Assignment of Configuration from Proton Spin–Lattice Relaxation Time Measurements

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Summary Measurement of proton spin–lattice relaxation times has differentiated the *syn-* and *anti*-isomers of substituted cyclobutanes, in accordance with calculated relative values.

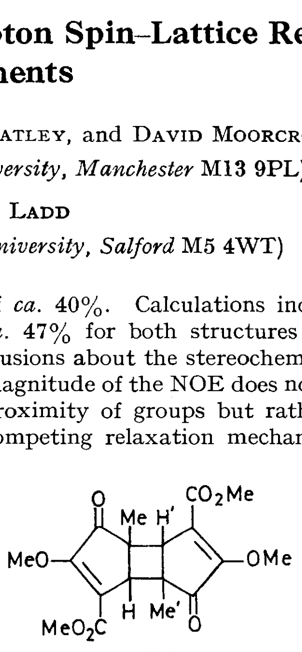
Synthetic studies of substituted cyclopent-3-ene-1,2-diones produced two series, (A) and (B), of related isomeric dimers which were assigned the *syn-* and *anti*-cyclobutane structures, typified by (I) and (II), respectively.[1] However, it was not possible to tell which series had which configuration, particularly since the ^{1}H n.m.r. spectra consisted only of singlets and no spin–spin coupling information was available. Examination of models of (I) and (II) showed that the structures had major differences in three internuclear distances (r) (see Table 1) and suggested that relative measurements of either nuclear Overhauser effects (NOE) or spin-lattice relaxation times (T_1) might provide the requisite information since both phenomena are dependent[2] on (r^{-6}).

Table 1

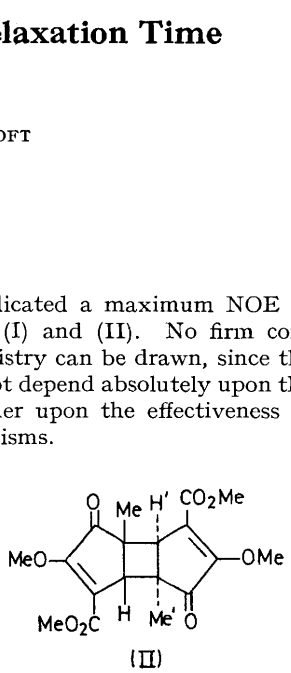
Average internuclear distances, r/Å

Structure	H–H′	H–Me	Me–H′	Me–Me′
(I)	3·5	3·0	3·0	4·7
(II)	3·8	3·0	3·8	5·6

Recent papers[3–5] have correlated the magnitude of the NOE with internuclear distance and it seemed likely that in the *syn*-isomer ($r_{\mathrm{HMe}} = r_{\mathrm{HMe}}{}' = 3{\cdot}0$ Å) the cyclobutane hydrogen should exhibit a greater NOE enhancement upon irradiation of the methyl signal than in the *anti*-isomer ($r_{\mathrm{HMe}} = 3{\cdot}0$, $r_{\mathrm{HMe}}{}' = 3{\cdot}8$ Å). Initial measurements indicated a large NOE (42%) for isomer (A) and a small one (15%) for isomer (B), the latter value agreeing with that estimated graphically.[3] However, as the observing field was reduced and the time for relaxation between successive measurements increased, the difference became less until finally both isomers had an enhancement of *ca.* 40%. Calculations indicated a maximum NOE of *ca.* 47% for both structures (I) and (II). No firm conclusions about the stereochemistry can be drawn, since the magnitude of the NOE does not depend absolutely upon the proximity of groups but rather upon the effectiveness of competing relaxation mechanisms.



(I)



(II)

The spin–lattice relaxation time for proton systems is given by the sum of intramolecular and intermolecular components according to equation (1). Under conditions

$$1/T_1 = 1/(T_1)_{\mathrm{intra}} + 1/(T_1)_{\mathrm{inter}} \tag{1}$$

such that the intermolecular contribution is negligible, $T_1 = (T_1)_{\mathrm{intra}}$. In the absence of exceptionally free rotational motion, proton relaxation is dominated by dipole–dipole coupling with other protons, and for dilute non-viscous solutions the relaxation time of a proton i can then be written as in equation (2),[2] where τ_c is the correlation

$$1/T_{1i} = \gamma_{\mathrm{H}}^4 \hbar^2 \tau_c [\Sigma_2^3 r_{ij}{}^{-6} + \Sigma r_{ik}{}^{-6}] \tag{2}$$

time for rotational diffusion of the molecule (assumed isotropic), γ_{H} is the proton magnetogyric ratio, $\hbar$ is $h/2\pi$, and r_{ij} is the distance between nuclei i and j; the first sum is over nuclei j which are identical to nucleus i and the second sum over nuclei k which are not identical to i. If the correlation times of two molecules are approximately equal, then the ratio of T_1's of nuclei in the two molecules, say (I) and (II), should be given by a function of ratios of internuclear distances, as in equation (3).

$$\frac{T^{\mathrm{II}}_{1i}}{T^{\mathrm{I}}_{1i}} = \frac{\frac{3}{2}\Sigma(r_{ij}{}^{-6} + \Sigma(r^{\mathrm{I}}_{ik})^{-6}}{\frac{3}{2}\Sigma(r^{\mathrm{II}}_{ij})^{-6} + \Sigma(r^{\mathrm{II}}_{ik})^{-6}} \tag{3}$$

The ^{1}H n.m.r. spectra of dimers (A) and (B) (in degassed $CDCl_3$ at 33°) consisted of four singlets and T_1 for each resonance was determined for a range of concentrations by two separate methods, (a) adiabatic rapid passage with sampling[5] (ARPS), and (b) saturation recovery[6,7] (SR) to give the results in Table 2. There was no variation of T_1 with concentration and hence the predominant relaxation mechanism must be intramolecular since in deuteriated solvents solute–solvent interaction is very small.[8] The T_1's for CO_2Me and OMe were approximately the same for both isomers, as expected for groups on the periphery of the molecule where they are little affected by differences in the centre. This similarity indicated that the two isomers have approximately the same correlation time τ_c and justified comparison of T_1's for structural assignments.

TABLE 2

Method	Isomer	$T_1 \pm 0{\cdot}2$/s CO_2Me	OMe	CMe	CH
ARPS	(A)	2·50	1·70	0·85	3·40
SR	(A)	2·60	1·50	0·90	3·40
ARPS	(B)	2·25	1·60	0·55	4·70
SR	(B)	2·55	1·40	0·65	4·80

The most striking difference was in the T_1's of the cyclobutane protons which had a (B):(A) ratio of 1·4:1. This was supported by measurements using the progressive saturation method[9] which gave a value for this ratio of 1·3:1. In the *syn*-structure (I) each of these protons is close to two methyl groups and the other proton, whereas in the *anti* (II) it is adjacent to only one methyl group, and therefore intramolecular relaxation of this hydrogen might be expected to be more efficient in the former than the latter. Hence, the observation that the cyclobutane hydrogen in isomer (A) had a much shorter T_1 than in isomer (B) lead to the conclusion that (A) had the *syn*-configuration and corresponded to (I).

This qualitative argument could be substantiated by an estimate of the T_1 ratio for the cyclobutane hydrogens using equation (4).

$$\frac{T^{\mathrm{II}}_{1}}{T^{\mathrm{I}}_{1}} = \frac{\frac{3}{2}(r^{\mathrm{I}}_{\mathrm{HH'}})^{-6} + 6(r^{\mathrm{I}}_{\mathrm{HMe}})^{-6}}{\frac{3}{2}(r^{\mathrm{II}}_{\mathrm{HH'}})^{-6} + 3(r^{\mathrm{II}}_{\mathrm{HMe}})^{-6} + 3(r^{\mathrm{II}}_{\mathrm{HMe'}})^{-6}} \tag{4}$$

Substitution of the values for r given in Table 1 gives a ratio of 1·6:1. The approximation of considering only the dipole–dipole interactions within the cyclobutane ring is justified by the large NOE enhancements found for both isomers which show that this mechanism is predominant for the cyclobutane hydrogens.

Independent corroboration of the n.m.r. results could be obtained in this case using the symmetry properties of the two molecules. The *syn*-structure has a C_2 axis of symmetry whereas the *anti* is centrosymmetric, and the rule of mutual exclusion[10] would allow no coincidence of frequencies between the i.r. and Raman spectra of the latter. In the 500—3000 cm^{-1} region isomer (A) had 24 i.r. and 25 Raman bands, 14 of which were common, but in contrast none of the 27 i.r. and 25 Raman bands of isomer (B) coincided, confirming the above structural assignments. More general application of T_1 measurements to other problems involving configurational assignments, *e.g.* photodimers of $\alpha\beta$-unsaturated carbonyl compounds, is therefore likely.

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