BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 41 191—197 (1968)

Proton Magnetic Resonance Studies of 2, 2'-Anhydro-2-*C*-hydroxymethyl-1, 3 : 4, 6-di-*O*-isopropylidene-L-sorbitol[1]

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(Received July 8, 1967)

The PMR spectra of 2, 2'-anhydro-2-*C*-hydroxymethyl-1, 3 : 4, 6-di-*O*-isopropylidene-L-sorbitol were examined in several solvents to confirm its structure. The conformation of this molecule is also discussed.

In a recent paper,[2] we have reported that the treatment of 1, 3 : 4, 6-di-*O*-isopropylidene-β-L-sorbofuranose (I) with diazomethane in ether-methanol afforded a mixture of 2, 2'-anhydro-2-*C*-hydroxymethyl-1, 3 : 4, 6-di-*O*-isopropylidene-L-xylohexitol (II) and 2, 5-anhydro-2-*C*-hydroxymethyl-1, 3 : 4, 6-di-*O*-isopropylidene-L-iditol (III) accompanied with trace of methyl 1, 3 : 4, 6-di-*O*-isopropylidene-β-L-sorbofuranoside (IV), and that II was easily transformed to III even in the absence of an acid. Ring opening of an epoxide proceeds with inversion at that carbon atom which is attacked.[3,4] Therefore, it can be anticipated that the structure of II should be 2, 2'-anhydro-2-*C*-hydroxymethyl-1, 3 : 4, 6-di-*O*-isopropylidene-L-sorbitol but not 2, 2'-anhydro-2-*C*-hydroxymethyl-1, 3 : 4, 6-di-*O*-isopropylidene-L-iditol (V). This paper deals with the confirmation of the structure of II by means of PMR spectroscopy. Further the conformations of II in several solvents are discussed.

The 100 Mc PMR spectra of II were measured in carbon tetrachloride, chloroform-d, acetone-d_6, pyridine-d_5, and dimethylsulfoxide-d_6 in order to apply the solvent effects to the assignment of proton signals. The data obtained by the first-order approximation are shown in Table 1.

The spectrum of II in carbon tetrachloride shows the signal of epoxidic protons as an AB-type quartet at τ 7.06 and 7.45 ($J_{2'A,2'B}$=4.4 cps), as shown in Fig. 1a. The upfield-half of the quartet shows extra splittings of 0.8_5 cps. Double irradiation on this proton causes the collapse of the downfield-half of the quartet into a singlet and the change of a broad doublet due to H_3 at τ 5.90 ($J_{3,4}$= 3.0 cps) into a sharper doublet, but did not cause any changes to an AB-type quartet due to H_1 and $H_{1'}$ at τ 6.13 and 6.47 ($J_{1,1'}$=(−)12.5 cps) (Fig. 1b). Conversely, double irradiation at the resonance position of H_3 causes sharpning of the upfield-half of the quartet due to the epoxidic protons as well as the collapse of the multiplet arising from H_4 at τ 6.33 into a doublet ($J_{4,5}$= 2.0 cps) (Fig. 1c). Thus, the presence of a long-range spin coupling between only one of the epoxidic and C-3 protons was revealed. A doublet signal at τ 6.99 (J=7.0 cps) is thought to be due to the OH proton coupled to H_5. Decoupling of this proton by double irradiation (Fig. 1d) and by deuterium exchange by an addition of a small amount of deuterium oxide to the solution examined (Fig. 1f) made a broad multiplet at τ 6.58 narrower. Thus this multiplet was assignable to H_5 signal. The remaining AB-type quartet further split into doublets at τ 6.18 (J=(−)12.2 and 2.4 cps) and 6.38 (J=(−)12.2 and 2.5 cps) arises obviously from C-6 protons. Figures 1e and 1g show other examples of spin-decoupling experiments on II.

Similar decoupling experiments on II in chloroform-d (see Fig. 2) and acetone-d_6 (see Fig. 3) gave similar results. In these solutions the OH proton signals appear at positions so close to those

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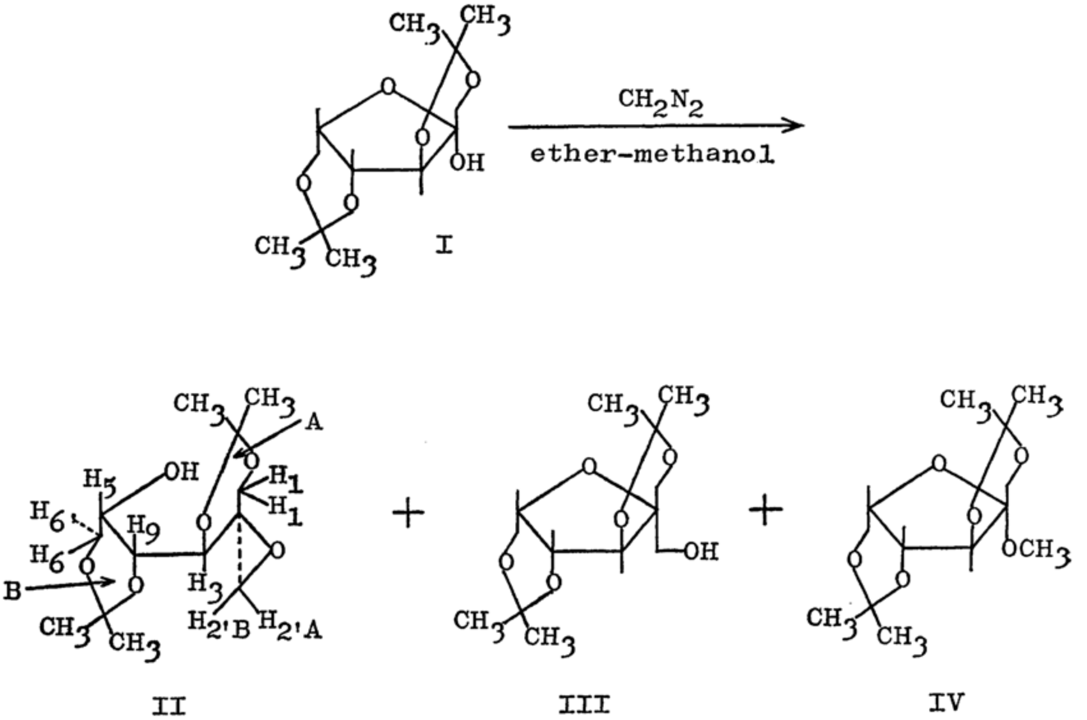
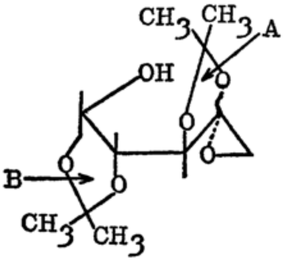
[1] Sorboses. X. For Part IX, see Ref. 2.

[2] T. Maeda, This Bulletin, **40**, 2122 (1967).

[3] S. Peat, *Advan. Carbohydrate Chem.*, **2**, 37 (1946).

[4] J. G. Buchanan and E. M. Oakes, *Tetrahedron Letters*, **1964**, 2013.





V

of H_5 signals that their patterns are much complicated, but the additions of deuterium oxide to the solutions examined make the signal patterns very clear with disappearing of the OH-signals. It is very interesting to note that decoupling of the OH proton in these solvents, particularly in chloroform-d, changes one of the C-6 methylene proton signals (at the lower field) into a sharp quartet. This observation implies the presence of long-range spin coupling between the OH- and the C-6 protons.

The infrared spectrum of II in a dilute solution of carbon tetrachloride shows two OH bands at 3539 and 3578 cm^{-1}; the former indicates the presence of a strong intramolecular hydrogen-bonding (the distance between OH–O is claculated about 1.76 Å) and the latter (shoulder) does a weak hydrogen-bonding (the distance is about 2.18 Å).[5]

The values for $J_{3,4}$ (2.7—3.6 cps) led us to determination of the dihedral anagle between H_3 and H_4 according to the well known Karplus correlation;[6] the angle is about 60° in a very rough estimation.[7] The values for $J_{4,5}$, $J_{5,6}$, and $J_{5,6'}$ (2—2.5 cps) are essentially unchanged with the change of solvents. Applying the Karplus equation to these values likewise in a rather qualitative

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[5] The distances were calculated according to Y. Matsui, M. Takasuka and T. Kubota, *Ann. Rept. Shionogi Res. Lab.*, **15**, 125 (1965), and T. Kubota, M. Takasuka and Y. Matsui, *ibid.*, **16**, 63 (1966), provided that the absorption band of an ordinary secondary OH group appears at 3630 cm^{-1}.

[6] M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959); *J. Am. Chem. Soc.*, **85**, 2870 (1963).

[7] It is a well known fact that much caution should be exercised when deriving the dihedral angle between a set of protons from the Karplus equation. For example, see N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, Inc., San Francisco (1964).

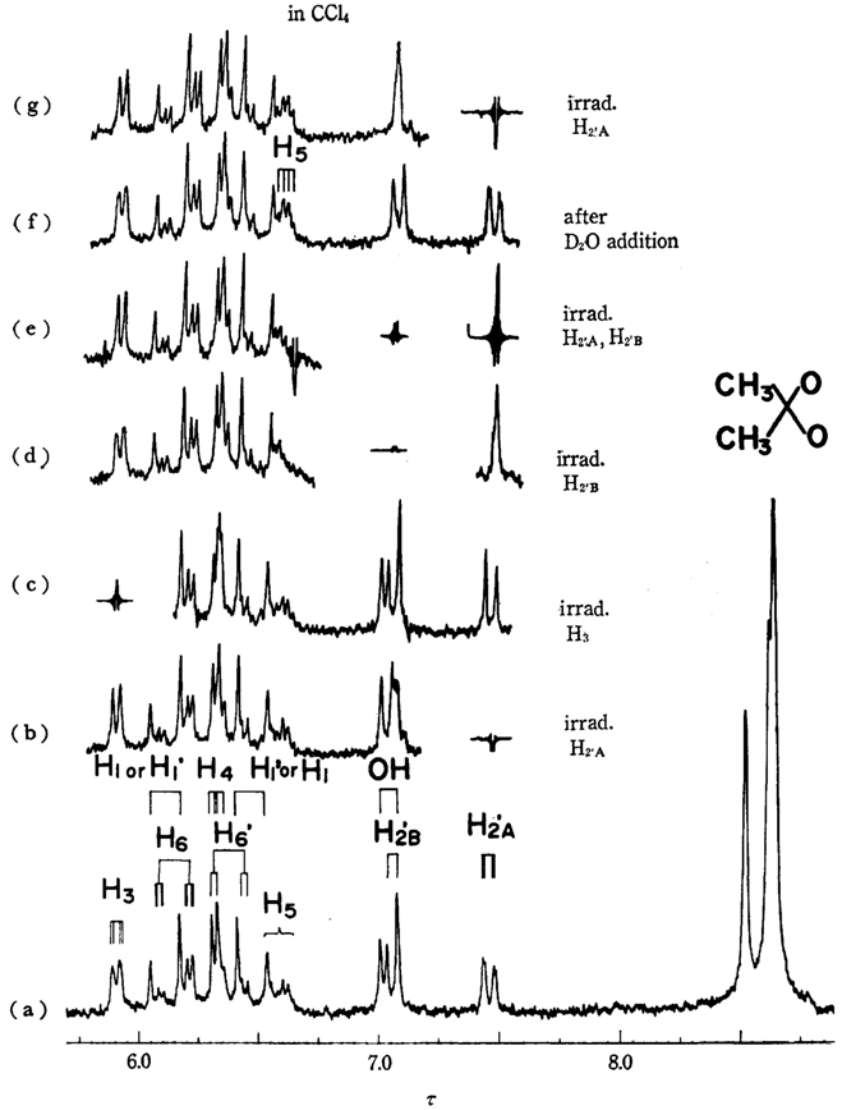

Fig. 1. PMR spectra of II in carbon tetrachloride at 100 Mc.
(a) Normal spectrum, (b)—(e) double and triple resonance spectra, (f) normal spectrum measured after adding a small amount of D_2O to the solution, and (g) double resonance spectrum.

sense, we can conclude that the 4, 6-*O*-isopropylidene ring (ring B) has a chair form; the C-5 OH group has an axial conformation. Examination of Dreiding models shows that it is difficult to form the molecular conformation so as to enable the intramolecular hydrogen-bonding of this OH group toward the epoxide ring owing to strong steric hindrance. Therefore, the OH group should possibly, and perhaps dominantly, be hydrogen-bonded to the oxygen atom at C-3; but partly, as the infrared spectrum indicates, a weak hydrogen-bonding between the OH group and either of oxygen atoms in ring B is thought to be formed. The presence of the long-range spin couplings between one epoxidic and C-3 protons and between the OH- and one C-6 protons is useful for inferring the stereochemistry of II. The stereochemical relationship between these protons should obey the "W-letter" rule for the long-range spin coupling across four single bonds.[8] The "W-letter" arrangement between the OH- and the axial C-6 protons also explains the coupling constant between the OH- and C-5 protons in carbon tetrachloride; the dihedral angle between these two protons is

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[8] For example, see S. Sternhell, *Rev. Pure and Appl. Chem.*, **14**, 15 (1964); K. Tori, K. Aono, Y. Hata, R. Muneyuki, T. Tsuji and H. Tanida, *Tetrahedron Letters*, **1966**, 9, and references therein.

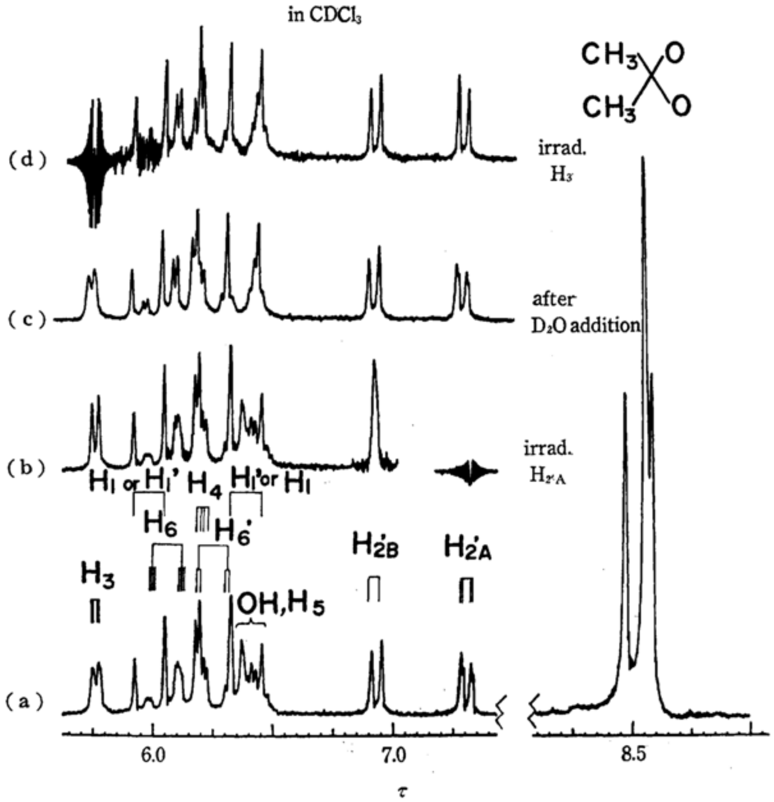

Fig. 2. PMR spectra of II in chloroform-d at 100 Mc.
(a) Normal spectrum, (b) double resonance spectrum, (c) normal spectrum measured after adding a small amount of D_2O, and (d) double resonance spectrum.

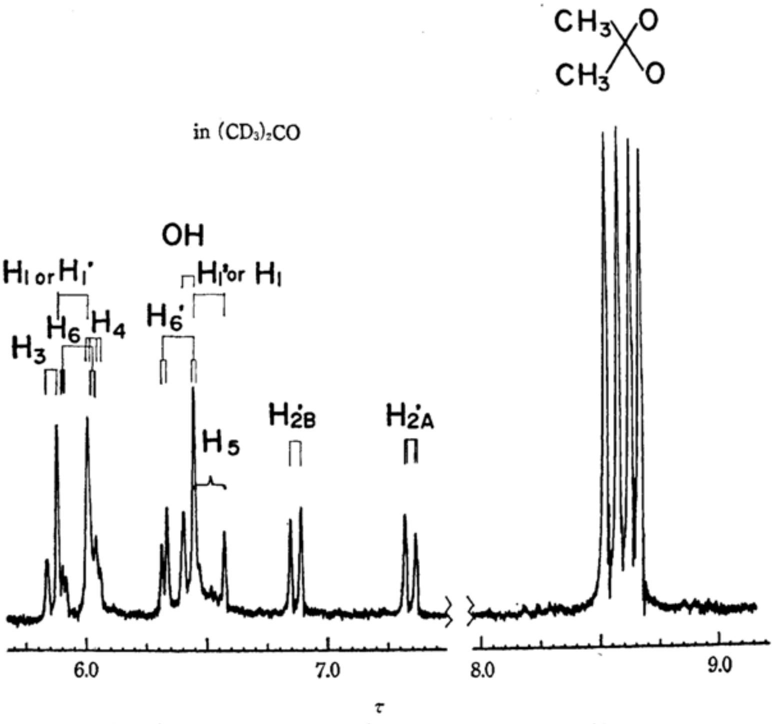

Fig. 3. PMR spectrum of II in acetone-d_6 at 100 Mc.

TABLE 1. CHEMICAL SHIFTS (τ) AND COUPLING CONSTANTS (J, cps) OF 2, 2′-ANHYDRO-2-*C*-HYDROXYMETHYL-1, 3 : 4, 6-DI-*O*-ISOPROPYLIDENE-L-SORBITOL (II) IN VARIOUS SOLVENTS

	Solvent				
	Carbon tetrachloride	Chloroform-d	Acetone-d_6	Pyridine-d_5	Dimethyl-sulfoxide-d_6
Chemical shift					
H_1 and $H_{1'}$	6.13 6.47	5.98 6.36	5.93 6.49	5.78 6.25	5.95 6.57
$H_{2'A}$	7.45	7.28	7.31	7.20	7.31
$H_{2'B}$	7.06	6.90	6.85	6.56	6.90
H_3	5.90	5.76	5.84	5.42	6.06
H_4	6.33	6.13	6.00	5.75	5.96
H_5	6.58	6.37	6.45	6.30	6.65
H_6	6.18	6.03	5.95	5.93	6.04
$H_{6'}$	6.37	6.20	6.37	6.03	6.47
OH	6.99	~6.37	6.43	4.17	5.69
C-CH_3	8.51 8.61 8.63(6H)	8.46 8.55(6H) 8.57	8.51 8.56 8.62 8.66	8.41 8.53 8.54 8.55	8.58 8.62 8.63 8.69
Coupling constant					
$J_{1,1'}$	(−)12.5	(−)12.8	(−)12.5	(−)12.5	(−)12.5
$J_{2'A,2'B}$	4.4	4.0	4.3	4.5	4.5
$\|J_{2'A,3}\|$	0.8_5	1.0	0.7	—	—
$J_{3,4}$	3.0	2.7	3.6	5.5	6.4
$J_{4,5}$	2.0	1.5	2.0	1.8	1.8
$J_{5,6}$	2.5	2.0	2.0	2.2	2.0
$J_{5,6'}$	2.4	1.8	1.8	2.0	2.0
$J_{6,6'}$	(−)12.2	(−)12.5	~(−)12.5	(−)12.4	(−)12.4
$J_{5,OH}$	7.0	a)	a)	—	5.4
$\|J_{6,OH}\|$	0.7	0.7	0.7	—	—

a) Obscured.

about 30—40°. The fact that in contrast to the general rule, the axial C-6 proton signal appears at a lower field than the equatorial C-6 proton is accounted for by the long-range shielding effects of the OH group in *trans*-diaxial relation to the axial C-6 proton and of the isopropylidene methyl group 1, 3-diaxial to this proton.[9] Provided that the OH group is strongly hydrogen-bonded to C-3 oxygen, only one skew-boat conformation of 1, 3-*O*-isopropylidene ring (ring A) in II can satisfy the "W-letter" relationship between $H_{2'A}$ and H_3, as Dreiding models indicate. However, any conformations of ring A in the structure V cannot explain the presence of the long-range spin coupling only between one epoxidic proton and H_3. Thus, we reached in the conclusion that the product II was confirmed to be 2, 2′-anhydro-2-*C*-hydroxymethyl-1, 3 : 4, 6-di-*O*-isopropylidene-L-sorbitol which has the molecular conformation shown in Fig. 4 in carbon tetrachloride, chloroform-d, and acetone-d_6. This conformation also well explains the appearance of the $H_{2'B}$ signal at a lower field than the $H_{2'A}$ signal because $H_{2'B}$ is closely situated to one of the oxygen atom in ring B, which can exert deshielding effects on $H_{2'B}$.

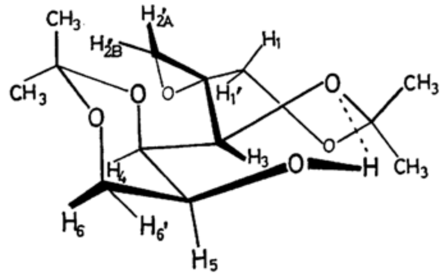

Fig. 4. The conformation of II.

This conclusion was further evidenced by the measurements of the spectra of II in pyridine-d_5 and dimethylsulfoxide-d_6; these solvents can be expected to remove the hydrogen-bonding owing to their strong basicity.[10-12] Seemingly, acetone

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[9] K. Tori and T. Komeno, *Tetrahedron,* **21**, 309 (1965).

[10] O. L. Chapman and R. W. King, *J. Am. Chem. Soc.,* **86**, 1256 (1964).

[11] D. Barnard, J. Fabian and H. Koch, *J. Chem. Soc.,* **1949**, 2442.

[12] A. Allerhand and P. von R. Schleyer, *J. Am. Chem. Soc.,* **85**, 1715 (1963).

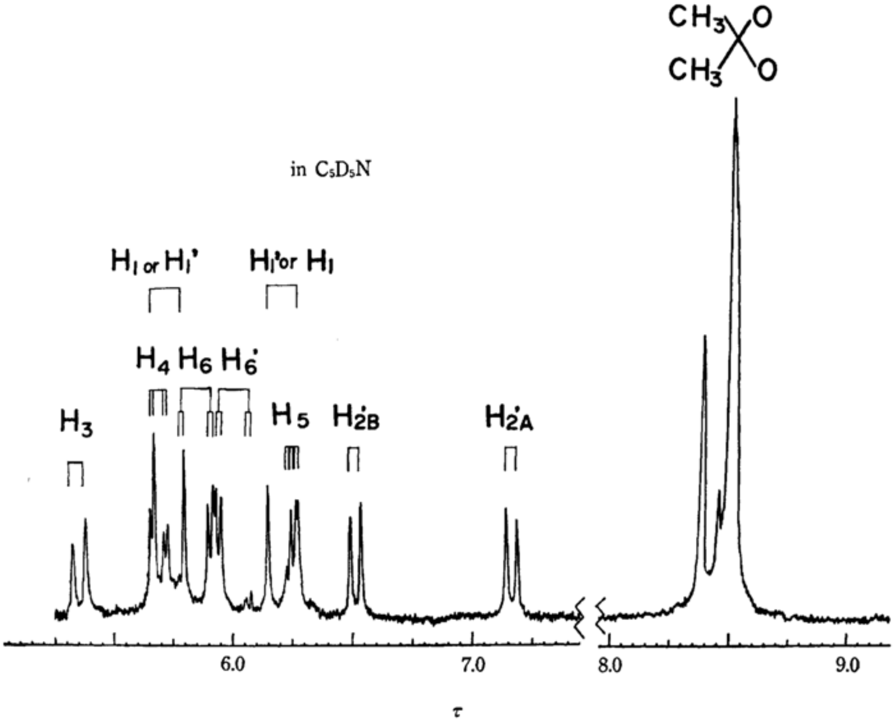

Fig. 5. PMR spectrum of II in pyridine-d_5 at 100 Mc.

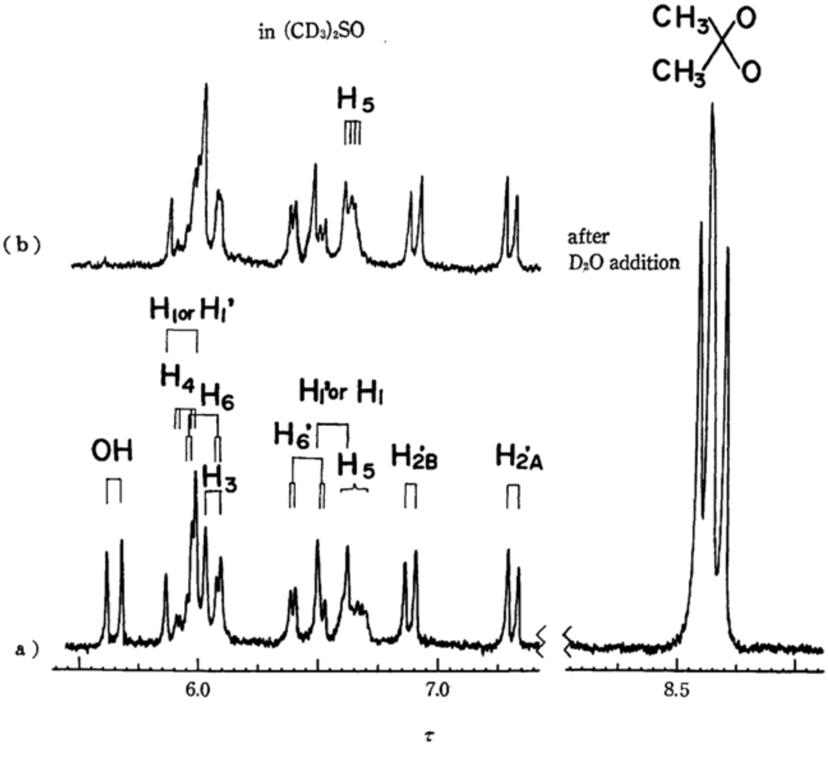

Fig. 6. PMR spectra of II in dimethylsulfoxide-d_6 at 100 Mc.
(a) Normal spectrum and (b) spectrum measured after adding a small amount of D_2O.

does not have sufficient basicity to remove such a strong intramolecular hydrogen-bonding between the C-5 OH and C-3 oxygen.

The spectrum of II in pyridine-d_5 shown in Fig. 5 exhibits well-separated signals, which were easily assigned. In the spectrum in dimethylsulfoxide-d_6 (Fig. 6a), the signals seemed somewhat complicated; but by an addition of deuterium oxide to the solution examined the lowest-field doublet (J=5.4 cps) disappears with the change of the H_5 signals (little changes in the chemical shift were caused as shown in Fig. 6b). This doublet is due to the C-5 OH proton. The signal assignment was made as indicated in Fig. 6. In these cases, the signals of $H_{2'A}$ appear as a clear doublet showing no further splittings. The larger values for $J_{3,4}$ obtained (5.5 and 6.4 cps) imply the increasing of population of the *trans*-conformation between H_3 and H_4 in these solvents. These observations can be due to the disappearance of the intramolecular hydrogen-bonding; instead, the intermolecular hydrogen-bondings between the OH group and the solvents were formed strongly. Thus, the above conclusion was amply justified by these facts also.

Experimental

The PMR spectra were taken with a Varian HA-100 spectrometer operating at 100 Mc by using about 5% solutions of the sample in carbon tetrachloride, chloroform-d, acetone-d_6, pyridine-d_5, and dimethylsulfoxide-d_6 in the frequency-swept and tetramethylsilane (TMS)-locked mode. Calibration of the spectrometer was checked by a Hewlett-Packard 5212A electronic counter. Spin-decoupling experiments were carried out by using two Hewlett-Packard 200ABR audiooscillators. Chemical shifts are expressed in τ unit ($\pm$0.02) and coupling constants in cps ($\pm$0.2 cps).

The infrared spectrum of II was measured with a Nippon Bunkō DS402G infrared spectrometer by using a 3.5 mg/8 cc (in 20 mm cell) solution in carbon tetrachloride.

We thank Dr. Ken'ichi Takeda, Director of this Laboratory, for his interest, and dedicate this paper to him in celebration of his sixtieth birthday.