

REVERSAL OF THE "TWIST" CONFORMATION OF 2,3-DIHYDRO-2,3-DIHYDROXYBENZOIC ACID  
WITH CHANGE OF SOLVENT

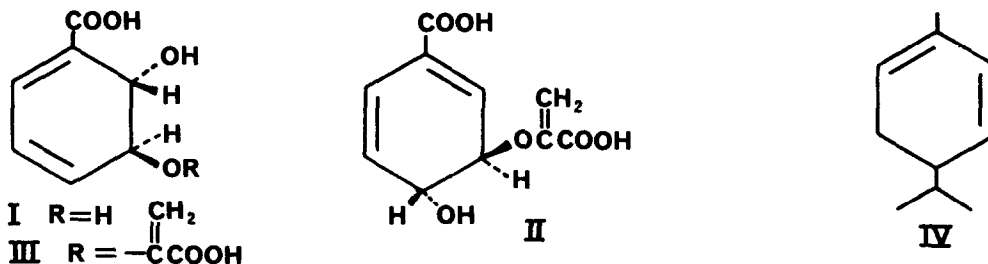
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Recently, the nuclear magnetic resonance (n.m.r.) spectra of

2,3-dihydro-2,3-dihydroxybenzoic acid (I) (1), chorismic acid (II) (2) and isochorismic acid (III) (3) have been reported. Unusually large solvent effects are observed for these compounds. In the present investigation the dramatic changes in spectral parameters observed for (I) in  $\text{CDCl}_3$ :DMSO mixtures are explained in terms of conformational mobility.



In these compounds the two oxygen substituents, and hence the corresponding methine hydrogen atoms are *trans* to each other and the predominant "twist" conformation can be determined from the size of the coupling between these two protons. With the hydrogens fixed in the *trans*-diquasial conformation the vicinal bond angle ( $\theta$ ) between them is about  $170^\circ$  (from Dreiding models) and a large coupling is expected. In the cyclohexane series the characteristic value for coupling between *trans*-diaxial protons is about 12 Hz (4) and in the present series of compounds the largest coupling of this type is  $J_{3,4} = 13.0$  Hz for (II) in  $\text{CDCl}_3 + 10\%$  DMSO. This value is taken as the upper limit. The expected coupling for the alternative conformation with hydrogen atoms quasiequatorial ( $\theta$  about  $65^\circ$ ) is 1 to 2 Hz and values for  $J_{2,3}$  of 2 Hz for (I) and  $\sim 1$  Hz for (III) are observed when DMSO is used as solvent.

The spectrum of (I) was first measured in  $\text{CDCl}_3 + 10\%$  DMSO and the value of  $J_{2,3}$  (8.3 Hz) (1) suggests that the 2,3-hydrogen atoms are predominantly quasiaxial. However, in DMSO this coupling is only 2 Hz, indicating that in DMSO the 2,3-hydrogens are almost completely quasiequatorial. The effect of solvent on the "twist" conformation has been studied for a range of  $\text{CDCl}_3$ :DMSO mixtures and the results are summarised in Table 1 and Figure 1. The n.m.r. spectra of (I) in  $\text{CDCl}_3 + 10\%$  DMSO and in DMSO alone are shown in Figure 2.

Table 1

Spectral Data for 2,3-Dihydro-2,3-Dihydroxybenzoic Acid in Mixtures of DMSO- $\text{CDCl}_3$

% DMSO	Chemical shifts (p.p.m.)					Coupling constants (Hz)						
	$\tau_2$	$\tau_3$	$\tau_4$	$\tau_5$	$\tau_6$	$J_{2,3}$	$J_{2,6}$	$J_{3,4}$	$J_{3,5}$	$J_{4,5}$	$J_{4,6}$	$J_{5,6}$
100	5.69	6.07	3.84	3.86	3.08	2.0		5.0		*	*	*
60	5.63	6.00	3.84	3.88	3.07	2.6		4.0		*	*	*
40	5.54	5.90	3.82	3.88	3.04	3.8		3.6		9.8	*	4.9
20	5.39	5.68	3.80	3.91	3.01	6.5	-1.0	3.5	-1.0	9.8	1.2	5.1
10	5.32	5.58	3.78	3.93	3.00	8.3	-1.3	3.4	-1.4	9.7	1.2**	5.4

\* Values could not be obtained due to deceptive simplicity. \*\* For the method used to determine the sign of this coupling constant, see the communication immediately following.

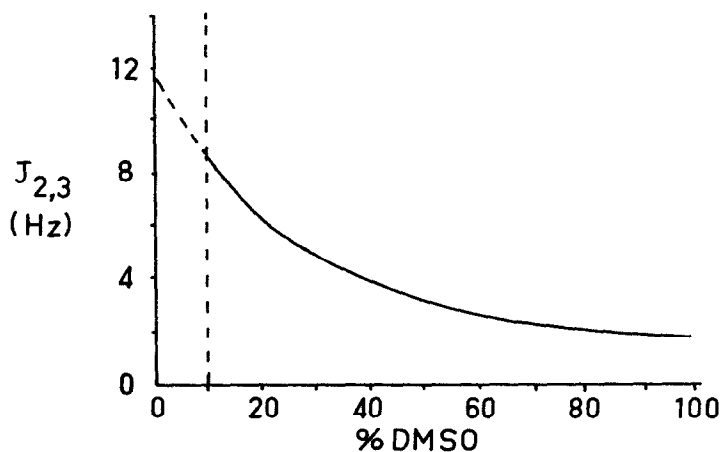


Figure 1. Variation of  $J_{2,3}$  with % DMSO in DMSO: $\text{CDCl}_3$  mixtures.

Dotted line indicates smooth extension of curve to 100%  $\text{CDCl}_3$ .

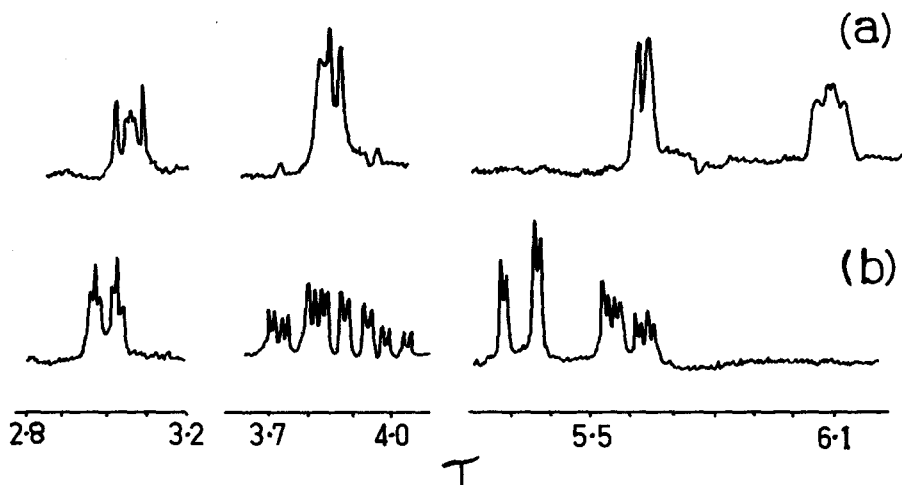


Figure 2. Spectra at 100 MHz of (I) in (a) 100% DMSO and (b)  $\text{CDCl}_3 + 10\%$  DMSO

The low solubility of (I) in  $\text{CDCl}_3$  prevents measurement of its spectrum in this solvent alone but smooth extension of the curve in Figure 1 gives a value for  $J_{2,3}$  of 12-13 Hz, the limiting value expected with H-2 and H-3 in the quasiaxial conformation. Thus the values given in Table I for  $J_{2,3}$  represent the weighted means of this coupling for the two interconverting forms. This is also true of the chemical shifts and the other couplings listed in Table 1, although as is described below, deceptively simple averaging of  $J_{3,4}$  and  $J_{3,5}$  also occurs.

In  $\text{CDCl}_3 + 10\%$  DMSO, the allylic couplings  $J_{2,6}$  and  $J_{3,5}$  are present because the quasiaxial protons H-2 and H-3 of the predominant conformer make an angle of about  $90^\circ$  with the plane of the adjacent double bonds. As the concentration of DMSO increases, the observed splittings due to these allylic couplings decrease and become negligible when the quasiequatorial conformer predominates. As the DMSO concentration increases,  $J_{3,4}$  and  $J_{3,5}$  experience two independent averaging effects. H-3 is weakly coupled to H-4 and H-5, which constitute a strongly coupled "AB group". Because the chemical shift between H-4 and H-5 decreases with increasing DMSO concentration (Table 1), deceptively simple averaging of  $J_{3,4}$  and

$J_{3,5}$  occurs. This is superimposed upon the conformational averaging and the observed values of these couplings can only be explained if both effects are considered.

Chorismic acid (II) also appears to undergo a similar but less dramatic change in "twist" conformation when the solvent is changed from  $\text{CDCl}_3$  to DMSO. In  $\text{CDCl}_3 + 10\% \text{ DMSO}$ ,  $J_{3,4}$  is about 13 Hz but in pure DMSO,  $J_{3,4}$  is only 9.6 Hz. This lower value indicates some conversion to the conformer with quasiequatorial hydrogens at positions 3 and 4.

The inversion of the "twist" conformations of these compounds with change of solvent is difficult to explain. Certainly the diene system offers little steric hindrance to large quasiaxial substituents and in systems such as  $\alpha$ -phellandrene (IV) this type of conformation is sometimes preferred (5). If the oxygen substituents are held in the quasiequatorial conformation by hydrogen bonding, then it is likely that DMSO would weaken these bonds, allowing the bulky oxygen substituents (probably highly solvated) to more readily assume the less crowded quasiaxial conformation. In agreement with this, isochorismic acid (III) in DMSO is also predominantly in the conformation with quasiaxial oxygen substituents (3). Sufficient isochorismic acid has not yet been obtained to allow measurement of its spectrum in  $\text{CDCl}_3$ .

A study of these systems using optical rotatory dispersion and circular dichroism is in progress.

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