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NUCLEAR MAGNETIC RESONANCE SPECTRUM OF 2,7,8-TRIOXA-1-PHOSPHABICYCLO [3.2.1] OCTANE

A FURTHER OBSERVATION OF THE "*THROUGH-SPACE*" LONG-RANGE COUPLING CONSTANT

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Abstract—The PMR spectrum of 2,7,8-trioxa-1-phosphabicylo[3.2.1]octane (I) has been fully analysed by the first order assumption and a preferred conformation of the molecule was determined on the basis of the coupling constants. Many ^4J (long-range coupling through four bonds) were observed both in the coplaner and non-coplaner systems. An unexpected ^5J was observed, which can be considered as a "*through-space*" long-range coupling. Attention has been directed also to the angular dependency of J_{POCH} and J_{POCCH}.

RECENTLY, Edmundson and Mitchel[1] reported the synsthesis of 2,7,8-trioxa-1-phosphabicyclo[3.2.1]octane (I) by the transesterification between trimethylphosphite and 1,2,4-butanetriol in a 75% yield. Although the molecular structure of I has been characterized by an elemental analysis and the reaction product with benzylchloride, detail examination of its stereochemistry was not given. In this paper we wish to report a complete first order analysis of the PMR spectrum of I and discuss the preferred conformation in solution.

RESULTS

Assignment of the absorptions. The 100 MHz PMR spectrum in deuterochloroform solution shows a very complex but well resolved pattern (Fig. 1). The whole spectrum

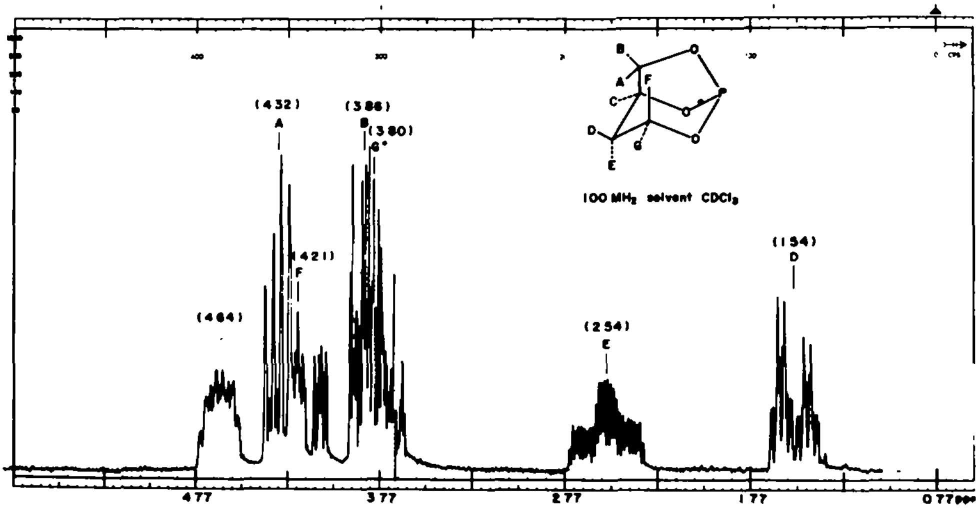


FIG. 1 PMR spectrum of 2,7,8-trioxa-1-phosphabicyclo[3.2.1]octane (I). Internal standard, TMS

can be divided into five bands at δ 4·6, 4·3, 3·8, 2·5 and 1·5 ppm. The integrated spectrum indicates that the bands are attributable to 1, 2, 2, 1, and 1 protons respectively. It was found that a small signal of the unremoved trimethylphosphite is hidden at ca. 3·8 ppm. These seven protons correspond to those of either Ia and Ib conformations shown in Fig. 2.

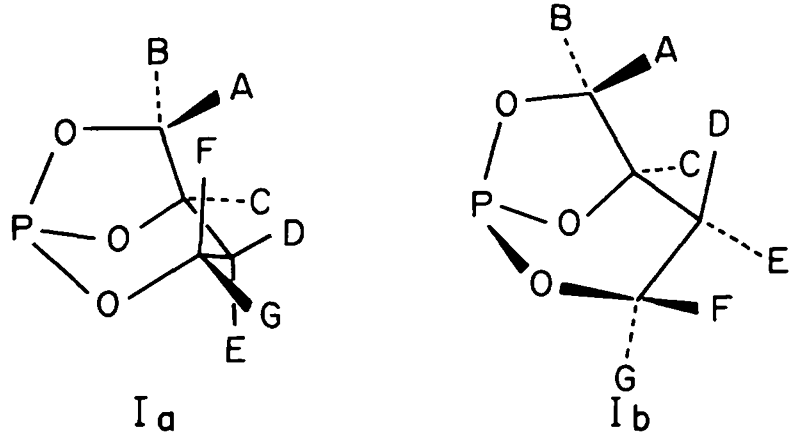


FIG. 2 Two alternative conformations of I

Signals at δ 1·5 and 2·5 ppm are assigned to D and E protons from their chemical shifts. Furthermore with its larger line width ($W\frac{1}{2}$ = ca. 40 Hz) the signal at 2·5 ppm can be assigned to either E of Ia or D of Ib. Further experiments including spin decoupling experiments show that this proton is E. Thus a strong irradiation at 2·5 ppm (Fig. 3, Table 1) caused a marked change of all the other signals, indicating that

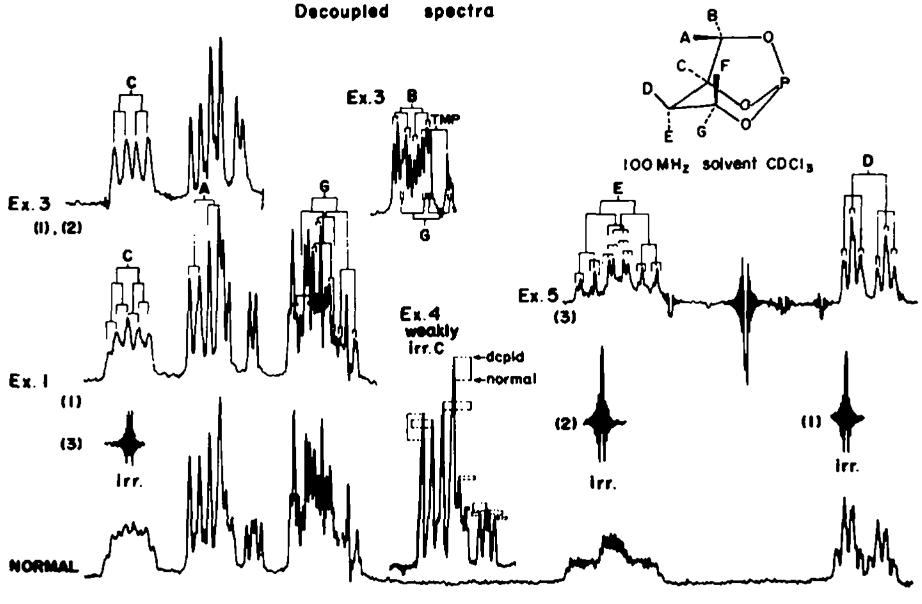


FIG. 3 Frequency sweep NMDR and NMTR spectra of I

TABLE 1. DECOUPLING EXPERIMENTS

Proton	Multiplicity[b]	Ex. 1	Ex. 2	Ex. 3	Ex. 4	Ex. 5	Ex. 6
A (4·32)[a]	d, d, d, d, d	n.e.	s.	s.	s.	—	p.
B (3·86)	d, d, d, d	n.e.	n.d.	dpl.	p.	—	→
C (4·64)	d, d, d, d, d, d, d	dpl.	n.d.	dpl.	→*	→	dpl.
D (1·54)	d, d, d, d, d	→[c]	p.	→	—	dpl.	n.d.
E (2·54)	d, d, d, d, d, d, d	p.	→	→	—	dpl.	n.d.
F (4·21)	d, d, d, d, d, d	dpl.	n.d.	dpl.	s.	—	—
G (3·80)	d, d, d, d, d	dpl.	n.d.	dpl.	p.	—	→

[a] Values in the parenthesis represent chemical shifts (δ, ppm) from internal TMS.

[b] Multiplicity is given as d, d . . ., which means doublet of doublets of . . .

[c] Arrows indicate the proton irradiated.

* Weakly irradiate. Abbreviations are following; n.e., no effect; dpl., decoupled; p., perturbed; n.d. nealy decoupled; s., sharpened.

this proton is coupled to each one. This situation can only be possible for E proton of Ia conformation, because D of Ib is considered to have nearly zero coupling constants with A and B protons. So the signal at 1·5 ppm must be assigned to D of Ia conformation. On strong irradiation at E the multiplet around 4·2 ppm was found to decouple. Although the change of the multiplicity of this complex signal is not so apparent in a $CDCl_3$ solution by the line overlapping, it becomes very clearcut in a acetone-d_6 solution by the solvent induced chemical shift (Fig. 4). As this signal is coupled also with D, the triple resonance spectrum appears as a slightly broad double doublets (Fig. 4). This signal was found to have ca. 10 and 4 Hz coupling constants with E and D respectively, indicating F is its origin.

The triple resonance experiment further realized the assignment of the very complex multiplet at 4·64 ppm. The rather broad quintet at 4·64 ppm of E-decoupled spectrum (Figs. 3, 4) changes to a simpler double doublets by D, E-irradiation. C-proton can be unequivocally assigned to this signal, for F is only slightly affected by the weak irradiation of this multiplet. It may be supported by a stereochemical consideration which shows the dihedral angle of A and C proton is 86°, i.e. J_{AC} must be nearly zero (Discussion).[2] The rather broad double doublets at 4·52 ppm is slightly perturbed by the irradiation of E and D, and also slightly sharpened by the weak irradiation of C proton. Therefore, the signal should be assigned to A proton. The two unassigned protons B and G must therefore be attributed to the complex signals around 3·8 ppm and the further assignment of these protons was completed by the following analysis of the expanded spectra.

Complete first order analysis of the expanded spectra. The preceding assignment of the PMR spectrum of I shows that the strongly coupled protons, fortunately, are sufficiently separated to permit a good first order approximation. A complete first order analysis of each of the seven protons of I has been achieved by the expanded spectra using a very slow scanning. All coupling constants were determined as the spacings of the multiplets and are summerized in Table 2. Details of the analysis are as follows.

Proton E. The signal of E proton consists of 128 lines and its splitting pattern is given in Fig. 5. The smallest spacing, 0·42 Hz, can be assigned to J_{AE} from the

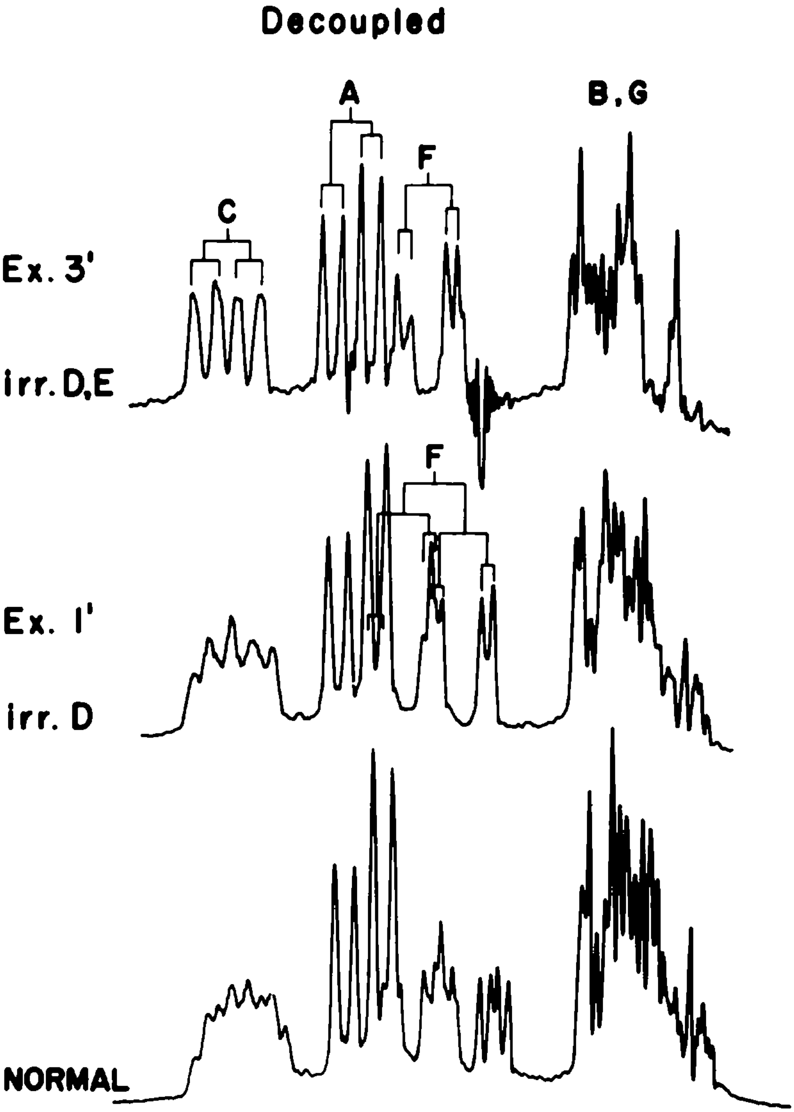


FIG. 4 NMDR and NMTR spectra in acetone-d_6, 100 MHz

decoupling experiments. One of the next smallest coupling constants may be assigned to the "W" coupling J_{BE}, and the other should be J_{EP}. J_{CE} was shown to be 3·1 Hz from the decoupling experiments, and the two large coupling constants, 14·4 and 13·0 Hz, are assignable to J_{DE} and J_{EF}. The further assignment of these two coupling constants, however, was done by the analysis of the spectrum of D proton. Consequently J_{GE} must be the splitting of 6·4 Hz.

Proton D. The splitting pattern is illustrated in Fig. 6. The largest coupling constant assigned to J_{DE}, so J_{EF} must be 13·0 Hz (see *Proton E*). The decoupling experiments show J_{DC} and J_{DF} are ca. 3–4 Hz and the corresponding spacings in D

TABLE 2. SPIN-SPIN COUPLING CONSTANTS[a]

	^{31}P	A	B	C	D	E	F
A	4·4						
B	1·7	8·8					
C	9·6	0·67	5·2				
D	3·8	—[b]	—[b]	2·8			
E	1·7	0·42	1·7	3·1	14·4		
F	2·5	0·22	—[b]	0·47	4·0	13·0	
G	9·3	—[b]	—[b]	1·1	1·0	6·4	12·2

[a] Coupling constants (Hz) are assumed to be approximately equal to the splittings and each of the components of this table shows a corresponding J value.

[b] not observed.

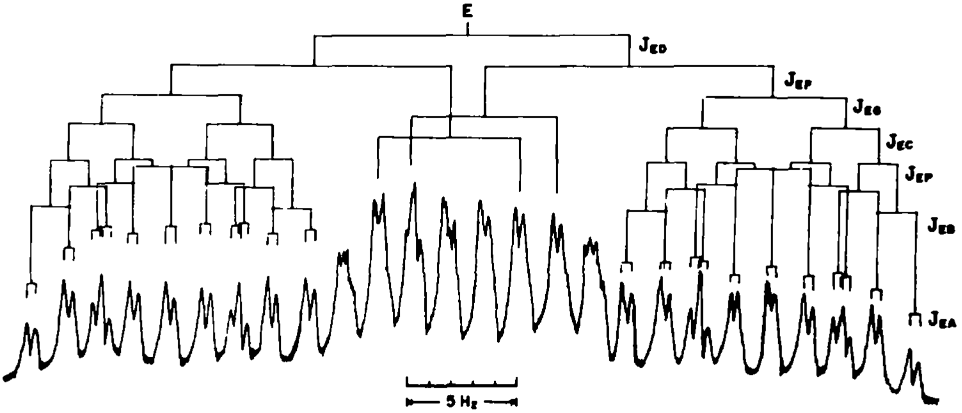


FIG. 5 Expanded spectrum of proton E, C_6D_6.

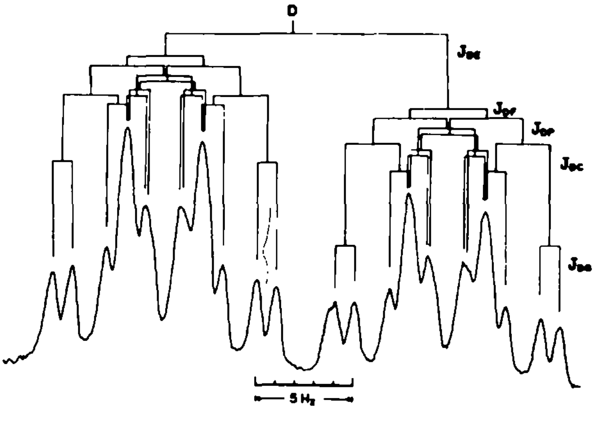


FIG. 6 Expanded spectrum of proton D, $CDCl_3$

signal are 2·8, 4·0, and 3·8 Hz. Further assignments were achieved by comparison of the other proton signals. Possibly one can assume that J_{DP} may be larger than J_{EP} (1·7 Hz), so the smallest spacing, 1·0 Hz, assigned to J_{DG}. J_{AD} was confirmed as almost negligible by the decoupling experiment (Ex. 1 of Table 1)

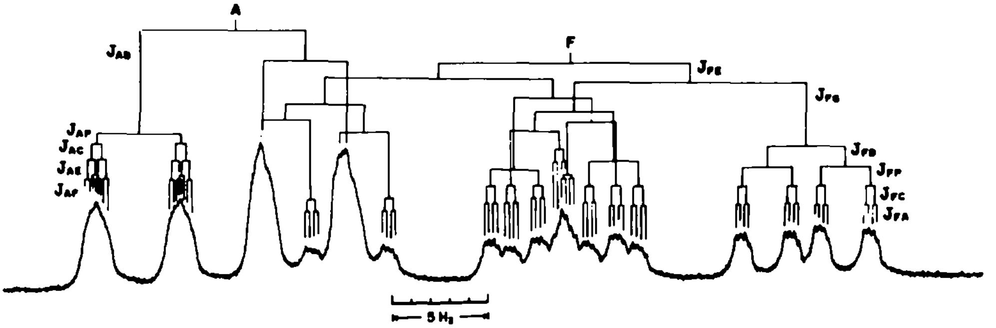


FIG. 7 Expanded spectrum of proton A and F, Acetone-d_6

Proton F and A. The expanded spectrum in acetone-d_6 solution, Fig. 7, permits the first order analysis of the complex signals of F and A by the solvent induced shift. Thus the signal of F proton consists of 64 lines and its multiplicity can be regarded as d, d, d, d except two small splittings. By the spin decoupled spectrum, J_{DF} and J_{EF} were found to be 4·0 and 13·0 Hz respectively. It is also apparent that J_{FG} and J_{FP} are 12·0 and 2·5 Hz. The remaining two small spacings, 0·47 and 0·22 Hz, should be attributed to J_{AF}, J_{CF} or J_{BF}. The expanded spectrum of A proton has three very small splittings 0·22, 0·42 and 0·67 Hz. By comparison of the spacings of F and A signals the smallest splitting 0·22 Hz was found to be the unexpected J_{AF}. This should be a real coupling because the chemical shift between these two interacting nuclei is sufficiently large with respect to the coupling constant to avoid a virtual coupling,[3] furthermore J_{AF} does not depend on the solvents ($CDCl_3$ and aceton-d_6). As a result J_{AC}, J_{AB} and J_{AP} are shown to be 0·67, 8·8 and 4·4 Hz respectively.

Proton B and G. The complex and overlapped multiplet around 3·8 ppm is assigned to B, G and the unremoved trimethylphosphite (TMP). Although these signals are completely overlapped, the careful decoupling experiment (Fig. 3) allowed the first order analysis as illustrated in Fig. 8. G proton's signal consists of 64 lines. The spacing of 12·0 and 6·4 Hz coincides with those of J_{FG} and J_{EG} obtained by the analysis of F and E. Then J_{GP} should be 9·3 Hz and two small splittings of 1·0 and 1·1 Hz are assignable to J_{DG} and J_{CG} respectively. B proton gives a rather simple spectrum, consisting of 16 lines, which can be readily analysed. J_{AB} (8·8 Hz) and J_{BE} (1·7 Hz) have been determined, J_{BC} and J_{BP} are found to 5·7 and 1·7 Hz respectively. As J_{BF} is not yet observed the unidentified J_{CF} (see *Proton F and A*) must be 0·47 Hz.

Proton C. C gives a very complex signal at 4·64 ppm. The first order splitting pattern, shown in Fig. 9, was elucidated with the aid of the coupling constants obtained as well as the decoupled spectrum (Fig. 3 and 4). In addition to the three small couplings ($J_{CG} = 1 \cdot 1$, $J_{CF} = 0 \cdot 47$, $J_{AC} = 0 \cdot 67$ Hz) four extra spacings were observed. J_{CP} and J_{CD} are easily determined as 9·3 and 2·8 Hz respectively. Consequently the unidentified J_{DP} (see *Proton D*) should be 3·8 Hz.

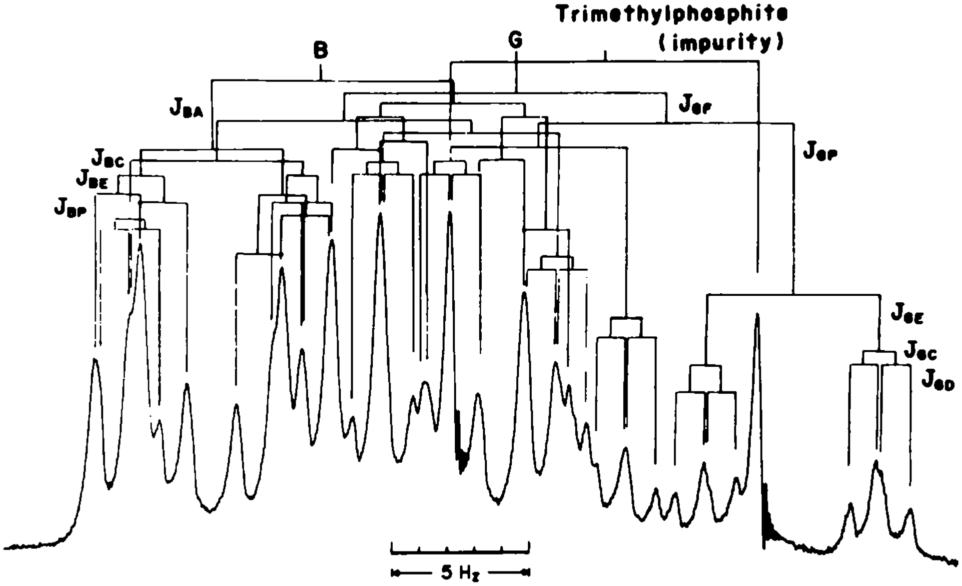


FIG. 8 Expanded spectrum of proton B and G, $CDCl_3$

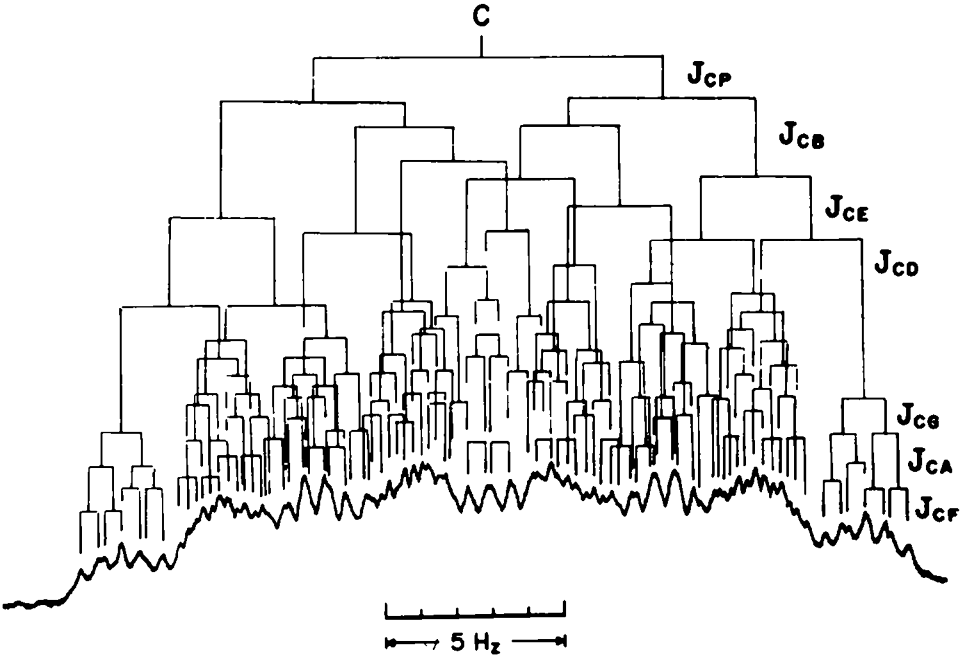


FIG. 9 Expanded spectrum of proton C, $CDCl_3$

DISCUSSIONS

Vicinal proton-proton coupling constants and the molecular conformation oj I. As described above, I can be assumed to exist as two alternative conformations (Ia and Ib) but they cannot be differentiated by the vicinal coupling constants (see the preceding paragraph). But, as was shown above, ^4J shows Ia to be the preferred conformation. This may be further supported by the values of vicinal phosphorus-proton coupling constants (see below). In Table 3, the dihedral angles and vicinal coupling constants are given.[4] These values fit the Ia conformation.

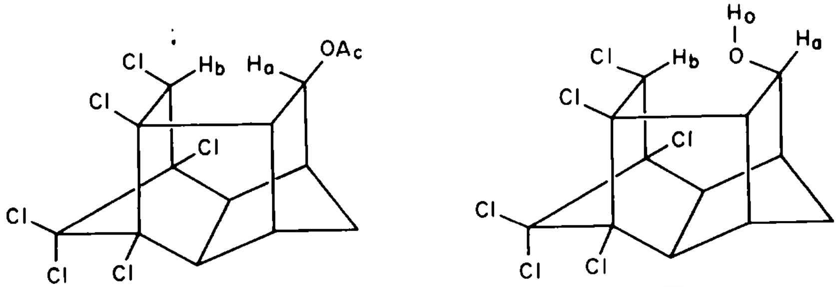
TABLE 3. VICINAL PROTON-PROTON COUPLING CONSTANTS (J_{vic}; Hz) AND DIHEDRAL ANGLES (ϕ°)[a]

J_{vic}		ϕ	J_{vic}		ϕ
J_{AC}	0·67	86	J_{EF}	13·0	179
J_{BC}	5·2	35	J_{EG}	6·4	60
J_{EC}	3·1	70	J_{DF}	4·0	57
J_{DC}	2·8	52	J_{DG}	1·0	62

[a] Estimated by the photographs of a dreinding model

Long-range proton-proton coupling constants through for σ bonds (^4J). It is known that ^4J shows a max value when two interacting nuclei are oriented as a co-planer zigzag form, i.e. "W" orientation.[5] I has two "W" or quasi "W" letter coupling constants, J_{GC} = 1·1 Hz and J_{BE} = 1·7 Hz, which are normal values.[5] Recently, several examples of non "W" coupling have been reported.[6-8] Two non "W" couplings, J_{AF} = 0·42 and J_{CF} = 0·47 Hz, have values similar to those reported by Hall *et al.*[8] for carbohydrates.

Coupling through five σ bonds (^5J). Several examples have been observed for long-range coupling constants through five σ bonds.[9-11] Most observations reported are confined to the systems having the hetero atoms[9] or cyclopropane ring [10] in their two or more equivalent coupling paths[9,10] which may enhance the coupling constants.[12] Only one instance has been reported to have ^5J (and ^6J) free from the above criteria, which is Winstein's half-cage molecules illustrated in Fig. 10. In these compounds the



II
J_{ab} < 1.0 Hz

III
J_{ab} = 0.24 Hz
J_{bo} = 1.1 Hz

FIG. 10 "*Through-space*" coupling in Winstein's half-cage compounds protons or OH oxygen of the inner side of cage (for example Ha, b of II) are highly compressed to each other, for the internuclear distance may be 1 Å or less. These situations appear as the anormalous high frequency shift of νC—H (inner proton),[13] down field shift of the compressed proton[14] and the mutual relaxation process (NOE).[15] So, it seems quite acceptable that the ^5J and ^6J are "*through-space*" coupling[16] instead of the conventional "*through-bond*". Particular attention must be directed to the molecules having a highly strained nature with $J_{H_{ab}}$ larger in III than in II. The latter feature may indicate that the internuclear distance is not necessarily a principal requirement for the "*through-space*" interaction between protons, instead, the existence of an O atom may be important.[14] Our observation of J_{AF} (0·22 Hz) may give further support to this result. In Ia conformation the distance between A and F is ca. 2·1 Å as estimated by a Dreiding model, which is much larger than that of II. Further, I may be almost strain-free. As the "*through-bond*" mechanism for J_{AF} seems less probable also in case of I, "*through-space*" mechanism has been assumed. An examination of a Dreiding model of Ia may show the lone pairs of three O Atoms and the phosphorus orbital possibly includes its 3d orbital, and form a convenient path for the interaction (Fig. 11). The necessity of the P atom in this coupling path has been supposed by the lack of J_{AF} in the PMR spectra of the corresponding orthoesters, i.e. 2,7,8-trioxabicyclo[3.2.1]octane and its 1-methyl derivative.[17]

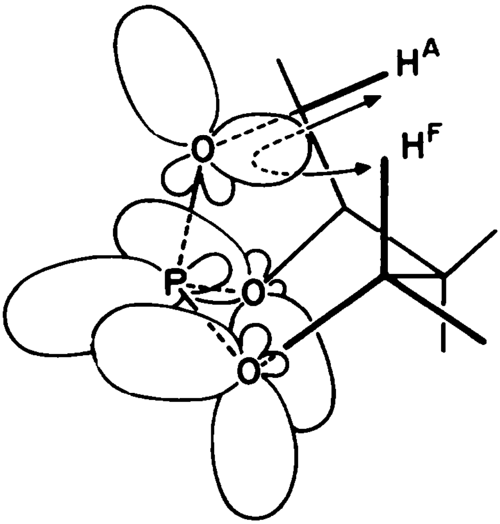


FIG. 11 Possible rout for the "*through-space*" interaction. 3d orbitals in phosphorus are not illustrated and the size of lone pairs are minimized

Phosphorus-proton coupling constants. As was previously reported [18-20] J_{POCH} shows a marked dihedral angle dependence, but no attempt has been made to get a Karplus relation-like curve[21] for J_{POCH}. In order to estimate all the dihedral angles of the P—O—C—H system, a half-chair conformation is assumed for the 5-membered ring of I on the basis of a Dreiding model examination (Fig. 12). In Table 4 the dihedral angles and J_{POCH} are listed, which gives a similar curve to the Karplus' one (Fig. 13). J_{POCCH} shows also a marked angular dependence, which has been already observed for several compounds,[19,20] similar to that of J_{POCH}.

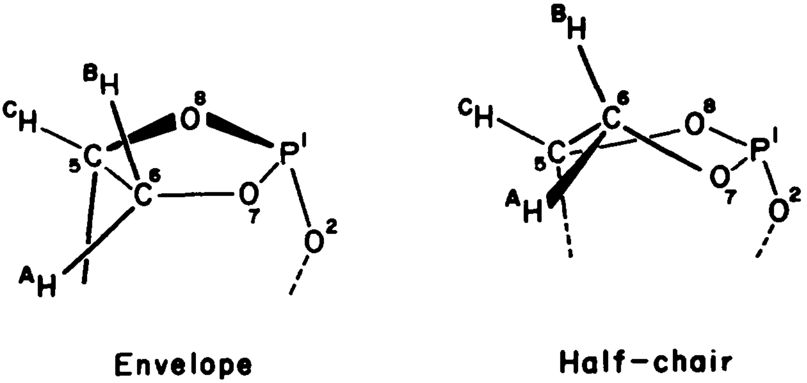


FIG. 12 Two alternative conformations of the five-membered ring in I

TABLE 4. DIHEDRAL ANGLE (ϕ)[a] VERSUS J_{POCH}

	J_{POCH} (Hz)	$\phi°$
J_{AP}	4·4	128
J_{BP}	1·7	113
J_{CP}	9·6	163
J_{GP}	9·3	180
J_{FP}	2·5	60

[a] Estimated by photographs of a dreiding model.

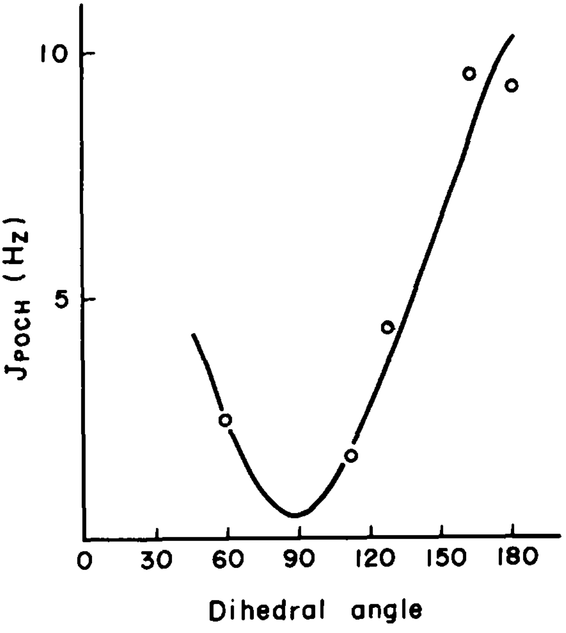


FIG. 13 Dihedral angular dependency of J_{POCH}

EXPERIMENTAL

NMR measurements. All spectra were run by a Varian HA-100 at 100 MHz by a field/frequency stabilized mode. For an integration of spectra was used a field sweep mode and the other spectra were recorded by a frequency sweep. Double and triple resonance experiments were done by two Hewlet-Puckard 200- ABR audio oscillators. Chemical shifts were calibrated by a digital frequency counter. The expanded spectra were recorded at a sweep-width of 50 Hz and a sweep time of 2500 sec. All coupling constants are obtained directly from the calibrated chart.

I was subjected for NMR measurements as the degassed soln (ca. 20% v/v).

2,7,8-*Trioxa*-1-*phosphabicyclo*[3.2.1]*octane* (I). Two drops of Et_3N was added to a mixture of freshly distilled 1,2,4-butantriol (53 g, 0·5 mol), b.p.$_{2\cdot0}$ 146–148°, and trimethylphosphite (62 g, 0·5 mol). The resulting inhomogenious mixture was heated slowly on an oil bath with continuous stirring. As the temp rose, the reaction mixture became homogeneous and MeOH began to distil off. In order to keep the rate of distillation of MeOH minimum, the temp of the oil bath was lowered below 90°. After 6 hr, when the rate of the distillation was extremely slow, the temp of the oil bath was gradually raised to 94°; 31·6 g of MeOH (63% of the theoretical) was recovered. After the low boiling material had distilled over under a reduced press, the residual oily product was fractionated. The fraction collected at 62–63°/1·0 was identified as I with a little unremoved TMP. Further two distillations however, did not completely remove TMP. The final product was pure enough for spectral measurements; b.p.$_{0\cdot8}$ 47–49°, n_D^{23} 1·4771. I has a characteristic phosphite odour and is a colourless oil at room temp which crystallizes into needles on cooling. It is fairly stable at a low temp but quite sensitive to moisture; MS; 134 (M^+, $C_4H_7O_3P$), 104, 77, 57, 41; IR (ν_{max} film); 2966, 2894, 1098m, 1072s, 1041vs. (Found, C, 35·92; H, 5·46. Calc. for $C_4H_7O_3P$: C, 35·83; H, 5·42%).

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