

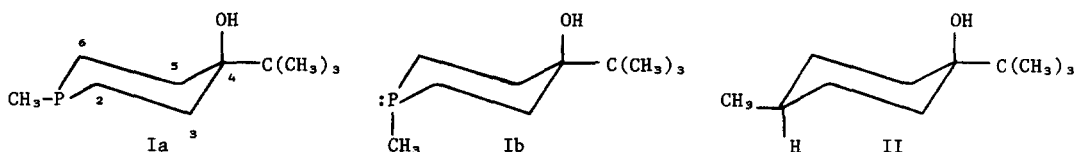
ASSIGNMENT OF STRUCTURE TO ISOMERIC 4-PHOSPHORINANOLS BY  $^{13}\text{C}$  NMR SPECTROSCOPY

Sidney I. Featherman and Louis D. Quin\*  
Paul M. Gross Chemical Laboratory, Duke University  
Durham, N. C. 27706, U.S.A.

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We have found that  $^{13}\text{C}$  nmr spectroscopy is a powerful tool for the determination of the structures of cis, trans isomers in the phosphorinane family. It is more definitive than  $^1\text{H}$  nmr spectroscopy; the carbon signals are well separated and have several unique features pointing to the structure, whereas proton signals are generally bunched together and are difficult to interpret. Furthermore, structural effects on chemical shifts are shown to be interpretable on the same grounds now well established for cyclohexane derivatives.

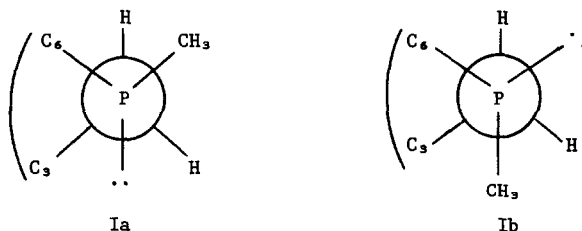
The cis (Ia)<sup>1</sup> and trans (Ib)<sup>2</sup> forms of the conformationally rigid 1-methyl-4-*t*-butyl-4-phosphorinanols, whose structures have been established unequivocally by x-ray analysis, serve as the basis for the assessment of structure-spectra correlations among the phosphorinanols.



Spectral assignments (Table I) were facilitated by the fact that trivalent phosphorus exerts a small shielding effect on  $\alpha$ -carbons; therefore the C-2,6 signal is upfield from C-3,5. This effect is apparent from a comparison with the chemical shifts of the ring carbons in cyclohexanol II. Here the signals for C-2,6 and C-3,5 occur close together (161.3 and 161.7, not yet assigned) and in similar position to C-3,5 of the configurationally related Ia (163.1); the C-2,6 signal of Ia is, however, at 168.9. Other assignments are straightforward.

A comparison of the spectra of Ia and Ib reveals that several features are associated with their configurations: (1) The signal for C-4 is at nearly the same position in the isomers ( $\Delta\delta = 0.2$ ), as would be expected from the configurational identity at this carbon; this is also true for the carbons of the substituent at C-4. In cyclohexanols, carbon bearing axial OH is upfield by about 5 ppm from that with equatorial OH<sup>3</sup>. (2) Steric compression between the axial P-CH<sub>3</sub> in Ib and axial protons at C-3,5 results in substantial upfield shifts for the CH<sub>3</sub> and

C-3,5 signals, an effect well known in cyclohexane derivatives<sup>4</sup> and seen in 1,3,2-dioxaphosphorinanes<sup>5</sup> as well. (3)  $^{31}\text{P}$  coupling with the  $\text{CH}_3$  carbon is stereo-related, being larger for that isomer (Ib) with axial  $\text{PCH}_3$ . A steric effect on  $^1J_{\text{P-C}}$  has been noted both in phospholenes<sup>6</sup> and phosphetanes<sup>7</sup>, and may be associated with hybridization differences. The effect holds also for endocyclic  $\alpha$ -carbons;  $^1J_{\text{PC-2,6}}$  is slightly greater in Ib than in Ia. (4) The magnitude of coupling between  $^{31}\text{P}$  and a  $\beta$ -carbon has been shown to be related to the disposition of this carbon relative to the lone pair on phosphorus. This effect has previously been found useful in assigning cis, trans structure when the  $\beta$ -carbon is located in an exocyclic substituent at the  $\alpha$ -carbon<sup>6,7</sup>. The effect appears to hold also for  $\beta$ -carbons located in a ring; in Ia, the value for  $^{31}\text{P}$  coupling with C-3,5 is 7.5 Hz, while no coupling is observed in Ib. The geometric relation of C-3,5 to the lone pair is apparent from the Newman formulas:



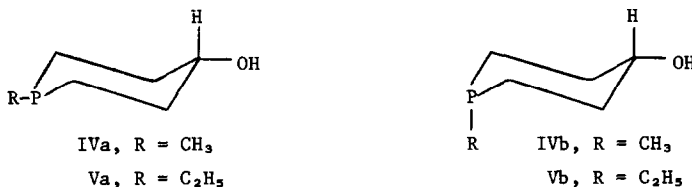
The relation of small dihedral angle with large coupling, and vice-versa, is exactly that seen in cases where the  $\beta$ -carbon was exocyclic<sup>6,7</sup>. (5) An equatorial P-substituent deshields C-2,6 ( $\beta$ -effect) more strongly than does an axial substituent, an effect known also in cyclohexanes<sup>4</sup>.

That these relationships hold for conformationally mobile systems and are useful for structural assignment in other isomer pairs is immediately obvious from an examination of the data for the 1,4-dimethyl-4-phosphorinols (III). The spectrum for a roughly 1:1 mixture of the cis (IIIa) and trans (IIIb) forms could be interpreted easily (Table 1); the only uncertainty, of little consequence, was in the assignment of the C-4 and C- $\text{CH}_3$  signals to particular isomers. The proximity of the C-4 signals, and marked differences of P- $\text{CH}_3$  and C-3,5 signals, clearly show that the configurational difference must occur at P, and support structures IIIa and IIIb as suggested previously for such phosphorinols from other studies<sup>8,9</sup>.

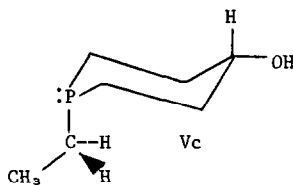


The more upfield position of C-3,5 in I relative to III may be attributed to  $\gamma$ -shielding in the former by the methyls of the t-butyl group.

Isomeric secondary phosphorinanol isomers are also seen to have  $^{13}\text{C}$  spectra possessing similar differences to those for tertiary alcohols. Previous work<sup>8,9</sup> has suggested that the isomeric forms of 1-methyl-4-phosphorinanol (IV) differ in configuration at P, and not at C-4, and this is evident in their  $^{13}\text{C}$  spectra (Table I).



It is also true for the previously unstudied isomeric 1-ethyl-4-phosphorinanol (V), although a somewhat larger difference in  $\delta$  for C-4 (1.1 ppm) may suggest a greater contribution of conformers with axial OH. These isomers exhibit yet another case of stereo-related coupling. The methyl carbon of the equatorial ethyl group in Va is not noticeably coupled to  $^{31}\text{P}$ , but when the ethyl group is axial (Vb) small but definite coupling (2 Hz) is observed. This can be attributed to a conformational effect; in the axial position, rotation is hindered by interactions with the ring, so that a preferred conformation (Vc) can be visualized:

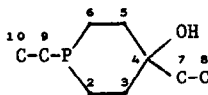


In this conformation, the methyl-lone pair orientation is that already seen to permit maximal coupling.

II was prepared by addition of  $t\text{-C}_4\text{H}_9\text{Li}$  to 4-methylcyclohexanone; it had mp  $36\text{--}38^\circ$ , bp  $73\text{--}76^\circ$  (0.1 mm) and gave the correct analysis. The IIIa-IIIb mixture (1:1), bp  $60\text{--}64^\circ$  (0.25 mm) was prepared from addition of  $\text{CH}_3\text{MgBr}$  to 1-methyl-4-phosphorinane<sup>8</sup>; the methide prepared from the mixture had mp  $255\text{--}257^\circ$  and gave the correct analysis. The Va-Vb mixture (1:1), bp  $66\text{--}68^\circ$  (0.15 mm), came from reduction of 1-ethyl-4-phosphorinane<sup>8</sup> with  $\text{LiAlH}_4$ , and was analyzed as the mixed methiodides, mp  $250^\circ$  dec. Proton noise-decoupled  $^{13}\text{C}$  spectra were obtained at 22.62 MHz with a Bruker HFX-10 Spectrometer using the Fourier transform method. An external heteronuclear lock of  $\text{C}_6\text{F}_6$  in a 3-mm coaxial tube was employed.

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Table I.  $^{13}\text{C}$  NMR Data for 4-Phosphorinanol<sup>a</sup>



	<u>C-2,6</u>	<u>C-3,5</u>	<u>C-4<sup>d</sup></u>	<u>C-9</u>	<u>C-7</u>
Ia <sup>b</sup>	168.9(10)	163.1(7.5)	117.9	178.9(12)	154.0(s)
Ib <sup>c</sup>	174.7(12)	168.7(s)	118.1	188.1(16)	154.0(s)
IIIa	168.8(6)	154.9(4.5)	121.1 <sup>e</sup>	180.5(10)	160.9(s) <sup>e</sup>
IIIb	171.0(10)	157.3(s)	121.5 <sup>e</sup>	184.1(13)	161.3(s) <sup>e</sup>
IVa	168.3(10)	160.2(4)	122.3 <sup>e</sup>	181.2(14)	
IVb	170.8(10)	163.1(s)	122.9 <sup>e</sup>	185.8(14)	
Va <sup>f</sup>	168.0(10)	158.0(4)	120.0 <sup>e</sup>	169.8(11)	
Vb <sup>g</sup>	170.9(12)	160.4(s)	121.1 <sup>e</sup>	175.2(12.5)	

<sup>a</sup>Chemical shifts ( $\pm 0.1$  ppm) are upfield from  $\text{CS}_2$ ; values in parentheses are  $^{31}\text{P}$ - $^{13}\text{C}$  coupling constants ( $\pm 1.2$  Hz). Spectra of I and IV were obtained in  $\text{CH}_2\text{Cl}_2$  solution, all others in  $\text{CH}_3\text{OH}$ . All spectra, except that of Ib, were obtained on mixtures of the isomers. <sup>b</sup>C-8 had  $\delta$  167.1(s). <sup>c</sup>C-8 had  $\delta$  167.6(s). <sup>d</sup>Coupling to  $^{31}\text{P}$  was not clearly observable with the resolution employed except for Va, Vb (both 1.8 Hz). <sup>e</sup>Assignments to particular isomers are uncertain. <sup>f</sup>C-10 had  $\delta$  180.5(s). <sup>g</sup>C-10 had  $\delta$  181.2(2).

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