

NMR AND STEREOCHEMICAL STUDIES OF NON AROMATIC HETEROCYCLIC COMPOUNDS—II^a

¹³C AND ³¹P NMR OF 2-METHOXY-1,3,2-DIOXAPHOSPHORINANES

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(Received UK 10 February 1973; Accepted for publication 11 May 1973)

Abstract—¹³C and ³¹P chemical shift data for eight 2-methoxy-1,3,2-dioxaphosphorinanes are reported. Examination of pairs of geometrical isomers, which differ only in the orientation of the OMe substituent on P^{III}, have shown that both the ³¹P and the ¹³C signals of C_{4,6} atoms appear 3–4 ppm at higher field when the OMe is axial compared with the equatorial isomer. This observation can be associated with the 1–3 syn diaxial interaction between the phosphorus axial substituent and the axial hydrogens on C_{4,6} and should thus constitute, in the future, a supplementary tool for the structural analysis of this kind of compound. Important long range δ effects were observed both on ¹³C and especially on ³¹P chemical shifts. It is suggested that the high field δ_e effects could reflect a direct stereoelectronic interaction between the P atom and the cyclic C-5 atom. This interpretation is supported by a study of the ³¹P...¹³C coupling constants and their stereochemical dependence.

As part of our stereochemical studies on phosphorus containing derivatives by NMR spectroscopy,^{1–3} we have investigated the ³¹P and ¹³C NMR spectra of a series of closely related compounds: the 1,3,2-dioxaphosphorinanes.

Since the early observation of Katz *et al.*,⁴ some examples can be found showing differences of ³¹P^{III} chemical shifts for stereoisomers.⁵ Nevertheless, the origin of these differences (generally of the order of a few ppm) has not yet been elucidated. It must be noted that the semi-empirical or theoretical approaches proposed^{6,7b} to solve the ³¹P chemical shift problem are inadequate to describe the small differences between chemical shift values. The Van Wazer approach, which attempts to correlate a 10 ppm chemical shift of ³¹P in phosphites with an angular variation of 0.25°⁸ seems, in itself, inappropriate to treat the problem of small chemical shift differences between stereoisomers. When a physical parameter is so sensitive to slight geometrical variations, it seems evident, *a priori*, that no simple rules like additive substituents effects or systematic differences between axial and equatorial phosphites should be observed. However, we have observed such simple rules and there are other

examples in the literature.⁹ Moreover, before using the relation proposed by Van Wazer,† $\Delta\delta = K\Delta\Theta$, to “calculate” $\Delta\Theta$ values of the order of 0.2°, it is necessary to ask: “What is the physical meaning of an angular difference of 0.2° between two compounds?” NMR does but reflect averaged geometries and, in particular, an angular value obtained via the measurement of J or δ is always an average value on all the populated vibrational states. Even in the lowest state, the vibrational zero point energy (or the Heisenberg principle) introduces a probability function for the angular value and thus leads to an uncertainty in Θ . It is possible to give an image of this uncertainty using a semi-classical approach. For a harmonic motion, we can easily calculate the abscissa of the intersection points of the parabola $E = k/2(\Theta - \Theta_0)^2$ with the horizontal line having $1/2 h\nu$ as ordinate. We can take the two abscissa of the intersection points as a semi-classical measurement of the uncertainty in Θ . Thus, in the case of the O-P-O angle, Θ varies between $\Theta_0 + 3.9^\circ$ and $\Theta_0 - 3.9^\circ$. Obviously, these limits can differ from one compound to another, as can Θ_0 . Having in hand an estimation, even a crude one,‡ of the uncertainty in Θ (Θ being $\Theta_0 \pm \Theta'$), the physical significance of a so-called $\Delta\Theta$ of 0.2° does not appear to be very clear. We must agree that only a $\Delta\Theta_0$ has a physical significance but, to obtain a true $\Delta\Theta_0$ it is not only necessary that the relation between δ and Θ be strictly linear (which seems the case in the Van Wazer theory) but also that the vibrational motion be harmonic. This is certainly not the case for the low frequency O-P-O bending mode ($\sim 290 \text{ cm}^{-1}$).¹¹

^aPart I: see Ref 2

^bChargé de Recherches du Fonds National de la Recherche Scientifique Belge

†For some remarks concerning this relation see also ref. 9b.

‡In the case of H-C-H, Gutowski has shown that the “classical” limits are in very good agreement with the quantum mechanic value.¹⁰

For all the reasons previously expressed, we have preferred to use an empirical approach in the treatment of our experimental results concerning phosphorus chemical shifts. The empirical approach used in this work is similar to the method applied in ^{13}C spectroscopy by many authors to rationalise, if not always to explain, experimental results and, especially small chemical shift differences between stereoisomers. We must also say that, historically, the problem of ^{31}P chemical shifts was first approached in terms of additive group contributions,¹² this concept being favorably and unfavorably criticized.^{9a}

It seems possible to describe the phosphorus electronic structure in phosphites using only 3s and 3p electrons. For carbon, 2s and 2p electrons are needed. We shall try to see if some similarities exist between the NMR behaviour of these two nuclei. Such comparisons between ^{13}C and ^{11}B ,^{13a} ^{13}C and ^{15}N ^{13b} and even ^{13}C and ^{31}P ^{13c} NMR spectroscopies have been proposed in the literature but, in this last case, the author concludes that "the major factor affecting ^{31}P and probably ^{13}C chemical shifts appears to be the bond angle changes at the nucleus in question".

EXPERIMENTAL

NMR experiments. All ^{13}C and ^{31}P NMR Spectra were obtained using a Bruker-Spectrospin HFX90 Spectrometer operating near 22.63 MHz for ^{13}C and near 36.43 MHz for ^{31}P . The field frequency stabilisation was achieved using the proton signal (90 MHz) of tetramethylsilane as lock for the ^{31}P NMR experiments and the fluorine signal (84.69 MHz) of hexafluorobenzene (contained in a capillary tube) as lock for the ^{13}C NMR experiments.

Proton spectra were obtained using a Varian A60 Spectrometer.

The ^{13}C spectra were obtained under broad band decoupling conditions of the proton spectra and were accumulated in a T.M.C. 1000 time averaging computer. The samples contained in 10 mm o.d. tubes, were approximately 2 M/l chloroform solutions. Chloroform is used as the internal chemical shifts standard.

Neat liquids were used for the ^{31}P spectra.* The capillary tube containing the external reference (H_3PO_4 85%) was centered in the 5 mm o.d. sample tube. The values of ^{31}P chemical shifts were not corrected for differences of volume diamagnetic susceptibilities (χ_v) between the sample and the reference. For triethylphosphite for instance, for which $\chi_v = -0.611 \times 10^{-6}$,¹⁴ $\chi_v(\text{H}_3\text{PO}_4)$ being -0.447×10^{-6} ,^{7c} this correction is of the order of 0.5 ppm. The correction on the observed chemical shift difference between any pair of the phosphites studied should be even smaller and thus, there is no doubt that differences greater than 0.5 ppm are certainly significant.

*The neat liquid spectrum of derivative 2 and the spectrum for an approximately 50% solution in CCl_4 give the same ^{31}P chemical shift.

‡The attribution given by White *et al*^{5d} to the ^{31}P signals of the isomeric phosphites 4A and 4B is the reverse of that given in this paper.

Synthesis of the 2-methoxy-1,3,2-dioxaphosphorinanes. The phosphites 1, 2A, 3, 4A and 5A were obtained, via the corresponding chlorophosphites, following the method described.¹⁵

The thermodynamically less stable isomers of an A/B pair were prepared by Aksnes' procedure.¹⁶ When special care is taken,¹⁷ this method gives pure 4B and 5B (B > 95% via NMR) and a 80/20 mixture of 2B to 2A (integration of the Me proton signals).

All the compounds studied are liquids at ordinary temp. They were purified by fractional distillation under reduced pressure and their purity was established on the basis of their proton NMR spectra. The respective b.ps are as follow: 1: 60–61°/30 mm; 2A/B: 59–60°/60 mm; 3: 69°/15 mm; 4A/B: 75–76°/20 mm; 5A/B: 67–69°/0.25 mm.

Preparation of the starting 1,3-diols. Propanediol and 2,2-dimethylpropanediol are commercial products. 2-methyl-1,3-propanediol was obtained by reduction of diethyl-methylmalonate by LAH.

Meso and racemic forms of 2,4-pentanediol were separated from the commercial mixture through fractional distillation of the corresponding cyclic sulphites followed by hydrolysis of the isolated *meso* and *d,l*-sulphite isomers.¹⁸ *trans*-2-Hydroxymethylcyclohexanol was synthesised by the Prins reaction on cyclohexene.^{19,20}

RESULTS

^{31}P chemical shifts and ^{13}C chemical shifts of the 1,3,2-dioxaphosphorinane ring C atoms and of the Me and OMe C atoms are given in Table 1 together with literature values when available.‡

The ^{13}C signals of the four remaining carbocyclic C atoms, in compounds 5A/B, are given below with the respective ^{31}P ... ^{13}C coupling constants in parenthesis.

5A: 44.7 ppm (3.2 Hz); 50.4 ppm (2.4 Hz); 52.6 ppm; 52.7 ppm

5B: 43.8 ppm (2.3 Hz); 49.7 ppm (1.5 Hz); 52.7 ppm; 52.9 ppm

On the basis of chemical shift and coupling constant values, the signal at lowest field can tentatively be attributed to C_7 and the next one to C_{10} (see Scheme in Table 2).

The signals in the proton decoupled ^{13}C spectra were assigned on the basis of relative intensities measurements and off-resonance partial-proton decoupling experiments.

The 5-Me signals in the spectrum of compound 3 were assigned by selective ^{13}C - $\{^1\text{H}\}$ decoupling.²¹

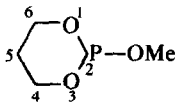
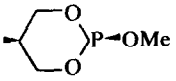
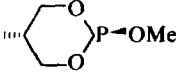
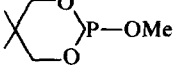
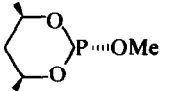
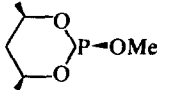
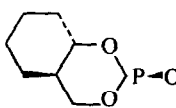
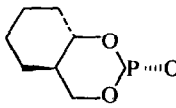
DISCUSSION

For all the compounds studied, except 2, it was shown by proton NMR Spectroscopy that the 1,3,2-dioxaphosphorinane cycle has a chair conformation.^{1,2,21–23}

Moreover, there seems to be no doubt that the preferred orientation of the OMe substituent on phosphorus is axial.^{2,16,24}

The PMR spectra of stereoisomers 4A/B or 5A/B

Table 1. $^{13}\text{C}^a$ and $^{31}\text{P}^b$ chemical shifts in 2-methoxy-1,3,2-dioxaphosphorinanes

Derivative	$^{13}\text{C}_{\text{H}_3\text{O}}$	$^{13}\text{C}_{4,6}$	$^{13}\text{C}_5$	$^{13}\text{C}_{\text{H}_3}^{4,6}$	$^{13}\text{C}_{\text{H}_3}^3$	^{31}P
1 	27.7	18.3	48.8			-130.1 -131 (5d)
2A 	27.8	12.7	45.4		64.1 (eq.)	-123.5
2B 	c	13.2	46.0		62.3 (ax)	-129.8
3 	27.7	8.7	44.8		54.7 (eq.) 55.0 (ax.)	-122.6 -122.7 ²¹ -123 ^{5d}
4A 	27.8	11.5	34.5	54.7 (eq.)		-127.2 -133 ^{5d}
4B 	29.0	7.5	36.4	53.9 (eq.)		-131.5 -129 ^{5d}
5A 	27.8	13.4 (C ₄) 4.1 (C ₆)	34.2			-129.3
5B 	28.5	10.2 (C ₄) 1.2 (C ₆)	36.3			-132.0

^aIn ppm at high field relative to the ^{13}C signal of the solvent CHCl_3 . For the purpose of comparison, these values can be converted to the CS_2 scale using the following relation:

$$\delta_{\text{C}}\text{CS}_2 = \delta_{\text{C}}\text{CHCl}_3 + 115.3.$$

^bIn ppm at low field relative to the ^{31}P signal of external H_3PO_4 —85%

^cThe ^{13}C spectra of stereoisomers **2A,B** were obtained for an equilibrium mixture (**2A/2B** = 80/20) and the ^{13}C signal of the methoxy group **2B** could not be observed.

show that at the thermodynamical equilibrium, there is less than 5% of the less stable isomer (i.e. **B**: OMe equatorial²). These stereoisomers differing essentially in the orientation of the OMe group on P,² the conformational free energy difference between axial and equatorial P-OMe groups, in 1,3,2-dioxaphosphorinanes, is thus greater than 1.75 kcal/mole. A value of about 2 kcal/mole has been given previously.¹⁷

Equilibration of mixtures of **2A** and **2B** by traces of BF_3 in tetrachloride solution, followed by integration of the well separated Me protons NMR

signals, has shown that the free energy difference between the two isomers is about 0.9 kcal/mole at 32°. This value is very similar to the conformational free energy of a Me group in position 5 in 1,3-dioxanes ($\Delta G_{25}^\circ = 0.8$ kcal/mole)²⁵ and in 1,3,2-dioxanthianes-2-oxide ($\Delta G_{40}^\circ = 0.7$ kcal/mole).²⁶ These results seem to indicate that **2A** and **2B** differ mainly in the configuration at C₅ and that **2B** exists predominantly in a chair conformation with axial Me group in position 5 and axial OMe group on phosphorus.

Moreover, the proton chemical shifts of the Me

groups in compounds **2A**, **2B** and **3** are in agreement with a predominant diaxial conformation for **2B** as shown below:

3²¹: Axial Me at C₅ δ¹H = 1.25 ppm; equatorial Me at C₅ δ¹H = 0.70 ppm; **2A**: equatorial Me at C₅ δ¹H = 0.71 ppm; **2B**: Me at C₅ δ¹H = 1.31 ppm.

The derivatives **1** to **5** are adequate to study the relations between stereochemistry and ¹³C and ³¹P chemical shift parameters.

Effect of configuration at P^{III} on ¹³C and ³¹P chemical shifts. Comparison of ¹³C and ³¹P chemical shifts between **4A** and **4B** or **5A** and **5B** gives the effects associated with axial or equatorial orientation of the OMe substituent on P. These effects are summarized in Table 2.

First, we can observe that an axial OMe has a high field effect from 3 to 4 ppm, on the C_{4,6} ¹³C signals. This effect is analogous to the well known sterically induced diamagnetic γ effect,* which was observed in cyclohexane systems for Me²⁷ or OH²⁸

*Throughout this paper, we are using the terms "α, β, γ, δ effect" as defined in the paper of Dalling and Grant²⁷

†See also Ref 5e and 5h for similar observations in 2-R-5-t-butyl-1,3,2-dioxaphosphorinanes. However, in these cases, a conformational equilibrium for one of the two isomers is present^{5e} or cannot be excluded.^{5h} This situation makes the conclusions somewhat ambiguous especially concerning the ³¹P chemical shifts owing to the important δ effects discussed in the following section.

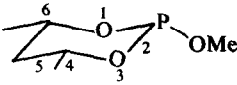
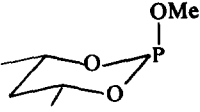
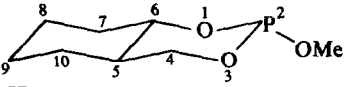
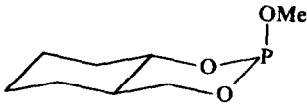
substituents and in norbornyl derivatives²⁹ for a fluoro substituent. To our knowledge, these are the first examples where such an effect can be unequivocally attributed to an axial substituent on trivalent phosphorus.†

If we admit, as a crude approximation, that the magnitude of the γ_a effect could be used as a semi-quantitative measure of the degree of steric interaction in a given molecule,^{29,30} the observation of a diamagnetic γ_a effect in the derivatives studied here is particularly interesting in relation to the preferred axiality of the OMe substituent on P.

Moreover, the ³¹P signal for the axially substituted P atom appears at higher field than for the equatorially substituted isomer, the ³¹P chemical shift difference between the A/B pair being of the same order as the corresponding γ_a effect (Table 2) observed in ¹³C NMR. The sequence δ³¹P(R_{eq}) > δ³¹P(R_{ax}) was also found for *cis* and *trans* 1-methyl-4-t-butyl-4-phosphorinanes^{5b} and seems thus to be quite general.†

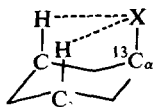
This situation is similar to that of the high field shift of the ¹³C signal of an axially substituted C atom in cyclohexane derivatives as compared with the corresponding signal in the equatorially substituted derivatives.^{27,28,31} The difference between the axial and equatorial α shifts on ¹³C chemical shifts can be ascribed to the steric effect of the γ carbons and their hydrogens on the 1-carbon, operating backwards through the axial substituent.²⁸

Table 2. Variation* (ppm) of ¹³C and ³¹P chemical shifts with OMe group orientation

Derivative	¹³ CH ₃ -O	¹³ C ₄	¹³ C ₆	¹³ C ₅	¹³ CH ₃	³¹ P
 4B	-1.2	+4.0	+4.0	-1.9	+0.8	+4.3
 4A						
 5B	-0.7	+3.2	+2.9	-2.1	+0.9	+2.7
 5A					<u>C₇[†]</u>	

*A + sign indicates a high field effect tentative attribution (see text)

This effect could be called the reciprocal of the γ_a effect.



Similarly, the high field shift of the ^{31}P signal in derivatives **4A** and **5A**, relative to the signal in the corresponding **B** isomer, could be attributed to the reciprocal of the γ_a effect associated with the axial methoxy substituent in compounds **4A** and **5A**.

As we said in the introduction, this parallelism between ^{31}P and ^{13}C NMR spectroscopy, which appears also for other substituent effects^{3,9,13c} is not unexpected on a theoretical basis. When we consider a factorization of the screening constant following Saika and Slichter,³² it is essentially the variation of the paramagnetic contribution to the screening constant which is responsible for the scale of chemical shifts for both ^{31}P ^{7a} and ^{13}C .³³ If we assume that the occupation of the d atomic orbitals on phosphorus is negligible in tricoordinated derivatives,^{7b} the expression of $\sigma_{\text{para}}^{\text{AA}}$ for ^{31}P takes a similar form as in the case of ^{13}C nucleus.

The δ effect in ^{13}C and ^{31}P NMR spectroscopy. Comparison of ^{31}P chemical shifts between **1** and **2A** shows that the addition of an equatorial Me group in position 5 has a high field effect of +6.6 ppm on the ^{31}P signal (δ_e effect).^{*} On the other hand, the effect of an axial Me at C_5 is negligible as is indicated by the +0.3 ppm difference between **1** and **2B** (δ_a effect).

Long range magnetic effects are generally considered unimportant in ^{31}P chemical shift studies.^{7a,b} The large value of the δ_e effect is thus particularly surprising.[‡]

Considering the high stereospecificity of the $\delta(\text{CH}_3)$ effect on ^{31}P chemical shift ($\delta(\text{CH}_3)_e \gg \delta(\text{CH}_3)_a$), we must conclude that the special spatial configuration between the equatorial Me at C_5 and the P atom plays an important role in the mechanism of the shift change.

In this context, it is important to note that the long range $^4J_{^{31}\text{P}, ^{13}\text{C}}$ coupling constant, in 1,3,2-dioxaphosphorinane compounds, is also found to be stereospecific, as was recently observed for analogous P^{IV} derivatives.³⁵ The ^{13}C nuclei of the

equatorial Me groups in **2A** and **3** are coupled to the P atom as indicated below:

$$\begin{aligned} {}^4J_{^{31}\text{P}, ^{13}\text{CH}_3 \text{ eq}} \quad \mathbf{2A} &= |1.5| \text{ Hz} \quad (\text{absolute value}) \\ {}^4J_{^{31}\text{P}, ^{13}\text{CH}_3 \text{ eq}} \quad \mathbf{3} &= |1.2| \text{ Hz} \quad (\text{absolute value}) \end{aligned}$$

On the contrary, the $^{31}\text{P} \dots ^{13}\text{C}$ coupling constant for the axial Me group in **3** is unobserved in the ^{13}C spectra.

The high field $\delta(\text{CH}_3)_e$ chemical shift effect and the stereospecificity of the $^4J_{^{31}\text{P}, ^{13}\text{CH}_3}$ coupling constant could well have a common origin.

It is known that there may be a contribution to the coupling constant which results from direct interaction between the bonds associated with the coupled nuclei (direct contribution).³⁶ This seems to be the case for long range H...H coupling constants when the interacting nuclei are in a W arrangement.³⁷

Increasing overlap between the back lobes of the P and C_5 bonding orbitals, when the Me on C_5 is equatorial, could thus be expected to increase $^4J_{^{31}\text{P}, ^{13}\text{CH}_3}$ and, at the same time, it should be an especially attractive explanation of the high field δ_e chemical shift effect on the ^{31}P nucleus.[†] A similar argument has already been invoked to explain the unusually large diamagnetic γ_e effect on ^{13}C chemical shift in norbornyl systems.²⁹

As is shown by the difference in ^{31}P chemical shift between **1** and **3**, gem dimethyl substitution at C_5 is accompanied by a +7.5 ppm upfield shift of the ^{31}P NMR signal. This upfield gem substituent effect was also observed by White *et al.*^{5d} in similar compounds and attributed to a narrowing of the O-P-O angle in response to the decrease in C-C-C angle on alkyl substitution of hydrogens on C-5. The results presented here seem to indicate that this is not the correct explanation since the equatorial Me group of a gem dimethyl could be responsible for nearly the whole observed effect.[‡]

On the other hand, the variation of both the ^{13}C chemical shift of carbon-5 and the $^3J_{^{31}\text{P}-\text{O}-\text{C}-^{13}\text{C}_5}$ coupling constant with OMe substituent orientation seems also to indicate a direct interaction between the P atom and the C-5-atom.

In Table 2, we see that the ^{13}C signal of C_5 appears 2 ppm at higher field in the phosphorus equatorially substituted derivatives **4B** and **5B** compared to **4A** or **5A**.

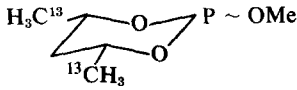
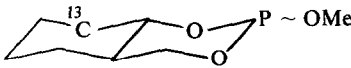
In cyclohexane²⁷ or dioxane^{30,38} derivatives the chemical shift variations associated with Me substituents δ to the observed C atom are generally smaller than 1 ppm. The same is true for the difference between the δ_e and δ_a effects. This situation appears quite normal since in ^{13}C NMR, the long range magnetic effects are also considered negligible.³³ The ^{13}C OMe substituent parameters in these two series of derivatives are not known but a chemical shift difference of 0.9 ppm is found for the C-4 atom of *cis*- and *trans*-4-t-butylcyclohexanols.²⁸

*The corresponding effects for the equatorial substituents 5-Et, 5-*i*Pr and 5-*t*-But are respectively of +5.0 ppm, +5.3 ppm and +5.5 ppm. Similarly in the analogous 2-chloro-5-R-1,3,2-dioxaphosphorinane derivatives, we have observed high field δ_e effects of +7.0 ppm (R = Me), +5.2 ppm (R = Et), +5.5 ppm (R = *i*Pr) and +5.5 ppm (R = *t*-But).³⁴

†To gain further information on the origin of the large diamagnetic δ_e effect on ^{31}P chemical shift, 5-X-1,3,2-dioxaphosphorinanes, where X is an electron withdrawing group, are presently under investigation.

‡See note added in proof.

Table 3

Derivative	Isomer	$^3J_{31P-O-C-^{13}C}$ *	POMe
	4A	3.2 Hz (4.2 Hz)	axial
	4B	1.6 Hz (13.5 Hz)	equatorial
	5A	3.2 Hz (4.7 Hz)	axial
	5B	2.3 Hz (14.0 Hz)	equatorial

*The corresponding value of $^3J_{31P-^{13}C}$ between P and C-5 is given in parenthesis.

It seems thus that in ^{13}C NMR also, the δ effects are more pronounced in 1,3,2-dioxaphosphorinane compounds than in the dioxane or cyclohexane series.* Moreover, we observe that the $^3J_{31P-O-C-^{13}C_5}$ coupling constant, which is 4.2–4.7 Hz for an axial P-OMe substituent (**4A** and **5A**), increases to 13.5–14.0 Hz when this substituent becomes equatorial (**4B** and **5B**). Such a large variation of $^3J_{31P-^{13}C}$ with P-OMe orientation is not observed for the labeled C atoms indicated in Table 3. It is interesting to note that the effect of OMe substituent orientation on the chemical shifts of these same C atoms, which is also a δ effect, is similarly smaller (Table 2).

The high field $\delta(P-OMe)_e$ effect on C-5 ^{13}C chemical shift and the increase of $^3J_{31P-O-C-^{13}C_5}$ in the equatorially substituted derivatives **4B** and **5B** compared to **4A** and **5A** could reflect a more pronounced interaction of the orbitals on C₅ and P in **4B** and **5B**.^{4*}

Ring substituent effects on ^{13}C resonances. The effect of Me groups on the appropriate ^{13}C resonances can be used to confirm some of the assignments made.^{27,30,38} In this context, it is worth noting that the low field effect due to Me substitution on C₅ is of the same order for an equatorial Me ($\alpha_e = -3.4$ ppm in **2A**) and for an axial Me group ($\alpha_a = -2.8$ ppm in **2B**) in contrast to what is observed in cyclohexane derivatives.²⁷ In 1,3-dioxane derivatives, the α_e and α_a Me substituent parameters on C-5 ^{13}C chemical shift are also found

equal.^{†30,38} This was attributed to a reduction of the steric compression by the 1,3 ring oxygens on an axial C₅ Me as compared with the syn 1,3-axial hydrogens in cyclohexane.³⁸ The same explanation should hold in the case of 1,3,2-dioxaphosphorinane derivatives.

Similarly, in the two series of heterocyclic compounds, the lack of a steric effect at C₅ can explain why the ^{13}C signal of an axial Me on C₅ appears at lower field than the corresponding equatorial Me signal.³⁸ Again, this is the reverse of what is observed in methylcyclohexanes.

CONCLUSIONS

It seems to us that the comparison between substitution effects in ^{31}P NMR spectroscopy on the one hand, and in ^{13}C NMR spectroscopy on the other hand, appears as a powerful approach to the ^{31}P chemical shift problem in relation with stereochemistry. The number of substituent effects (α , β , γ , . . . effects) studied in ^{13}C NMR is important and additivity rules appear useful in various systems, especially from the stereochemical point of view. Similarities or differences observed in this study between substituent effects in ^{31}P NMR and in ^{13}C NMR can be rationalised using simple concepts. Similarities can be considered as normal if we admit that like the C atom, the P atom in phosphites forms bonds using essentially s and p orbitals. Differences of behaviour could also be considered as normal if we take into account the spatial extension of 3s and 3p orbitals relative to 2s and 2p orbitals. Study of the so-called δ effect in ^{31}P NMR is in progress in our laboratory.

*The C₄ signal in the series lithium piperidine, piperidine, N-methylpiperidine and N,N-dimethylpiperidinium iodide appears over a range of 6.8 ppm.³⁹ The shift from the piperidine to N-methylpiperidine being of 1.8 ppm to higher fields (1.3 ppm in Ref. (40)). These anomalous variations were attributed to intramolecular field effects associated with the N–X polar bonds.³⁹ Although such an explanation cannot be rejected in the case studied here, it is actually impossible to check this hypothesis owing to the lack of the appropriate geometrical and partial electric moments parameters.

†That the two effects are not exactly the same in the 1,3,2-dioxaphosphorinane derivatives could be due to the presence of the diequatorial conformation in **2B** (see text).

Acknowledgments—The authors are indebted to Professor K. Mislow for his helpful comments and to Professor G. Chirudoglu for his interest. We are grateful to Mr. O. Fabre for his technical assistance. We thank the F.R.F.C. (Fonds de la Recherche Fondamentale Collective) for his financial support.

Note added in proof: This work being achieved, Hutchins *et al.* reported $\delta(\text{CH}_3)_e$ effects of +6.7 and +6.1 ppm on the ^{31}P signal in 2-ethyl- and 2-phenyl-5-methyl-1,3,2-diazaphosphorinanes (*J. Am. chem. Soc.* **94**, 9151 (1972)).

The same authors also discuss briefly the δ gem-dimethyl effect on P chemical shifts (see text) and conclude that "the overall picture is more complex than it would seem from the suggested explanation". This comment is in agreement with our conclusions. They present some preliminary results on spirocompounds in the 1,3,2-dioxaphosphorinane series, the second ring, fixed in position 5, being three- and four-membered. We have also measured the P chemical shifts of the corresponding spirocompounds with five and six membered rings in position 5. For spirophosphites, our $\delta^{31}\text{P}$ are -126.6, -124.1, -125.6 ppm, the ring fixed in position 5 being respectively three-, four-, five- and six-membered; for the analogous chlorophosphites, the values are as follows: -150.1, -148.3, -147.9, -149.7 ppm (3).

These results will be discussed in a forthcoming paper together with ^1H and ^{13}C NMR results.

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