coupling to C–CH proton; see text. † The coupling to the N–CH proton in (IIc) was found to be 0.5 Hz; the corresponding coupling in (IIa + b) was <0.2 Hz (unresolved). ‡ This coupling was unresolved in CDCl$_3$ solution, and was assumed to have the same value as that found in [$^2H_6$]acetone solution.

Apparatus and Measurements.—All spectra were recorded on a Varian XL-100-15 spectrometer, mostly in the continuous wave mode, and utilizing an internal proton lock (tetramethylsilane). Slow sweep rates (0.1—0.2 Hz s^{-1}) were used to minimize distortion of the signals, and great care was taken to avoid saturation by maintaining an appropriately low level of radio frequency power. For several spectra at the high temperature end of the temperature range, the Fourier transform mode was employed, with an acquisition time of 2 s, a pulse width of 60 μs, and a spectral width of 1 000 Hz, resulting in a resolution of 0.5 Hz.

The temperature was measured by means of a thermocouple fixed inside a normal 12 mm insert, with the sensing point *ca.* 2 cm above the receiver coil. It was not possible to have the thermocouple closer to the receiver coil without affecting the observed bandshape. The temperature readings from this thermocouple were calibrated against a second thermocouple held inside a spinning 10 mm n.m.r. tube containing approximately the same amount of liquid as the actual sample tube. The resulting correction was found to vary from −0.5 at −20 to +1.5° at +120°. At the temperatures used for the determination of rate constants, the variation in temperature did not exceed 0.2°.

Bandshape Calculations.—A simple two-site exchange was assumed, and the theoretical bandshapes were calculated using equations based on McConnell's treatment.[15] Multiplet structure was taken into account by the superposition of an appropriate number of lines with the spacing between them given by the coupling constant(s). The simulations of the less complex cases (=CH and isopropyl methyl) were made on a Hewlett–Packard desk calculator model 9820A, equipped with a model 9862A plotter, whereas the methine proton spectra were calculated on a Univac 1108 computer. The τ values were obtained by means of visual fitting of calculated to experimental spectra.

RESULTS

Only two sets of signals were observed for rotamers (IIa—c) down to −80° (in [$^2H_6$]acetone solution †). We assume that one set belongs to (IIc), and consequently the other set arises from (IIa + b) in rapid interconversion. The relative populations of (IIa + b) could not be determined directly (see below). The chemical shifts and coupling constants for the various protons in rotamers (IIa + b) and (IIc) at −20° in deuteriochloroform and [$^2H_6$]acetone

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* The literature on this topic is fairly extensive, and refs. 7—12 make no pretence of completeness.

† Roussel *et al.*[14] observed only two sets of signals down to −150° in dichlorofluoromethane solution.

[7] F. A. L. Anet and A. J. R. Bourn, *J. Amer. Chem. Soc.*, 1967, **89**, 760.

[8] P. T. Inglefield, E. Krakower, L. W. Reeves, and R. Stewart, *Mol. Phys.*, 1968, **15**, 65, and later papers by Reeves and his coworkers.

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[11] R. R. Shoup, E. D. Becker, and M. L. McNeel, *J. Phys. Chem.*, 1972, **76**, 71.

[12] D. G. Bickley and N. Serpone, *Canad. Spectroscopy*, 1974, **19**, 40.

[13] (*a*) L. M. Jackman, T. E. Kavanaugh, and R. C. Haddon, *Org. Magnetic Resonance*, 1969, **1**, 109, and references cited therein; (*b*) T. Liljefors, *ibid.*, 1974, **6**, 144; (*c*) L. D. Colebrook, H. G. Giles, A. Granata, S. Idi, and J. R. Fehlner, *Canad. J. Chem.*, 1973, **51**, 3635.

[14] C. Roussel, R. Gallo, M. Chanon, and J. Metzger, *Bull. Soc. chim. France*, 1971, 1902.

[15] H. M. McConnell, *J. Chem. Phys.*, 1958, **28**, 430.

solutions, as well as the averaged values at rapid interconversion (+120°) in deuteriochloroform solution, are collected in Table 1. The coupling constants are those resulting from iteration in connection with the bandshape analyses.

In $[^2H_6]$acetone solution, the difference in rotamer populations (60 : 40) allowed a straightforward assignment of the two sets of signals. The essentially equal populations in deuteriochloroform solution made assignments somewhat ambiguous in this solvent, but they have been made in analogy with the data for $[^2H_6]$acetone solution, assuming the absence of shift crossovers.

The assignments of the shifts to specific protons in the rotamers were made ($[^2H_6]$acetone solution) primarily on the basis of the shielding effect of the thiocarbonyl group, and the stereospecificity of the long-range coupling between the 5-H and the 3-isopropyl methine proton. The anisotropy of the thiocarbonyl group is known[16] to have a deshielding effect on proximate protons in the $\rangle$C=S plane. The resonance of the 3-isopropyl methine proton in rotamer (IIc) is thus expected to occur further downfield than that of the corresponding proton in (IIa + b). The deshielding effect is of the order of 1.5 p.p.m., which is quite reasonable by comparison with shifts observed in other molecules with 'spatially analogous' $\rangle$C=S and C–H groups.[16,17] The relative shifts of the 3-isopropyl methyl protons are also in accordance with those expected on the basis of the anisotropic effect of the thiocarbonyl group. Irradiation of the low-field 4-isopropyl methine proton at δ 3.47 changed the poorly resolved triplet structure of the low-field 5-H resonance (δ 6.78) to a nicely resolved doublet with a separation corresponding to a coupling of 0.5 Hz. This coupling is thus over five bonds to the 3-isopropyl methine proton. In rotamer (IIc), the two protons involved presumably lie in an ideal 'zig-zag' relationship, whereas in rotamers (IIa + b) the steric relationship between these two protons is unfavourable for such a coupling. Analogous couplings have for example been observed in pyrrolecarbaldehydes.[18]

TABLE 2

Representative pre-exchange lifetimes (τ) obtained from bandshape analyses of spectra from the various groups in rotamers (IIa + b) and (IIc)

	τ/s				
T/°C	=CH	$CCCH_3$	$NCCH_3$	CCH	NCH
9.9	0.175	0.18	0.17	0.20	0.18
22.4	0.063	0.060	0.060	0.068	0.065
33.9			0.022	0.022	0.020
46.4			0.0090	0.0090	0.0090
66.9			0.0022	0.0021	0.0020
93.4 *			0.000 40	0.000 35	0.000 40

* The spectra at this temperature were obtained by the Fourier transform technique.

TABLE 3

Activation parameters derived from the bandshape analyses, including statistical errors (95% confidence limits) from the least-squares treatment of the rate data

Group	n [a]	Temp. interval/°C	$\Delta\nu^{b}{}_{T_c}$/Hz	T_c/K	$\Delta G^{\ddagger}_{298.2}$/ kJ mol^{-1}	$\Delta H^{\ddagger}$/kJ mol^{-1}	$\Delta S^{\ddagger}$/J K^{-1}mol^{-1}
$C-C(CH_3)_2$	4	10.0—22.1	3.4	284	65.4	61.5 ± 1.7	−13 ± 4
$N-C(CH_3)_2$	15	10.0—66.9	36.9	313	65.3	58.2 ± 0.8	−18 ± 2
C–CH	13	10.0—66.9	50.3	316	65.4	61.1 ± 1.7	−14 ± 4
N–CH	20 [c]	9.9—113.7	163.4	333	65.4	60.7 ± 1.7	−16 ± 5
=C–H	6	9.9—29.7	5.5	288	65.6	57.3 ± 2.5	−29 ± 8
Data from all five analyses	58	10.0—113.7			65.4 [d]	59.8 ± 0.6 [d]	−18 ± 2 [d]

[a] Number of points in the Eyring plot in the given temperature interval. [b] Chemical shift between sites; extrapolated from low-temperature data. [c] Includes Fourier transform data. [d] From plot of $\Delta G^{\ddagger}$ against T.

The splitting in the high-field 5-H signal due to coupling with the 4-isopropyl methine proton was found to be 0.95 Hz, while the corresponding coupling in the low-field 5-H signal was 0.3 Hz. The relative magnitudes of these cisoid allylic couplings may be tentatively rationalized on the basis of their expected dihedral angle dependence,[19] and the stereochemical relationships suggested by the structures given for the rotamers. However, since these arguments do not further our assignments of the two sets of signals, they will not be given detailed consideration here.

In an attempt to distinguish between rotamers (IIa and b), we have carried out a series of nuclear Overhauser effect (N.O.E.) experiments at −60 and −80° in $[^2H_6]$acetone solution. Saturation of the 4-isopropyl methyl signals would be expected to give rise to an N.O.E. of the 5-H signal from rotamers (IIb and c), but not of that from (IIa). The observation of an N.O.E. in the case of (IIa + b) would not however exclude the presence of (IIa) in rapid interconversion with (IIb). At both −60 and −80°, N.O.E.s of *ca.* 30% were observed for *both* 5-H signals, demonstrating the presence of rotamer (IIb). Pre-exchange lifetimes (τ) at these temperatures of the order of 1×10^3 and 5×10^3 s, respectively, can be estimated for the interconversion (IIa + b) $\longrightarrow$ (IIc) from the activation parameters obtained in deuteriochloroform solution (see Table 3). These relatively long residence times make it very implausible that the observed N.O.E. in the signal from (IIa + b) could arise from saturation transfer *via* the (IIc) $\longrightarrow$ (II a + b) interconversion. The possibility that rotamer (IIa), if present in a detectable amount, may interconvert rapidly with (IIb) is quite reasonable in view of the results obtained by Lidén *et al.*[1e] on the corresponding thiazolinethione (I: R^5 = Me) with a methyl group in the 5-position. In this case, rotamer (Ib; R^5 = Me) was actually observed, and a value of $\Delta G^{\ddagger}_{226\,K}$ = 49.8 kJ mol^{-1} (11.9 kcal mol^{-1}) for the (Ia; R^5 = Me) $\longrightarrow$ (Ib; R^5 = Me) interconversion could be estimated. Replacement of the 5-methyl group by a proton, to give (II), would presumably lower this barrier, leading to a rapid (IIa) $\rightleftarrows$ (IIb) interconversion.

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[16] (*a*) W. Walter and R. F. Becker, *Tetrahedron*, 1972, **28**, 1705; (*b*) W. Walter, E. Schaumann, and H. Paulsen, *Annalen*, 1969, **727**, 61.

[17] E. U. Elam, F. H. Rash, J. T. Dougherty, V. W. Goodlett, and K. C. Brannock, *J. Org. Chem.*, 1968, **33**, 2738.

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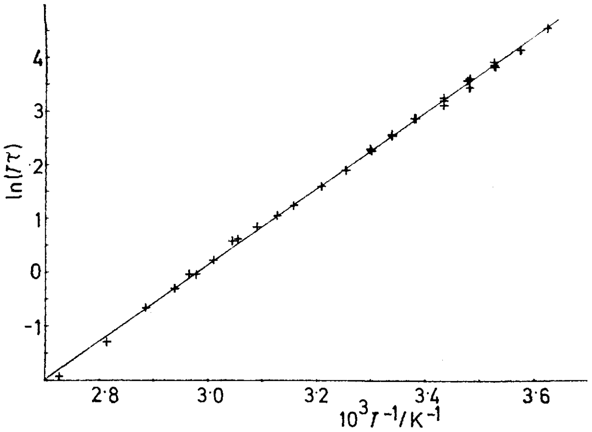

FIGURE 1 Plot of $\ln(\tau T)$ against $1/T$ for internal rotation of isopropyl groups in (II). Data from all five possible groups of protons in the molecule are included

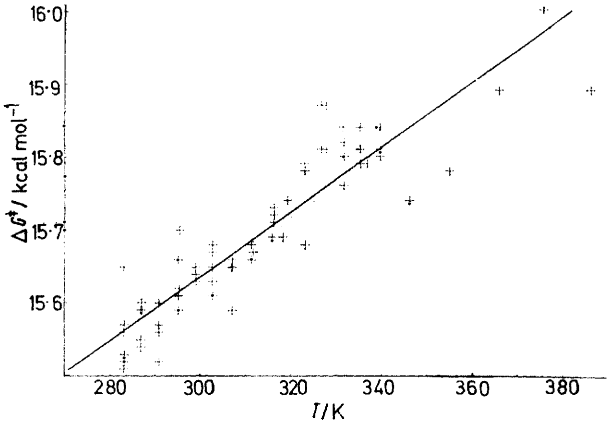

FIGURE 2 Plot of $\Delta G^{\ddagger}$ against T for internal rotation of isopropyl groups in (II)

The pre-exchange lifetimes in deuteriochloroform solution were determined separately from the bandshape due to each group of protons over appropriate temperature intervals, from a range of 12° for the 4-isopropyl methyl to a range of 104° for the 3-isopropyl methine signals (see Table 3). At +10°, the lowest temperature used for the extraction of rate constants from the bandshapes, the population ratio [(IIa + b) : (IIc)] was found to be 50 : 50, and this ratio was subsequently used throughout the temperature intervals studied. Quite acceptable agreement among the τ values was achieved, as indicated by the representative data collected in Table 2, and as shown in the form of a plot of $\ln(\tau T)$ against $1/T$ in Figure 1. This plot leads to the following thermodynamic activation parameters (and statistical error limits at the 95% confidence level): $\Delta H^{\ddagger}$ 60.2 ± 0.6 kJ mol^{-1} (14.4 ± 0.1 kcal mol^{-1}) and $\Delta S^{\ddagger}$ −18.3 J mol^{-1} K^{-1} (−4.3 ± 0.6 cal mol^{-1} K^{-1}). A plot of $\Delta G^{\ddagger}$ against T is, however, more eloquent, and also allows an estimate of the error in $\Delta G^{\ddagger}$. We used the pre-exchange lifetimes to calculate values of $\Delta G^{\ddagger}$ at each temperature, and then derived $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ parameters from plots of $\Delta G^{\ddagger}$ against T. The complete plot of $\Delta G^{\ddagger}$ against T for all five bandshape analyses is shown in Figure 2, from which the following thermodynamic activation parameters (and statistical errors at 95% confidence) may be derived: $\Delta H^{\ddagger}$ 59.8 ± 0.6 kJ mol^{-1} (14.3 ± 0.1 kcal mol^{-1}), and $\Delta S^{\ddagger}$ −18 ± 2 J mol^{-1} K^{-1} (−4.4 ± 0.4 cal mol^{-1} K^{-1}). A value of 65.4 kJ mol^{-1} (15.64 kcal mol^{-1}) for $\Delta G^{\ddagger}_{298.2\,K}$ was calculated, and it should be noted that essentially all of the points are included within ±0.4 kJ mol^{-1} (±0.1 kcal mol^{-1}). The data for each bandshape analysis are summarized in Table 3, and a series of experimental and theoretical spectra for the 4-isopropyl methine proton bandshape is shown in Figure 3.

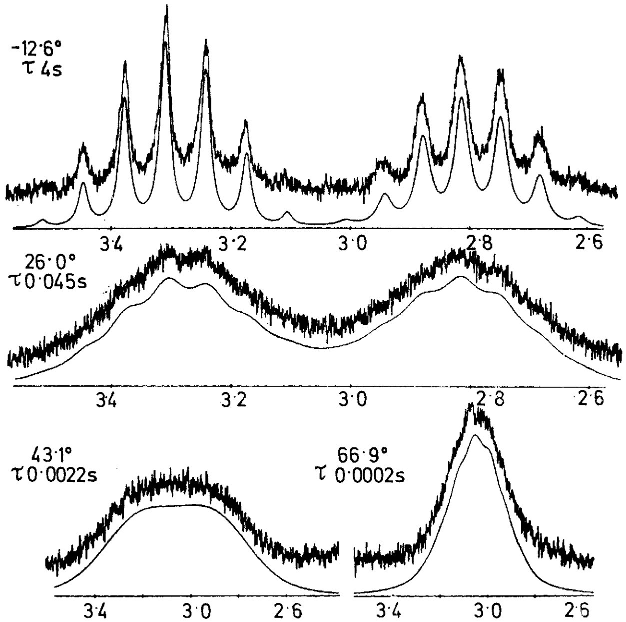

FIGURE 3 Experimental and theoretical spectra for 4-isopropyl methine proton bandshape analysis

DISCUSSION

The two most troublesome parameters involved in total bandshape calculations are without a doubt the relaxation time parameter, T_2, and the chemical shift in the absence of exchange, $\Delta\nu_{\infty}$, both of which must usually be determined as functions of temperature. The accuracy in the determination of these parameters is often decisive for the overall accuracy ultimately attainable in a bandshape analysis.[7-13]

Determination of T_2.—In the 'ideal' case, T_2 should be directly determined at both the high and low temperature limits of the exchange process, and at intermediate temperatures it should be obtained by the use of equation (1) from the width of a reference line, preferably due

$$1/T_2 = 1/T_2^{\mathrm{ref}} + \pi\Delta\nu^{\mathrm{corr}} \qquad (1)$$

to nuclei in the same molecule, which remains unaffected by the exchange. In equation (1), $\Delta\nu^{\mathrm{corr}}$ is a correction necessary if the linewidths of the exchanging lines and that of the reference line are not the same. $\Delta\nu^{\mathrm{corr}}$ should be measured at the high and low temperature limits, and is determined at intermediate temperatures by (linear) interpolation. Unfortunately, this ideal case is seldom realized in practice, and was not so for most of the signals observed in the present study. The low-temperature limit was not attainable before broadening of the signals occurred, presumably due to viscosity effects. This has been noted previously,[3b,11] and it would appear that viscosity broadening effects in deuteriochloroform solution may in some instances already be of significance above $-30°$. The T_2 values thus had to be determined in a less direct way, and furthermore no signal from (II) could be used as reference since all were affected by the exchange process. Instead, the proton signal from residual chloroform in the solvent was chosen as reference.

An almost 'ideal' procedure was applicable to the 3- and 4-isopropyl methyl proton bandshape calculations. In the case of the 3-isopropyl methine proton bandshape, the high temperature limit was not attained. However, a small error in the high temperature T_2 value is not of any great significance in this case, since line broadening due to exchange is quite evident (*ca.* 5 Hz) even at the highest temperature employed.

In the calculation of the 4-isopropyl methine proton bandshape, three different methods were used for the estimation of the T_2 values at the high- and low-temperature limits. In the first method (A), we attempted to use the 'ideal' procedure by measuring the linewidth of the reference and sample signals at -20 and $+120°$, and using equation (1). Significant deviations from linearity at both ends of the subsequent Eyring plot strongly indicated that the bandshapes at both -20 and $+120°$ were still affected by the exchange process. We thus proceeded to correct for this in method (B): the linear portion of the Eyring plot was extrapolated to $-12°$, which was the lowest temperature in our series at which no effects of viscosity could be observed, and the resulting τ value was used to iterate a new T_2 value at this temperature. The high temperature T_2 value was the same as in method (A). In method (C), both the high- and low-temperature T_2 values were corrected, the latter as in method (B), and the former by using the τ value at $+120°$ from the bandshape analysis of the 3-isopropyl methine signal, which even at this temperature was considerably broadened (see above), and thus relatively insensitive to the choice of T_2. It was not feasible to obtain spectra at higher temperatures in deuteriochloroform solution (sealed tube). The thermodynamic activation parameters derived from these three methods of T_2 determination are collected in Table 4, from which it is obvious that even in such a favourable case (with a large chemical shift difference), quite significant effects on both $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ are observed. It is thus easily understandable that serious errors can readily arise in other cases with more 'normal' shift differences (10—20 Hz).

TABLE 4

Activation parameters and statistical errors (at 95% confidence level) derived from bandshape analysis of 4-isopropyl methine spectrum, using different methods of T_2 evaluation (see text)

Method	$\Delta H^{\ddagger}$/kJ mol^{-1}	$\Delta S^{\ddagger}$/J mol^{-1} K^{-1}
(A)	68.6 ± 1.7	$+9.6 \pm 4.2$
(B)	63.6 ± 1.7	-6.7 ± 4.2
(C)	61.1 ± 1.7	-14.2 ± 4.2

It should be noted that the linearity of the Eyring plot is not a sufficient criterion for the reliability of the derived activation parameters. In the present case (Table 4), the statistical errors are essentially the same for all three methods, but the differences in $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ are much larger than these error limits.

To obtain the low-temperature T_2 value for the 5-H signals, the τ value at $-12°$ found for the 4-isopropyl methine proton with method (B) was used. The fast-exchange limit at high temperature was easily attainable due to the small chemical shift difference (5.5 Hz). Three coupling constants, one for the (IIa + b) conformer(s) (0.95 Hz), and two for the (IIc) conformer (0.5 and 0.3 Hz), were taken into account by summation of four pairs of signals.

Entropy of Activation.—The activation parameter of most interest in the present case is $\Delta S^{\ddagger}$, which, as may be gleaned from the data in Table 3, is small and negative, of the order of -18 J mol^{-1} K^{-1} (-4 cal mol^{-1} K^{-1}). Since all five values of $\Delta S^{\ddagger}$ in Table 3 are accommodated within ± 11 J mol^{-1} K^{-1} ($< \pm 3$ cal mol^{-1} K^{-1}), we feel that the observed entropy of activation has a firm experimental basis. In connection with previous work on 1,3,5-trineopentylbenzenes, it was estimated[20] that the contribution to $\Delta S^{\ddagger}$ from the complete loss of rotation of a methyl group was -15 J mol^{-1} K^{-1} (-3.6 cal mol^{-1} K^{-1}). Accordingly, a small negative $\Delta S^{\ddagger}$ value is certainly reasonable in the present case, in which intermeshing is assumed to occur during the exchange process, with a concomitant decrease in the rotational freedom of the methyl group(s) in the transition state.

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[20] B. Nilsson, P. Martinson, K. Olsson, and R. E. Carter, *J. Amer. Chem. Soc.*, 1974, **96**, 3190; see footnote 36.