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CONFIGURATION AND CONFORMATION OF 2,3-DIMETHYL-1,4-DIOXAN BY NMR

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Abstract—The NMR spectrum of the two isomers of 2,3-dimethyldioxan have been analysed.

The steric structure of the two compounds is discussed on the basis of the values of the parameters obtained.

The diequatorial conformation and *trans* configuration are assigned to the lower-boiling isomer, the equatorial-axial conformation and the *cis* configuration to the higher-boiling isomer.

THE present work initiates a study of the sterochemistry of the derivatives of 1,4-dioxan, so far limited to the two 2,3-dimethyl substituted isomers. At present, the only available structure assignments, based on chemical evidence and on the conformational rule, are those reported by Summerbell.[1] The diequatorial conformation (i.e. the *trans* configuration) for the two methyls has been assigned to the lower boiling isomer and the ea ⇄ ae conformation corresponding to a *cis* configuration to the other isomer. The purpose of our work is to check whether the proposed steric structures are in accord with the NMR spectra and to verify the validity of the conformational rule.

Analysis of the spectra

On the basis of chemical shift and peak intensity the absorption at ca. 1 and 3–4 ppm were assigned to Me and ring protons respectively. In order to obtain the δ and J parameters, the spin decoupling technique was used. The effect of solvent variation, the C_{13} side-bands, and the complete analysis of spectra are described.

For the α-isomer by irradiation of the Me protons the multiplet structure at ca. 3 ppm goes over into a single peak and therefore it is assigned to the CH group. The remaining absorption at 3·5 ppm is consequently assigned to the —OCH_2—CH_2O— fragment. The use of acetone-d_6 (Fig. 1) and DMSO-d_6 (Fig. 2) allows the 3·5 ppm absorption to show a typical AA'BB' pattern. The peaks of the lower field half-spectrum belonging to the latter absorption are less sharp because of the coupling with tertiary CH protons. Next, the two multiplets at 1 and 3 ppm form a typical $AX_3A'X'_3$ pattern. It can then be carried out in terms of the sum of two sub-spectra AA'BB' and $AX_3A'X'_3$. For the β-isomer, methyl irradiation simplifies the absorption between 3 and 4 ppm. This decoupled spectrum (Fig. 4, A) can then be interpreted as an overlapping of the CH protons singlet with the AA'BB' pattern of the OCH_2CH_2O fragment. Therefore, as in the case of the α-isomer, the entire spectrum of the β-isomer may be regarded as the sum of two sub-spectra AA'BB' and $AX_3A'X'_3$.

The analysis of the AA'BB' part of the spectra of both isomers was performed in

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[1] R. K. Summerbell, A. A. Burlingame, D. R. Dalton and C. Dalton, *J. Org. Chem.* **27**, 4365 (1962).

the standard manner. With the aid of well known rules,[2] a set of parameters was obtained and these were adjusted to give the best fit of calculated to observed spectra (Figs. 1, 2 and 4).

It is known[3] that the relative sign of the parameters L and M cannot be determined from the above analysis. The best fit between experimental and calculated spectra was found for opposite relative signs for K and N. From the parameters K, L, M and N the following relations:

$$\begin{aligned} K &= J_A + J_B & \quad M &= J_A - J_B \\ L &= J - J' & \quad N &= J + J' \end{aligned}$$

give the values of J_A, J_B, J and J' and the three relative signs of the four coupling constants. However, there is no possibility yet of distinguishing between J and J', and between J_A and J_B. Since $K > M$, J_A and J_B have the same signs, and since $N < L$, J and J' have opposite signs; and finally, K and N have opposite signs, consequently the larger constant of the pair J_A and J_B has a sign different from that of the largest constant of the pair J and J'. Furthermore, since the constant J between the chemically different nuclei is in every case a J gem (Figs. 7 and 8) its value is chosen as $-11{\cdot}66$ for the α-isomer and $-11{\cdot}83$ for the β-isomer. The remaining three coupling constants are therefore determined on the basis of the foregoing considerations.

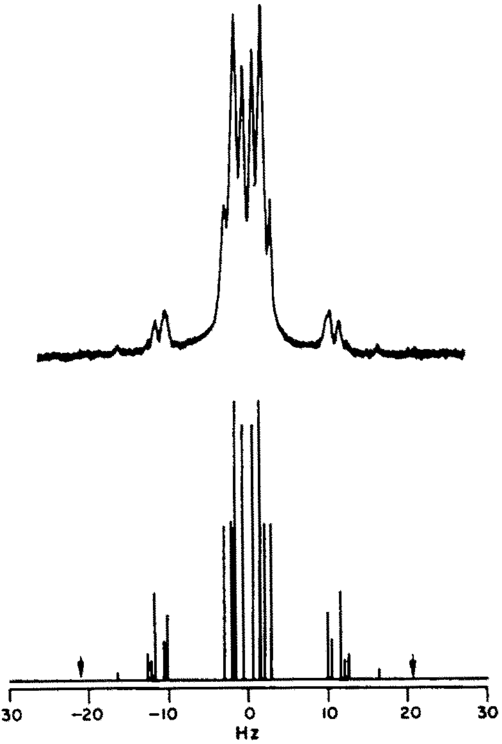

Fig. 1. Observed and calculated spectrum of the —OCH_2CH_2O— fragment in *trans*-2,3-dimethyldioxan in acetone-d_6.

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[2] J. W. Emsley, J. Feeney and L. H. Sutcliffe, *High Resolution NMR Spectroscopy*, Pergamon Press (1965).

[3] D. M. Grant, R. C. Hirst and H. S. Gutowsky, *J. Chem. Phys.* **38**, 470 (1963).

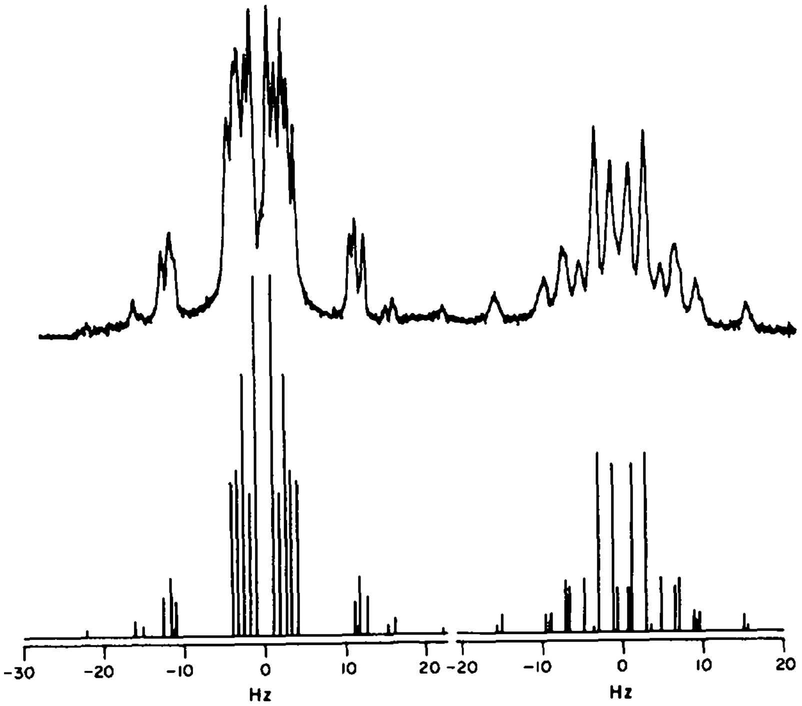

FIG. 2. Observed and calculated spectrum of the —OCH_2CH_2O— (left) and —OCHCHO— (right) fragments in *trans*-2,3-dimethyldioxan in DMSO-d_6.

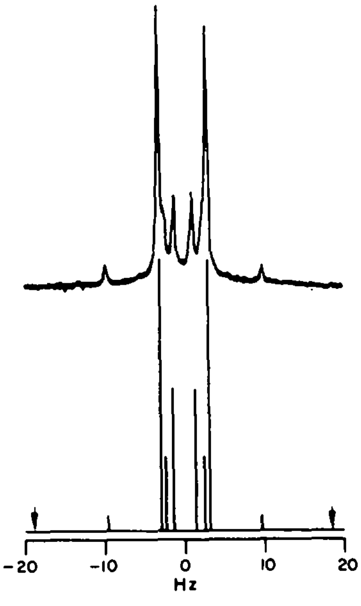

FIG. 3. Observed and calculated spectrum of methyl groups in *trans*-2,3-dimethyldioxan.

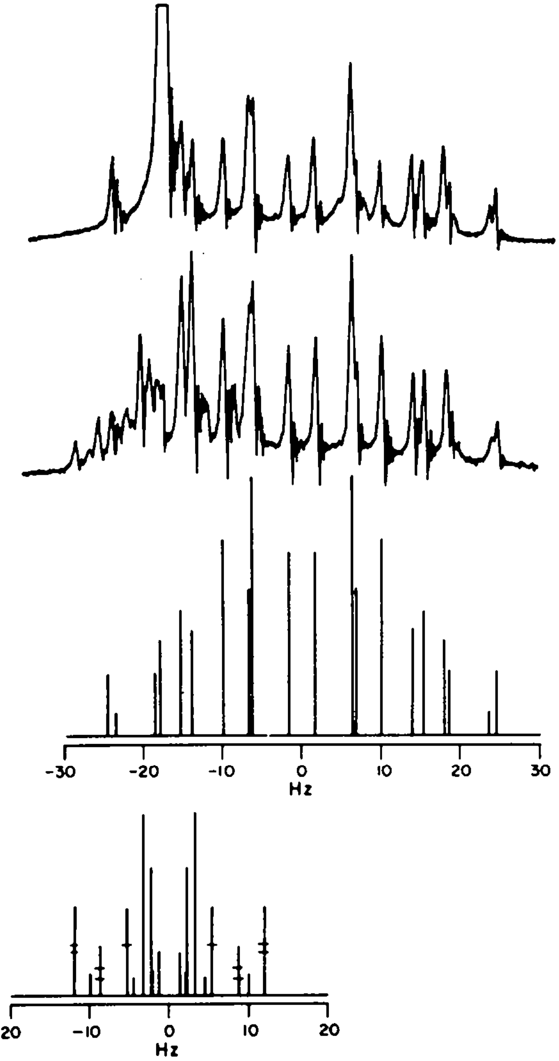

Fig. 4. Observed and calculated spectra of —OCH_2CH_2O— and —OCHCHO— fragments in *cis*-2,3-dimethyldioxan.

A: after irradiation of methyl groups;
B: undecoupled;
C: calculated spectrum of —OCH_2CH_2O— fragment;
D: calculated spectrum of —OCHCHO— fragment.

The portion of the spectrum corresponding to the —OCH(Me)CH(Me)O— fragment* was analysed as a $AX_3A'X'_3$ as in the case of 2,3-disubstituted-butanes;[4] in this approximation we considered the coupling constant $J_{CH_3-CH'} = 0$.

The parameters N, L and $J_{AA'}$ obtained from the observed spectrum was checked by calculating the theoretical spectrum, and the fit obtained is very satisfactory (Figs. 3 and 5). The value of J_{CH-CH} for the α-isomer was also obtained from the C^{13} satellite bands by irradiation of the methyl protons. The results of the analysis are indicated in Tables 1 and 2.

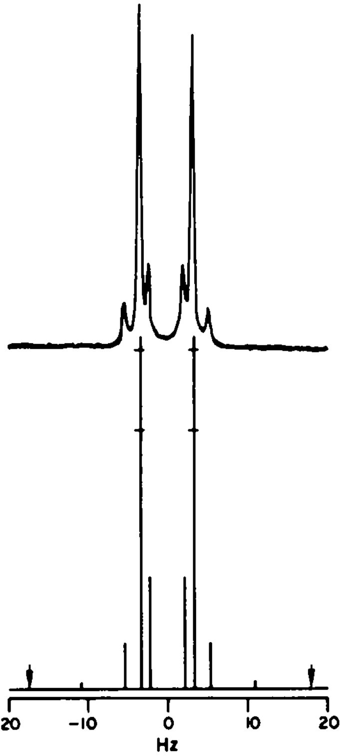

FIG. 5. Observed and calculated spectrum of methyl groups in *cis*-2,3-dimethyldioxan.

DISCUSSION

It is well known that the dioxan ring, like that of cyclohexane, can assume different conformations which may be classified as rigid and flexible. The two rigid conformations, "chair conformations", correspond to forms 1 and 2. Starting from the boat form with C_{2v} symmetry let us force a deformation of the molecule. One can then obtain first the twist form 4 (C_2 symmetry), then the boat form 5 (C_2 symmetry), then the twist form 6 (D_2 symmetry) and finally return to the starting boat form 3. All these forms and the intermediate ones which can be suitably obtained are the

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* Change of the solvent does not affect this portion.

[4] F. A. L. Anet, *J. Am. Chem. Soc.* **84**, 747 (1962); A. A. Bothner-By and C. Naar-Colin, *Ibid.* **84**, 743 (1962).

flexible forms. It is possible to predict that a rigid conformation is thermodynamically more stable than a flexible one. While in the C_{2v} boat form two eclipsed interactions of the ethane barrier type occur, in the C_2 boat form, there are two interactions of the methanol type. Deformation of the boat forms into the twist ones decreases the contribution of the methanol type interaction thus bringing the twist form to a minimum. Physical evidence from dipole moment measurements[5] suggests that the dioxan ring, at room temperature, preferentially takes up the rigid conformation, but boat forms are also present at higher temperatures. In the analysis of 2,3-dimethyldioxan, taking a more unbiased viewpoint, the NMR spectrum was analysed in terms of both the rigid and the flexible models. It has to be pointed out that among the models depicted in Figs. 7 and 8 isoenergetic pairs can be found (e.g. 10–10′; 11–11′, etc.) and necessarily they occur with the same concentration.

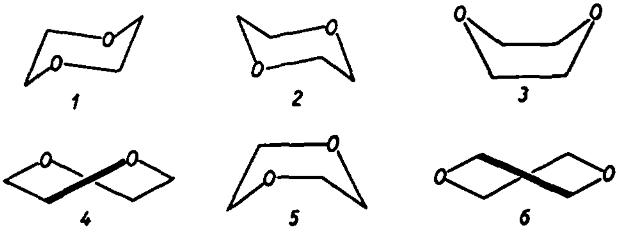

Fig. 6. Conformations of 1,4-dioxan.

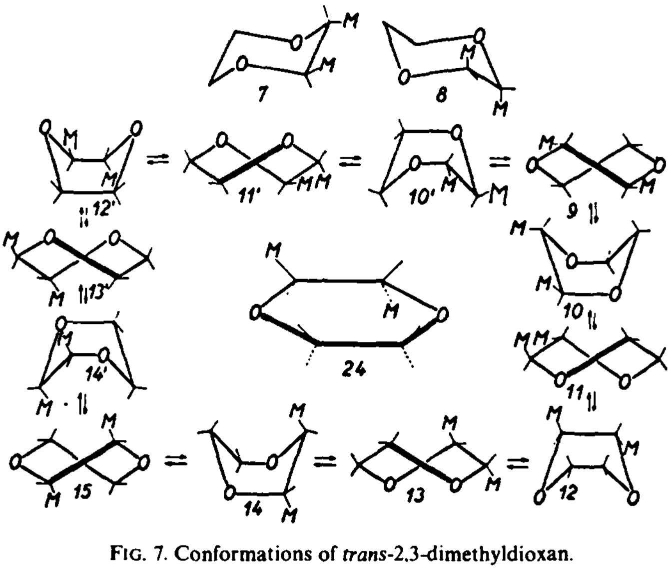

Fig. 7. Conformations of *trans*-2,3-dimethyldioxan.

In order to check which formulae (Figs. 7 and 8) agree with the NMR spectra of the α- and β-isomers, the symmetry of the spectrum and the value of the coupling constants were considered. The symmetry of the experimental spectrum of the OCH_2CH_2O portion of both isomers is of the AA′BB′ type and that of the OCH(Me)CH(Me)O fragment of the $AX_3A'X'_3$ type. The examination of the stereo

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[5] R. S. Armstrong, R. J. N. Le Fèvre and J. Yates, *Austral. J. Chem.* 11, 147 (1958).

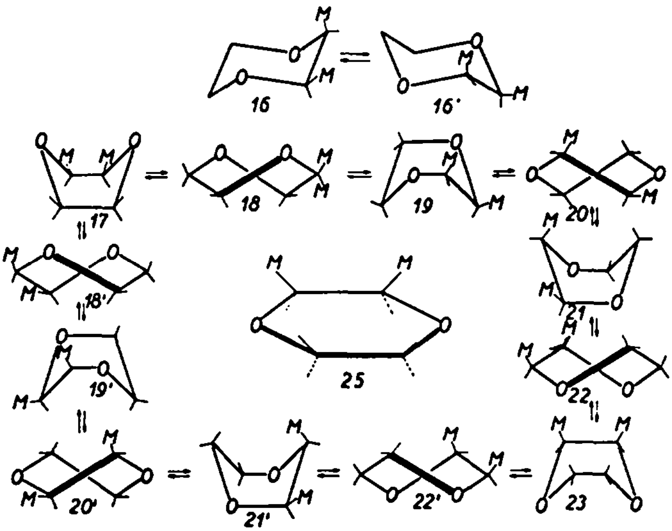

FIG. 8. Conformations of *cis*-2,3-dimethyldioxan.

models clearly shows that the simple conformations 7,8,9,15,17,23 have the forementioned symmetry and are therefore acceptable. The remaining forms, if considered individually, must be disregarded; but if they are considered as rapidly interconverting pairs with equal population, their conformation, as to NMR experiments at room temperature, is given by the average of the conformations of the two partners. For the *trans* isomer the average conformation of pairs 10,10' and 11,11' corresponds to the form 9. Pairs 13,13' and 14,14' give rise to form 15. The planar form 24 is obtained as average of pair 12,12'. Analogous combination of pairs can be found for the *cis* isomer. Namely pairs 18,18' and 19,19' → 17; pairs 21,21' → 23; 16,16' and 20,20' → 25 planar. As shown from the examination of the models, the symmetry of the average forms 9,15,17,23,24,25 is of the type experimentally observed. Therefore all rapidly interconverting pairs of partners cannot be disregarded. A further selection is based on the values of the coupling constants. As to the OCH_2CH_2O fragment, four different values of the coupling constants for the α-isomer and three for the β-isomer were obtained. Consequently, for the α-isomer, forms where $J_A = J_B$ must be excluded, i.e. the conformers and the pairs having a symmetry corresponding to 17,23,24,25. For the β-isomer the forms where $J_A \neq J_B$ (i.e. the conformers and pairs corresponding to 7,8,9,15), must be excluded. It follows, therefore, that the α-isomer has *trans* configuration, and its possible conformations are those corresponding to the models 7,8,9,15. The value of the coupling constant between the two methin protons of the OCH(Me)CH(Me)O fragment 8·46 Hz in the *trans* isomer does not fit with 8 and 15. Indeed, the two protons in synclinal position should give rise to a constant of the order of 2–3 Hz. We are left with the chair form 7, the twist one 9 and the pairs with average symmetry equal to 9. Measurement at lower temperature can give information on further selection of the models. As the spectrum of the *trans* compound, unlike that of the *cis*, does not vary by decreasing the temperature to −100°, this isomer must be present in a single form, i.e. either as 7 or as 9. Both forms account for the experimental spectrum. Furthermore for the OCH_2CH_2O fragment, the constant $J = -11{\cdot}66$ is acceptable as J_{gem}; the $J' = 2{\cdot}66$ and the $J_A = 0{\cdot}62$ as synclinal J_{vic} and the $J_B = 11{\cdot}54$ as antiperiplanar J_{vic}. The difference between the values of the two synclinal constants of 0·62 and 2·66 can be explained in terms of either ring distortion or to the known effect of the two oxygen atoms that decrease the value of the vicinal coupling constant of the two equatorial protons, with which they have an antiperiplanar relationship.[6] The difference between the values of the two antiperiplanar coupling constants in the OCH_2CH_2O and OCH(Me)CH(Me)O fragments (11·51 and 8·46 Hz respectively) may be attributed to the presence of two methyls.

The selection of possible forms for the β-isomer, based on the value of the coupling constants of the OCH_2CH_2O fragment limited them to the models 17,23,24 and 25. Form 24, which corresponds to a *trans* configuration, must be excluded *a priori*, since the isomer can be only *cis*. Furthermore, for the OCH_2CH_2O fragment the synperiplanar coupling which has to be found for model 17 and 23, should have a value of 10 Hz; the experimental value is only 3·18 Hz. Pairs 19–19′ and 21–21′ have the J' constant in both partners, corresponding to an antiperiplanar coupling, which is larger than that found (6·40 Hz). Therefore, conformers 17 and 23, pairs 19–19′ and 21–21′, and the intermediate situations like 18–18′ and 22–22′ must be discarded, leaving model 25 which may result from a rapid interconversion between conformers 16–16′ or 20–20′.

In both cases, the J_A and J_B ($\equiv J_{cis}$) constants are the average of two synclinal couplings: therefore they agree with the experimental value of 3·18 Hz. The average value of the J' constant ($\equiv J_{trans}$) between a synclinal and an antiperiplanar coupling, can be obtained by transferring the values of the related constants from the *trans* isomer; the value of $\frac{1}{2}(11{\cdot}51 + 0{\cdot}62) = 6{\cdot}06$ Hz obtained fits well with the experimental value of 6·40 Hz. Furthermore, the values of J_{trans} and J_{cis} obtained are also comparable with those of dioxan ($J_{trans} = 6{\cdot}10$; $J_{cis} = 2{\cdot}7$)[7] of *cis*-2,3-dichloro-1,4-dioxan ($J_{trans} = 6{\cdot}45$; $J_{cis} = 3{\cdot}1$)[8] of 4,4-dimethyl-1,3-dioxan ($J_{trans} = 6{\cdot}90$; $J_{cis} = 3{\cdot}9$)[9] of N,N′-dimethylpiperazine ($J_{trans} = 6{\cdot}8$; $J_{cis} = 3{\cdot}2$)[10]. A final check of the validity of the proposed structure is given by a study of the influence of temperature.

The spectrum of the β-isomer shows a progressive broadening of the bands with decreasing temperature. Under irradiation of the CH, the singlet due to the two Me groups broadens and finally splits into two peaks ($\delta = 0{\cdot}23$ ppm) corresponding to two different Me groups.

It can then be concluded that the configurations first assigned to the 2,3-dimethyldioxan are correct. Moreover, the result of our work shows that both the chair and twist ring conformations account for the NMR spectra. However, the former could be preferred because of its higher stability. Finally, the conformation of two substituents is ee in the *trans* isomer and ea in the *cis* isomer.

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[6] H. Booth, *Tetrahedron Letters* 411 (1965).

[7] N. Sheppard and J. J. Turner, *Proc. Roy. Soc.* A. **252**, 508 (1959); W. B. Smith and B. A. Shoulders, *J. Phys. Chem.* **69**, 579 (1965).

[8] R. R. Fraser and C. Reyes-Zamora, *Canad. J. Chem.* **13**, 3445 (1965).

[9] J. Delmau and C. Barbier, *J. Chem. Phys.* **41**, 1106 (1964).

[10] R. K. Harris and N. Sheppard, *J. Chem. Soc.* B, **1**, 200 (1966).

TABLE 1. PARAMETERS OBTAINED FROM THE ANALYSIS OF THE SPECTRUM AA'BB

Parameters	α-Isomer	β-Isomer
$\nu_0\delta_{AB}$	11·10[a]	24·66$_5$[b]
	8·07[c]	27·04[c]
J	−11·66	−11·83
J'	2·66	6·40
J_A	0·62	3·18$_5$
J_B	11·51	3·18$_5$

[a] In dimethylsulfoxide.

[b] In benzene

[c] In acetone.

TABLE 2. PARAMETERS OBTAINED FROM THE ANALYSIS OF THE SPECTRUM $AX_3A'X'_3$

Constant	α-Isomer	β-Isomer
J_{AX}	6·32	6·75
$J_{AX'}$	−0·33	−0·09
$J_{AA'}$	8·46	3·20

EXPERIMENTAL

The two 2,3-dimethyldioxans were prepared according to the literature and purified by gas chromatography. The spectra were recorded on a Varian HA 100 spectrometer. The line positions were obtained from the average of ten traces with sweep in both directions, the standard deviation in all line positions being less than 0·2 Hz. The samples consisted of 10 vol% solns accurately degassed in appropriate solvent containing TMS and benzene used as internal standards. A large series of solvents were tested in order to improve the resolution. At room temp, acetone and DMSO are good solvents for the α isomer (lower b.p.) and acetone and benzene for the β isomer (higher b.p.). At low temp CS_2 was used for both isomers, working with a concentration below 5%. The spin decoupling in frequency sweep conditions was carried out with a HP 200 J oscillator controlled by a frequency-meter model HP 5512 A.

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