Stereochemical Consequences of *C*-Methylation of 1-Methylphosphorinane and Its Sulfide and Oxide: A Carbon-13 and Phosphorus-31 Nuclear Magnetic Resonance Study[1]

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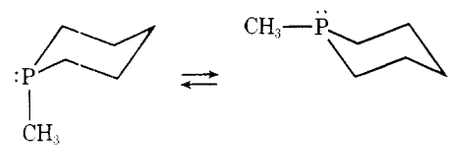
Placing a methyl at the 3 or 4 position of 1-methylphosphorinane results in conformational equilibria for both the cis and trans isomers that are strongly biased toward the form with equatorial *C*-methyl. This remains true when the phosphines are converted to sulfides, oxides, or methiodides. The steric demand of *C*-methyl is therefore considerably greater than that of *P*-methyl, a fact predicted for 1-methylphosphorinane by its $\Delta G°$ value of +0.35 kcal/mol. ^{13}C NMR spectroscopy was especially helpful in qualitatively analyzing the equilibria; the *C*-methyl and its carbon of attachment in a pair of isomers had little chemical shift variability, while *P*-methyl differed by 4–6 ppm, always with the axial methyl relatively upfield. Both the sulfides and the oxides have ring carbons 3 and 5 at higher field (2–3 ppm) when the sulfur or oxygen atoms are axial. This greater γ effect for a single-atom substituent on phosphorus over a methyl group has been observed previously for the case of S, but not for O. While ^{31}P NMR shifts were sensitive to the stereochemistry about phosphorus, no consistency in the direction of the effect was present. For the phosphines, axial methyl caused the expected relatively upfield shift. This was observed also for the sulfides, but the reverse effect prevailed for the oxides.

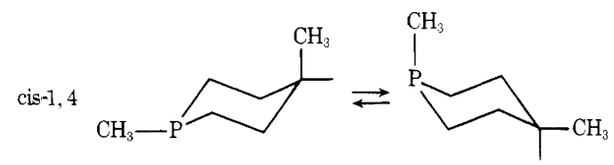
Phosphorus-substituted phosphorinanes are of considerable interest because of the predominance of the conformer with axial substituent over that with equatorial at room temperature.[2] For the 1-methyl derivative, the equilibrium constant (a ⇄ e) is estimated to be about 0.55, which gives $\Delta G°$ = +0.35 kcal/mol at 27 °C. This unusual result stems from a combination of a rather low enthalpy difference for the conformers ($\Delta H°$ = −0.68 kcal/mol) and a significant entropy effect ($\Delta S°$ = −3.4 eu). 1-Methylarsenane was later reported by another group to exhibit similar phenomena.[3] We have continued our investigation of the 1-methylphosphorinane system by considering the consequences of placing methyl at either the 3 or the 4 position, and then of adding sulfur, oxygen, or methyl to phosphorus to increase its covalency in these compounds. The synthesis and spectral properties of all of these compounds are reported in the present paper. Our major probe of the conformational changes occurring in these families has been ^{13}C NMR spectroscopy; we have previously employed this technique for hydroxy[4] and keto[5] derivatives of phosphorinanes and have witnessed a number of useful effects. ^{31}P NMR spectroscopy has also figured in our earlier studies and we have examined our new *C*-methyl compounds by this technique also.

The spectral data we have accumulated are best interpreted on the basis of perturbation of the conformational equilibrium for the parent 1-methylphosphorinane (**1**). Thus, a more

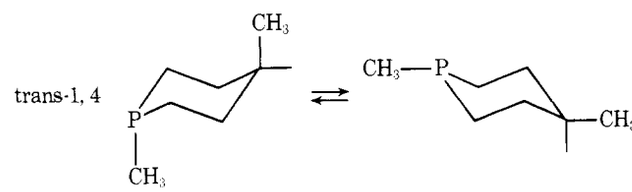


1a **1b**

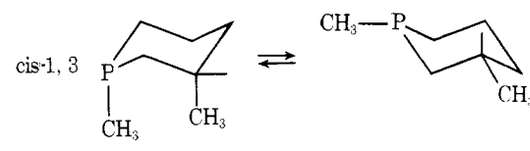
space-demanding group such as CH_3 ($\Delta G°$ = −1.7 kcal/mol in cyclohexanes; for thianes,[6] −1.80 ± 0.10 for 4-CH_3 and 1.40 ± 0.07 for 3-CH_3) placed on ring carbon 4 should control the equilibrium and the P-CH_3 group will be forced into greater occupation of the axial position (as in **2b**) in the cis isomer and of equatorial (**3b**) in the trans isomer. Similar consequences should result from methyl placed at the 3 position. Indeed, the principle of additivity of conformational free energies for remote substituents on a ring, most recently demonstrated to be valid in the related 1-methylthianium system,[7] should allow calculation of the position of these equilibria. For this purpose, we lack the $\Delta G°$ value for CH_3 on the phosphorinane ring, but



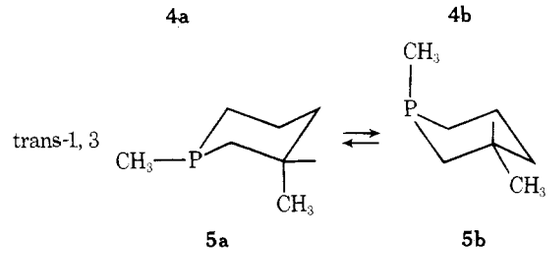
2a **2b**



3a **3b**



4a **4b**



5a **5b**

use of the cyclohexane value (−1.7) seems justified, which coupled with the value found for 1-methylphosphorinane (+0.35) leads to $\Delta G°$ = −2.05 kcal/mol for the *cis*-1,4-dimethyl system (**2**) and −1.35 for the *trans*-1,4-system (**3**). These values predict equilibrium constants of 92 and 9.9, respectively, or mixtures dominated by the *C*-methyl equatorial forms to a very large extent (99 and 91%, respectively). On comparing spectral properties for cis and trans forms, then, one should find significant differences about the P–CH_3 end, and considerable similarity at the C–CH_3 end. The same predictions would hold for the 1,3-dimethyl series, although we have refrained from making calculations in the absence of $\Delta G°$ for a 3-methyl group on this ring system.

When sulfur is added to 1-methylphosphorinane, it would be expected that a shift of the methyl group to the equatorial

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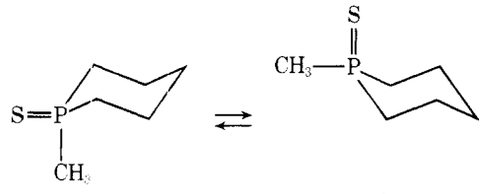
Table I. $^{13}C^{a}$ and ^{31}P NMR Spectra of 1,4-Dimethylphosphorinane and Derivatives

Compd no.	^{13}C-2,6	^{13}C-3,5	^{13}C-4	C-$^{13}CH_3$	P-$^{13}CH_3$	^{31}P-CH_3
2[b]	22.7 (14)	28.5 (0)[c]	34.1 (0)	23.5 (0)	5.7 (20)	−61.9
3[b]	28.5 (11)[c]	33.3 (6)	34.2 (0)	22.9 (0)	13.8 (18)	−55.7
7[d]	32.5 (50)	31.3 (7)	32.1 (0)	22.0 (0)[e]	15.9 (52)	+29.0
8[d]	31.1 (48)	28.8 (7)	32.7 (5)	22.0 (0)[e]	20.7 (52)	+30.8
11[d]	28.5 (63)	32.1 (6)	32.5 (5)	21.7 (0)[e]	12.0 (65)	+40.9
12[d]	27.6 (62)	29.0 (7)	32.3 (5)	21.7 (0)[e]	15.6 (66)	+38.7
15[f]	21.6 (50)	30.2 (5)	32.9 (7)	23.1 (0)	6.5 (55), 9.8 (55)	+17.2

[a] Values in parentheses are ^{13}C–^{31}P coupling constants in hertz. [b] ^{13}C spectrum neat; ^{31}P in benzene. [c] Overlapped signals. [d] Both spectra on $CHCl_3$ solutions. [e] Superimposed signals. [f] Both spectra on H_2O solutions; CH_3OH as internal ^{13}C reference.

position would occur. In this case of tetrahedral phosphorus, no mechanism is available to relieve the strain of 1,3-nonbonded interactions as is possible for the trivalent (pyramidal) system through expansion of bond angles.[2] Consequently, competition for the less crowded equatorial position should be won by the larger CH_3 group. This concept has already been tested and supported in other derivatives of phosphorinanes.[4a] Indeed, in another study in this Department directed by Professor A. T. McPhail,[8] it has been found by x-ray analysis of the crystalline 1-methylphosphorinane 1-sulfide that the methyl group is equatorial (**6b**). It is more difficult in advance



6a **6b**

of experimentation to predict what will occur when 3- or 4-CH_3 is placed on the ring with phosphorus in the tetrahedral condition, but as will be seen, the spectral data clearly reveal the control of the equilibria once again by the preference of the C–CH_3 group for the equatorial position.

The 1,3- and 1,4-Dimethylphosphorinanes. Carbon-13 NMR data for these compounds are conveniently discussed with reference to the 1-methyl parent, with two effects in mind: (1) replacement of ring hydrogen by methyl will produce the usual deshielding at α and β carbons and shielding at the γ carbon, by magnitudes dependent on axial–equatorial character; (2) the equilibria will shift so as to increase the axial P–CH_3 population in the cis compound of the 1,4 system and in the trans compound of the 1,3 system; it is quite clear from our earlier studies on hydroxyphosphorinanes[4] that axial P–CH_3 compounds have relatively upfield shifts at C-2,6, C-3,5, and at P–CH_3 due to steric crowding compared to the equatorial P–CH_3 compound. Indeed, these effects were used to assign cis,trans structure to the 1,4-dimethyl isomers that were obtained in unequal amount by the synthetic method used (CH_3PCl_2 added to the di-Grignard reagent of 1,5-dibromo-3-methylpentane). It is immediately evident from the ^{13}C spectra (Table I) that the isomers have nearly identical shifts for C-4 and for CH_3 on C-4, but that C-2,6 and C-3,5, as well as P–CH_3, are all markedly upfield in one (the minor) isomer. This leaves no doubt that both isomers have preferred conformations with equatorial C–CH_3 and that the minor isomer has the cis structure with a predominance of P–CH_3 axial (**2b**) and the major isomer is trans with a predominance of P–CH_3 equatorial (**3b**).

Comparison of the spectrum of *cis*-1,4-dimethylphosphorinane to that of the 1-methyl compound shows the following effects. (1) P–CH_3 is shifted upfield by 5.2 ppm; this is obviously the result of the increase in axial character of PCH_3 in the dimethyl compound (**2b**). (2) C-2,6 are also shifted upfield (4.0 ppm) by the increased axial P–CH_3 character (this upfield shift is not due to a γ effect of the 4-CH_3, since this is negligible for an equatorial group in cyclohexanes).[9] (3) C-3,5 feel opposite effects; they are shielded by the increased P–CH_3 axial character, but deshielded by the β effect of C–CH_3. The result is net deshielding (4.1 ppm). This is not unexpected, for the β effect of equatorial methyl on cyclohexane is a sizeable 8.9 ppm[9] and will dominate over the shielding. There is a marked difference in the ^{13}C–^{31}P coupling constant which also indicates the increased axial P–CH_3 character; there is no observable splitting in the dimethyl compound, while a doublet with J = 3 Hz is present for the 1-methyl compound. We have observed such stereodependence of $^2J_{PC}$ before,[2] and consistently have found that the value is largest (~6–7 Hz) with equatorial PCH_3 and is only 0–1 Hz in the axial case, as in the conformationally frozen 1-methyl-4-*tert*-butyl-4-phosphorinanols.[2] (4) C-4 is deshielded by the α effect of CH_3; the value (5.8 ppm) is nearly identical with the α-equatorial effect seen in cyclohexanes (5.6 ppm[9]).

The spectrum of the trans-1,4 isomer can be analyzed in the same way. (1) For PCH_3, there is increased equatorial character (**3b**) and consequently a downfield shift (2.9 ppm) relative to the 1-methyl case. (2) At C-2,6, there should also be deshielding accompanying the increased equatorial P–CH_3 character; the observed downfield shift is 1.8 ppm. (3) At C-3,5, deshielding is caused by both the increased equatorial P–CH_3 character and the β effect of the equatorial C–CH_3. The observed shift is 9.9 ppm. The expected increase in $^2J_{PC}$ also occurs; the value (6 Hz) is close to that (7 Hz) observed when P–CH_3 is frozen in the equatorial position in the 4-*tert*-butyl-4-phosphorinanol system.[2]

The chemical shift of the 4-CH_3 group in both isomers is very similar to that of 1-methylcyclohexane (δ 23.20[9]) and 4-methylthiane (δ 23.07[6]). That the shifts are not identical for the isomers, however, suggests that (1) the degree of equatorial character, while very large, is not precisely the same, and (2) the δ effect of the phosphorus function (+0.7 ppm in chain compounds[10]) is dependent on the configuration about phosphorus and is more important in the cis compound.

It is observed that some of the parameters (e.g., for P–CH_3 and C-2,6) for 1-methylphosphorinane fall between the extremes of the *cis*- and *trans*-1,4-dimethylphosphorinanes. Qualitatively, this is exactly what is expected for equilibria biased by *C*-methyl. It is not possible to use the data for quantitative conformational analysis, however, since the 4-methyl group is not an adequate anchoring group. Furthermore, the 4-methyl group clearly has an influence on the chemical shift of the phosphorus atom (vide infra) that may well be transmitted to carbons attached to phosphorus. To determine a conformational equilibrium constant by the chemical shift method requires assurance that a 4-substituent effect is absent.[11]

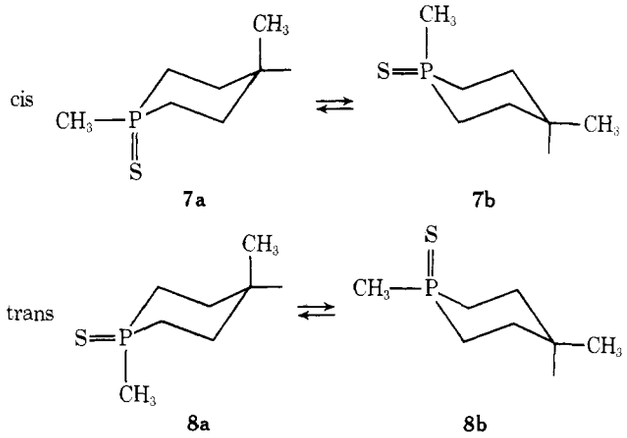
The synthesis of the 1,3-dimethylphosphorinanes proceeded similarly from the di-Grignard reagent of 1,5-dibromo-2-methylpentane. Again the cis and trans isomers were

formed in unequal amount. Here the cis isomer will have equatorial P–CH_3, in an equilibrium controlled by the greater demand of C–CH_3 for the equatorial position (**4b**), while the trans isomer will have axial P–CH_3 (**5b**). The differences in the P–CH_3 signals (*major* δ 14.3; *minor* δ 6.8) are immediately explainable on this basis and reveal the major isomer to have cis structure (**4b**). The similarity seen in the C–CH_3 signals (**5b**, δ 26.2; **4b**, δ 25.2) is then rationalized. These chemical shifts are noticeably downfield of those of the 1,4-dimethyl compound and we attribute this to the fact that phosphorus, rather than carbon, now occupies a γ position relative to 3-methyl. From our earlier study of open-chain phosphorus compounds, we know that trivalent phosphorus (as in the $(CH_3)_2P$ group) has a γ-shielding effect of only 0.5 ppm, while CH_3 has an effect of 2.4 ppm, a difference similar to that now seen on comparison of a 1,4- to a 1,3-dimethylphosphorinane with comparable disposition of the *P*-methyl group. Some other features of the spectra of these isomers are also notable. (1) C-2 and C-6 are easily recognizable in both isomers by the size of the coupling to ^{31}P. Of these, C-2 is the more deshielded due to the β effect of 3-methyl (about 5–6 ppm). The shift at C-6 is not influenced by the 3-methyl; the downfield shift noted in the cis isomer relative to the trans is due to the increased equatorial character of P–CH_3. (2) C-4 in both isomers, easily assigned by the absence of ^{31}P coupling, is strongly deshielded by the β effect of the 3-CH_3, about 10 ppm in each isomer relative to the 1-methyl compound. It is thus seen that the β effect of CH_3 is larger at C-4 than at C-2, but this effect has been found for 3-methylthiane also.[6] (3) C-5 is sensitive to two effects. The increased crowding due to P–CH_3 acquiring greater axial character is responsible for the noticeably upfield value for the trans isomer (δ 20.4) relative to the 1-methyl (δ 23.4), while relief of this crowding due to increased equatorial character of P–CH_3 in the cis isomer accounts for the downfield shift observed (δ 25.5). The value for $^2J_{PC}$ again supports these assignments; the isomer with axial P–CH_3 has the expected small constant (2 Hz), while the isomer with equatorial PCH_3 has the larger value (8 Hz). (4) The effect of CH_3 on C-3 is remarkably large for both isomers; relative to the 1-methyl compound, shifts of 13–14 ppm are observed. This shift greatly exceeds the expected α effect (5.8–5.9 ppm) seen in the 1,4-dimethyl compounds. The difference cannot be accounted for on any of the usual grounds; reassignment of the shifts to other carbons does not lead to any better interpretation.

The ^{31}P NMR shifts[12] (in benzene) for the axial P–CH_3 isomers (**2b**, −61.9; **5b**, −55.4) in each of the 1,4- and 1,3-dimethyl sets are upfield of the equatorial P–CH_3 isomers (**3b**, −55.7; **4b**, −54.3). This is the expected relation, based on our earlier studies with other phosphorinane derivatives,[2,4a] and is in common with the effects felt at ring carbon in cyclohexanes. However, the effect is noticeably more pronounced in the 1,4 isomers. The effect has not been considered previously for any 3-substituted phosphorinane, although it is known[13] for the 1,3-dimethylphospholanes that the difference in the cis and trans forms is small (δ −33.8 and −33.4, unassigned). In the 1,2-dimethylphospholenes,[13] the effect is actually reversed; the more crowded cis form (−16.7) is downfield of the trans (−28.2) and it would be of interest to determine values for the 1,2-dimethylphosphorinanes. Our attempts to prepare these compounds by the di-Grignard method have so far been unsuccessful, however. Another ^{31}P NMR feature of note is that the value[2] for 1-methylphosphorinane (neat, δ −53.7) falls outside the range for both of the pairs of dimethyl compounds, even allowing for the medium difference, and it is obvious that ^{31}P is influenced by other factors than just the degree of axial–equatorial character about the substituent it bears.

Sulfides of the Dimethylphosphorinanes. Addition of sulfur to the isomeric mixtures of 1,3- and 1,4-dimethylphosphorinanes produces the corresponding mixtures of 1-sulfides in good yield with retention of the isomer ratio. The effects on carbon of the conversion $R_3P \rightarrow R_3PS$ have been discussed in detail elsewhere;[4,10] the present discussion will concentrate on conformational effects only, as will that on the oxides and methiodides subsequently.

The 1,4-dimethyl isomers can be expected to participate in the conformational equilibria shown below (**7a,b**, **8a,b**).



7a **7b**

8a **8b**

That the ^{13}C shifts (Table I) are virtually the same in both isomers for C-4 and for 4-CH_3 clearly indicates that the equilibria are dominated by the same structural effect, presumably that of equatorial 4-CH_3 (**7b** and **8b**). This is confirmed by the observation that P–CH_3 and C-3,5 are quite different in the isomers. The former signals (δ 15.9 and 20.7) fall close to values established for conformationally frozen models with axial and equatorial P–CH_3 (1-methyl-4-*tert*-butyl-4-phosphorinanol 1-sulfides:[4b] P–CH_3 axial δ 14.5; P–CH_3 equatorial, δ 20.5). The C-3,5 signals should then differ because of the stronger shielding of axial sulfur than of axial methyl, an unusual effect observed earlier,[4b] and indeed that isomer assigned structure **8b** from the P–CH_3 effect has the expected upfield signal (δ 28.8 vs. 31.3).

The above interpretation implies that the conformational free energy of CH_3 on carbon is substantially larger than CH_3 on phosphorus bearing sulfur, just as it is on trivalent phosphorus, or conversely that of sulfur on phosphorus bearing CH_3. We have earlier[4a] considered the relative influence of CH_3 vs. S on the conformational equilibrium of 1-methylphosphorinane 1-sulfide and predicted that the conformer with equatorial CH_3 (**6b**) would be in predominance. X-ray analysis later confirmed this predominance for the solid state.[8] That there could be a substantial amount of the conformer with axial CH_3 (**6a**) in solution remains a possibility, however, and is indeed indicated by the fact that the P–CH_3 signal (δ 18.5) falls between the extremes of the two 1,4-dimethyl isomers. Were P–CH_3 in **6** very largely in the equatorial position, a value more like that of the trans compound (**8b**) should have been observed.

Analysis of the ^{13}C NMR data (Table II) for the 1,3-dimethyl compounds points to the same conclusion of control of the conformational equilibrium by the C–CH_3 group. Thus, the isomers have very similar shifts for C–CH_3 and for C-4, but quite different ($\Delta\delta$ 5.3 ppm) values for P–CH_3. Also, the greater γ-shielding effect of axial sulfur, relative to axial CH_3, is evident at both C-3 and C-5 in the isomer suspected to prefer structure **9b**.

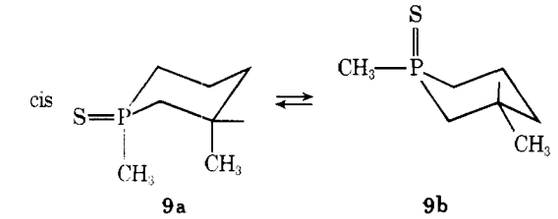
Another effect is present in both the 1,4 and 1,3 compounds: when sulfur is predominantly equatorial, small but noticeable deshielding occurs at the adjacent ring carbons (1.9 ppm at C-2, 1.8 ppm at C-6) relative to the form with axial sulfur. An effect of just this magnitude has been observed in the sulfides of the 1,4-dimethyl-1-phosphorinanols.[4]

There are two three-bond ^{13}C–^{31}P couplings in each of **9** and

Table II. $^{13}C^{a}$ and ^{31}P NMR Spectra of 1,3-Dimethylphosphorinanes and Derivatives

Compd no.	^{13}C-2	^{13}C-3	^{13}C-4	^{13}C-5	^{13}C-6	C-$^{13}CH_3$	P-$^{13}CH_3$	^{31}P-CH_3
4[b]	32.0 (8)	37.1 (3)	37.8 (0)	25.5 (8)	28.5 (10)	25.2 (5)	14.3 (16)	−54.3
5[b]	31.4 (10)	36.2 (2)	38.3 (0)	20.4 (2)	26.2 (12)[c]	26.2 (2)[c]	6.8 (18)	−55.4
9[d]	39.3 (39)	27.6 (4)	35.1 (6)	20.5 (5)	30.6 (50)	24.2 (18)[e]	21.7 (53)	+32.6
10[d]	41.2 (43)	30.8 (5)	34.1 (5)	23.1 (5)	32.4 (49)	24.2 (18)[e]	16.4 (52)	+30.5
13[d]	36.6 (62)	28.1 (6)[f]	35.3 (6)	20.6 (7)	27.4 (66)	24.6 (16)[c]	16.2 (68)	+40.6
14[d]	37.3 (63)	31.5 (4)	34.5 (6)	22.9 (4)	28.1 (65)[e]	24.3 (17)[c]	12.3 (66)	+42.2
16[g]	28.9 (49)	30.1 (5)	34.7 (7)	22.1 (5)	21.0 (51)	25.2 (16)	6.8 (53), 10.0 (54)	+19.2

[a] Values in parentheses are ^{31}P–^{13}C coupling constants in Hz. [b] ^{13}C spectrum neat; ^{31}P in benzene. [c] Overlapped signals. [d] Both spectra on $CHCl_3$ solution. [e] Signals nearly superimposed. [f] Overlapped signals. [g] Both spectra on H_2O solutions with CH_3OH as internal ^{13}C reference. Resolution was poor for C-2 and C-3 and C-5 and C-6, but a spectrum obtained at 15.0 MHz on a JEOL FX-60 spectrometer gave excellent resolution of all peaks and confirmed the assignments.



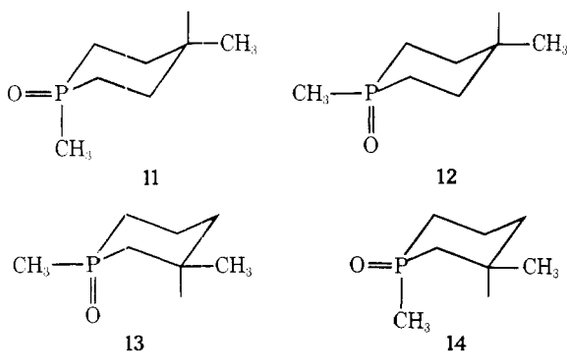
9a 9b

10a 10b

10, and a very large difference exists in their magnitude. The coupling to 3-CH_3 is a sizeable 18 Hz, while that to ring carbon 4 is only 5–6 Hz. We have previously noted a dihedral angle control of $^3J_{PC}$ in dimethylcyclohexylphosphine sulfides[14] and this appears to be the explanation for these phosphorinane derivatives as well. This effect will also be seen to prevail for the phosphine oxides and phosphonium salts to be discussed in later sections of this paper. The effect is useful in the present research since it supports the conclusion from chemical shift considerations that 3-CH_3 is in the same steric environment in both the cis and trans isomers.

The ^{31}P NMR shifts (in $CHCl_3$) for the sulfides of phosphorinanes are not as sensitive to structural changes as are those of the phosphines.[4a] Thus, the cis-1,4 compound (**7**) has δ +29.0 and the trans-1,4 compound (**8**) has δ +30.8. The 1-methyl compound falls out of this range (δ +33.9). For the 1,3-dimethyl compounds, similar values are found (**9**, +32.6; **10**, +30.5). In both sets of isomers, the upfield shift is associated with the form exhibiting an axial P–CH_3 preference.

Oxides of the Dimethylphosphorinanes. Equilibria for the oxides resemble those for the sulfides, and the ^{13}C NMR data (Tables I and II) reveal again that C–CH_3 is dominant over the phosphorus function. Thus the cis (**11**) and trans (**12**)



11 12

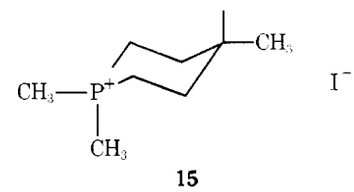
13 14

forms of the 1,4 compounds have very similar C-4 and 4-CH_3 signals, as do the cis (**13**) and trans (**14**) forms of the 1,3 compounds. The expected differences in the P–CH_3 signals are present. We have observed for the first time that the γ-shielding by axial oxygen exceeds that of axial CH_3, just as was true for sulfur. For the 1,4-dimethyl compounds, δ C-3,5 is 29.0 when axial oxygen is in predominance (**12**) and 32.1 for axial methyl (**11**). Similarly, for the 1,3-dimethyl compound with axial oxygen (**13**), δ C-3 (28.1) and C-5 (20.6) are upfield of the values for the isomer with axial CH_3 (**14**, δ C-3 31.5, δ C-5 22.9). The range for the axial oxygen effect is 2.3–3.1 ppm, which is like that of the axial sulfur effect (2.5–3.2 ppm). These shielding effects are clearly not interpretable on the usual basis of steric compression, and as we have pointed out elsewhere[4] probably require an explanation taking into account the polar character of the axial substituent.

The oxides also exhibit an effect at C-2 and C-6 like that seen for the sulfides; compounds with equatorial oxygen consistently have these carbons at lower field than do those with axial oxygen.

The ^{31}P NMR shifts for the oxides (Tables I and II) show exactly the opposite relation as seen for the phosphines and the sulfides; greater shielding is associated with an equatorial, not axial, *P*-methyl group. While the cause of this reversal is not known at present, it is evident that ^{31}P NMR spectroscopy must be used cautiously in conformational analysis, since other exceptions may exist to the rule that in isomeric cyclic compounds upfield shifts are always associated with greater apparent 1,3-steric crowding. In the conformationally rigid 3,5-dimethyl-2-R-2-oxo-1,3,2-dioxaphosphorinanes, exceptions to the rule have also been encountered.[15]

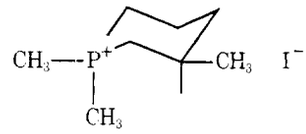
Methiodides of the Dimethylphosphorinanes. Based on the ^{13}C chemical shifts of C-4 and the 4-methyl group, which are found in the same region as the sulfide and oxide, it is possible to assign preferred conformation **15** to the methiodide



15

of 1,4-dimethylphosphorinane. If there was a significant amount of axial *C*-methyl, an upfield shift would have been noted. On the contrary, a weak deshielding due to the δ effect of the phosphorus function is seen. The *P*-methyl groups are nonequivalent; the axial CH_3 absorbs at higher field (δ 6.5) than the equatorial (δ 9.8).

The same spectral relations are found in the methiodide of 1,3-dimethylphosphorinane; the *C*-methyl group is assigned the equatorial position as in **16**, since it is again slightly downfield of the position in the oxides and sulfides. Again



16

there is a substantial difference in the two P–CH_3 groups (δ 6.8 and 10.0).

Conclusions

^{13}C NMR spectroscopy is eminently suited for the determination of cis,trans structure in 1,4- and 1,3-dimethylphosphorinanes and in their sulfides and oxides as well. These spectral data are also compelling in pointing to the consistent preference of methyl on carbon 3 or 4 of the phosphorinane ring for the equatorial position in all structures studied, regardless of the phosphorus oxidation state, thus forcing *P*-methyl in some structures into the axial position. This is consistent with observations we have made previously[4] for 1,4-dimethyl compounds also bearing a 4-hydroxy group, where x-ray analysis provided unequivocal proof of structure. It is therefore implied that the net of nonbonded interactions for the two substituents on phosphorus in the sulfides and oxides must be of smaller magnitude than that of *C*-methyl, and it would be desirable to assess this competition on a quantitative basis by determining $\Delta G°$ values. Thus, groups such as $CH_3(S)P$ and $CH_3(O)P$ must have $\Delta G°$ values of size considerably smaller than the −1.7 kcal/mol assigned to 4-CH_3. This raises the question of relative preferences when 4-CH_3 is pitted against phosphorus functionalities having larger alkyl substituents than methyl. It is possible that the domination by 4-CH_3 will prevail for some of these groups, and great caution must be used in assigning configurations solely on group size parameters that are really applicable only when the groups are present on the cyclohexane ring. No data are presently available for such compounds, although the isomeric 1-phenyl-4-methylphosphorinane 1-oxides have recently been considered from a number of standpoints (not ^{13}C NMR) and the judgement has been made that *P*-phenyl is equatorial in both.[16]

The γ effect of ^{13}C NMR is frequently used to assign configurations to cis,trans isomers, although it is evident that the full nature of this effect is not well understood and at least for nonalkyl groups appears to have a component unrelated to group size.[17] We have previously seen[4] that axial P=S causes greater shielding at C-3,5 of the ring of the 4-phosphorinanols than does axial P–CH_3, and the present study is the first to report the same property for axial P=O in a pair of cis,trans isomers.[18] Another cautionary note is therefore required in the use of ^{13}C NMR for stereochemical assignment: relative "size" of the two substituents attached to tetracovalent phosphorus is not the sole factor causing shielding at γ ring carbons, and specific information about a particular system is required before the technique is useful. The problem does not exist, of course, for trivalent phosphorus, where an axial substituent routinely causes greater upfield shifts at C-3,5 than does an equatorial substituent.

^{31}P NMR has played an important role in studying conformational equilibria of 1-substituted phosphorinanes,[2] but it is now seen to have only limited utility in the *C*-methylphosphorinanes and in their sulfides and oxides. Thus, the chemical shift for 1-methylphosphorinane does not fall within the range set by the cis and trans isomers of 1,4-dimethylphosphorinane, as it should if the degree of axial and equatorial character were in control of the shift. Still, greater shielding of phosphorus does occur in the cis-1,4 and trans-1,3 isomers which have largely axial P– substituent, as has been observed for the individual conformers of 1-methylphosphorinane when examined at very low temperatures.[2] This is true also for the sulfides. For the oxides, however, it is the isomer with oxygen in the axial position that has the more upfield ^{31}P signal. ^{31}P NMR anomalies do exist among other related systems; in the oxides of the 1,3-dioxaphosphorinane system,[15] equatorial P=O usually, but not always, is associated with the more upfield ^{31}P NMR signal.

In spite of the anomalies in the ^{31}P spectra, methyl groups on phosphorus give ^{13}C signals that have invariably been of aid in assigning cis,trans structure. We have not yet encountered a case where the generality that an axial P–CH_3 falls upfield of an equatorial P–CH_3 is not observed, regardless of the phosphorus functionality, and this measurement is the method of choice in studying this stereochemical feature.

Experimental Section

General. All manipulations of phosphines were conducted in a nitrogen atmosphere in a glovebag. Melting points are corrected. Proton NMR spectra were taken on Varian A-60 or JEOL MH-100 spectrometers. Phosphorus NMR spectra were obtained with a Bruker HFX-10 spectrometer at 36.43 MHz, using the continuous wave technique with proton decoupling; shifts are referenced to prerun 85% H_3PO_4, with downfield shifts positive. Carbon NMR spectra were taken with the Bruker instrument at 22.62 MHz using the Fourier transform technique with proton decoupling; shifts are referenced to internal tetramethylsilane.

Interpretation of ^{13}C NMR Spectra. In both the 1,4- and 1,3-dimethylphosphorinane syntheses, unequal mixtures of the cis and trans isomers were obtained. The mixtures were used without separation in all spectral studies. Generally the complete set of peaks for each isomer could be observed with signals readily assigned to a particular isomer by the relative intensities. In the 1,4 compounds, signals for C-2,6 were obvious from their intensity and relatively large coupling to ^{31}P, while C-3,5 were revealed by their intensity and confirmed by their stereospecific coupling to ^{31}P. Other signals presented no difficulty. In the 1,3 compounds C-2 and C-6 were again recognized by their relatively large coupling to ^{31}P; the more downfield signal was assigned to C-2, since it experiences a β effect from the 3-methyl. This effect also shifts C-4 well downfield, making it an easily recognized singlet. Other carbons are also easily assigned. Similar reasoning sufficed to make assignments for the tetravalent derivatives, coupled with known shift effects at α, β, and γ carbons accompanying the conversion from trivalent phosphorus. These have been described elsewhere.[4,10] The spectra were sometimes quite complex, since two isomers were present and many signals were split. Occasional superposition or overlapping of lines occurred, making some assignments tenuous. These are noted in Tables I and II. No important uncertainties in the assignments remain, however.

3-Methyl-1,5-dibromopentane. A known procedure for the preparation of this compound from *N*-benzoyl-4-methylpiperidine and PBr_5 was used.[19] The product (43%) had bp 71–81 °C (0.8 mm) [lit.[19] bp 59–61 °C (0.3 mm)].

***cis*- and *trans*-1,4-Dimethylphosphorinane (2 and 3).** The Grignard reagent was prepared from 48.8 g (0.20 mol) of 3-methyl-1,5-dibromopentane and 12.8 g (0.50 g-atom) of magnesium in 300 mL of anhydrous ether. To the reagent was added a solution of 23.4 g (0.20 mol) of methylphosphonous dichloride in 50 mL of ether. After the exothermic reaction had subsided, the mixture was stirred overnight and then hydrolyzed with saturated NH_4Cl solution. The organic layer was collected and the aqueous layer was extracted with four 80-mL portions of ether. The combined ether solutions were dried ($MgSO_4$) and distilled to give 2.5 g (10%) of product at 68–74 °C (45–49 mm). The ^{31}P NMR spectrum (benzene)

showed the presence of both the cis (**2**, δ −61.9, 35%) and trans (**3**, δ −55.7, 65%) isomers. The ^{1}H NMR spectrum was uninformative, consisting of highly complex signals clustered at δ 0.74–1.00 (P–CH_3 and C–CH_3) and 1.00–2.22 (ring protons). No attempt was made to separate the isomers. ^{13}C NMR parameters obtained for the mixture are reported in Table I.

***cis*- and *trans*-1,4-Dimethylphosphorinane 1-Sulfide (7 and 8).** A solution of 1.0 g (0.008 mol) of the mixture of phosphines **2** and **3** in 20 mL of benzene was treated with 0.4 g (0.013 mol) of sulfur. The mixture was refluxed for 3 h and filtered while hot to remove unreacted sulfur. Evaporation of solvent left a crystalline residue which was purified by vacuum sublimation to give a product of wide melting range (71–94 °C) because of the presence of isomers. The mixture was analyzed directly.

Anal. Calcd for $C_7H_{15}PS$: C, 51.82; H, 9.32; P, 19.09. Found: C, 51.53; H, 9.15; P, 18.97.

^{1}H NMR ($CDCl_3$) δ 1.71 (d, $^2J_{PH}$ = 13 Hz, P–CH_3 for both isomers), 0.95 (d, $^3J_{HH}$ = 6 Hz, C–CH_3 for both isomers), 1.28–2.40 (m, ring protons); ^{31}P NMR ($CHCl_3$) δ +29.0 (cis (**7**), 32%) and +30.8 (trans (**8**), 68%); ^{13}C NMR, Table I.

***cis*- and *trans*-1,4-Dimethylphosphorinane 1-Oxides (11 and 12).** A 0.8-g sample of the mixture of phosphines **2** and **3** was stirred with 10 mL of 3% hydrogen peroxide for several hours. The solution was extracted with chloroform; the extract was dried ($MgSO_4$) and evaporated to leave a colorless liquid (0.6 g, 67%): ^{1}H NMR ($CHCl_3$) δ 0.88–1.12 (m, C–CH_3 for both isomers), 1.53 and 1.57 (both d, $^2J_{PH}$ = 13 Hz, P–CH_3 for both isomers), 1.44–2.88 (m, ring protons); ^{31}P NMR ($CHCl_3$) δ +40.9 (cis (**11**), 33%) and +38.7 (trans (**12**), 67%); ^{13}C NMR, Table I.

1,1,4-Trimethylphosphorinanium Iodide (15). The salt was prepared in ether from the mixture of phosphines **2** and **3** and methyl iodide; the product recrystallized from chloroform–hexane began to darken near 200 °C and decomposed sharply at 313 °C: ^{1}NMR (Me_2SO-d_6) δ 0.92 (d, $^3J_{HH}$ = 6 Hz, C–CH_3), 1.94 (d, $^2J_{PH}$ = 14 Hz, P–CH_3), 1.20–2.64 (m, ring protons); ^{31}P and ^{13}C NMR, Table I.

Anal. Calcd for $C_8H_{18}IP$: C, 35.33; H, 6.62; P 11.39. Found: C, 35.36; H, 6.14; P, 11.14.

2-Methyl-1,5-Dibromopentane. This compound was prepared by the same procedure used for the 3-methyl isomer, employing *N*-benzoyl-3-methylpiperidine. It was obtained in 38% yield: bp 76–78 °C (1.1 mm) [lit.[20] bp 110–112 °C (21 mm)].

***cis*- and *trans*-1,3-Dimethylphosphorinane (4 and 5).** These compounds were prepared by the same procedure used for the 1,4-dimethyl isomers (**2** and **3**), employing 48.8 g (0.20 mol) of 2-methyl-1,5-dibromopentane and 12.8 g (0.50 g-atom) of magnesium in 300 mL of ether for di-Grignard preparation and 23.4 g (0.20 mol) of methylphosphonous dichloride. The product (5.4 g, 21%) distilled at 81–85 °C (57 mm). The ^{1}H NMR spectrum (C_6H_6) was uninformative (overlapping P–CH_3 and C–CH_3 at δ 0.68–1.00, ring H at 1.13–2.00); ^{31}P NMR (C_6H_6) δ −55.4 (trans (**5**), 41%) and −54.3 (cis (**4**), 59%); ^{13}C NMR, Table II.

***cis*- and *trans*-1,3-Dimethylphosphorinane 1-Sulfides (9 and 10).** The mixture of phosphines **4** and **5** was sulfurized as before; after vacuum sublimation, the isomeric sulfide mixture had mp 43–58 °C and was analyzed as such.

Anal. Calcd for $C_7H_{15}PS$: C, 51.82; H, 9.32; P, 19.09. Found: C, 51.96; H, 9.43; P, 19.23.

^{1}H NMR ($CDCl_3$) δ 1.74 and 1.75 (both d, $^2J_{PH}$ = 13 Hz, P–CH_3 of both isomers), 0.96–1.18 (m, C–CH_3), 1.60–2.60 (m, ring H); ^{31}P NMR ($CHCl_3$) δ +32.6 (cis (**9**), 56%) and +30.5 (trans (**10**), 44%); ^{13}C NMR, Table II.

***cis*- and *trans*-1,3-Dimethylphosphorinane 1-Oxides (13 and 14).** The procedure used for the formation of **11** and **12** was applied to the mixture of phosphines **4** and **5**, forming a liquid product: ^{1}H NMR ($CHCl_3$) δ 1.54 and 1.55 (both d, $^2J_{PH}$ = 13 Hz, P–CH_3 of both isomers), 1.00–1.16 (two overlapping doublets, C–CH_3), 1.20–2.80 (m, ring H); ^{31}P NMR ($CHCl_3$) δ +40.6 (cis (**13**), 72%) and +42.2 (trans (**14**), 28%); ^{13}C NMR, Table II.

1,1,3-Trimethylphosphorinanium Iodide (16). Prepared by the method used for **15** as applied to the mixture of phosphines **4** and **5**, this compound had mp 213–214 °C after recrystallization from ethyl acetate–ethanol: ^{1}H NMR (Me_2SO-d_6) δ 1.04 (d of d, $^4J_{PH}$ = 3 Hz, $^3J_{HH}$ = 6 Hz, C–CH_3), 1.95 (d, $^2J_{PH}$ = 13 Hz, both P–CH_3 groups), 1.56–2.68 (m, ring H); ^{31}P and ^{13}C NMR, Table II.

Anal. Calcd for $C_8H_{18}IP$: C, 35.33, H, 6.62; P, 11.39; Found: C, 35.50, H, 6.52; P, 11.26.

Registry No.—**2**, 64999-61-7; **3**, 64999-62-8; **4**, 64999-63-9; **5**, 64999-64-0; **6**, 1661-16-1; **7**, 64999-65-1; **8**, 64999-66-2; **9**, 64999-67-3; **10**, 64999-68-4; **11**, 64999-69-5; **12**, 64999-70-8; **13**, 64999 71-9; **14**, 64999-72-0; **15**, 64999-73-1; **16**, 64999-74-2; 3-methyl-1,5-dibromopentane, 4457-72-1; methylphosphonous dichloride, 676-97-1; methyl iodide, 74-88-4; *n*-benzyl-3-methylpiperidine, 19202-02-9; 2-methyl-1,5-dibromopentane, 25118-31-4.

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