Phosphorus-31 Nuclear Magnetic Resonance Spectroscopy in the Determination of Conformational Free Energies of Phosphorus Groups on the Cyclohexane Ring[1]

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Abstract: The proton-decoupled ^{31}P NMR spectra were obtained for cyclohexyl, *cis*- and *trans*-4-methylcyclohexyl, and *cis*- and *trans*-4-*tert*-butylcyclohexyl derivatives of six different phosphorus functions (PH_2, PMe_2, PCl_2, $P(OMe)_2$, $P^+Me_3(I^-)$, and $PSMe_2$). The ^{31}P shifts for the conformationally rigid *tert*-butyl derivatives revealed a strong dependence on the steric disposition of the group; for PH_2 and PMe_2, the signal was considerably more upfield when the group was axial, while for all the other groups greater shielding was experienced in the equatorial position. All groups biased the conformational equilibrium for the cyclohexyl derivatives strongly to the equatorial side, and the shifts differed only slightly from those of the *trans*-4-*tert*-butyl derivatives. While the *trans*-4-methyl and *trans*-4-*tert*-butyl compounds also had similar shifts, the *cis*-4-methyl compounds had signals between the extremes of the *cis*- and *trans*-4-*tert*-butyl compounds, and for the trivalent derivatives this allowed calculation of their conformational equilibrium constants by the method of Eliel. By the principle of additivity of group conformational free energies, the first A values for phosphorus functions were obtained: PH_2, 1.6; PMe_2, 1.6; PCl_2, 2.0; $P(OMe)_2$, 1.9. Peak separation of the tetravalent functions was not adequate to allow accurate determination of their A values, but they appeared to be much greater. On lowering the temperature during the ^{31}P NMR experiment on the *cis*-4-methyl trivalent derivatives, the signal virtually vanished into the baseline in the vicinity of the coalescence temperature (210–220 K), and then resolved into two sharp peaks by 183 K, with shifts very close to those for the rigid *cis*- and *trans*-4-*tert*-butyl derivatives. Peak intensity measurements at 183 K provided K_{equil}, and these led to a second set of A values: PH_2, 1.6; PMe_2, 1.5; PCl_2, 1.9; $P(OMe)_2$, 1.5. The agreement with the earlier set is excellent except for $P(OMe)_2$ where the low-temperature value is believed to be more accurate. The A values for phosphorus functions are seen to be larger than for comparable nitrogen (NH_2) and sulfur functions (SH and SMe).

That ^{31}P NMR shifts are sensitive to steric factors seems quite clear from data reported for cyclic phosphorus compounds (e.g., in the phosphorinane system[2]) as well as for some aryl derivatives.[3] It has also been suggested that the upfield shifts seen among noncyclic aliphatic phosphorus compounds on increasing the number of γ carbons are a consequence of increased steric interactions.[4] It follows that sizable differences in ^{31}P shifts can be expected when phosphorus functions occupy axial or equatorial positions on six-membered rings, although this point appears to have received no prior attention. We will show in this paper that shift differences indeed can be appreciable in cyclohexylphosphorus compounds when the phosphorus function is placed in a differing steric environment. It will be seen, however, that some groups are relatively more shielded in the axial position while others are more shielded when in the equatorial position.

Regardless of their origin, these shift differences provide a basis for the utilization of ^{31}P NMR spectroscopy for the establishment of conformational free energy differences (A values[5]) of phosphorus functions. Although the field of conformational analysis remains very active,[6] no A values have ever been reported for phosphorus functions, and indeed surprisingly little effort has been directed to the determination of A values for groups based on the heavier elements.[6]

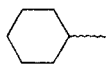
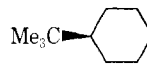
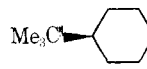
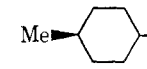
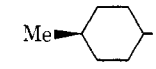
Nuclear magnetic resonance has long been used as a tool in determining conformational preferences of substituents on the cyclohexane ring.[6] The two NMR methods that have been most successful are the chemical shift method[7] and the direct measurement of conformer concentrations at low temperature.[8] While the methine proton on the carbon bearing the substituent has usually been the focus of ^1H NMR studies, nuclei in the substituent group can also provide useful NMR signals. Thus, A values of F,[9] CF_3,[10] and COF[11] groups have been determined by ^{19}F NMR, while values for CH_3[12] and CH_2OR[13] groups have been obtained from ^{13}C NMR. These nuclei when attached to the ring exhibit substantial shielding in the axial position, relative to equatorial. Thus, the ^{19}F resonance for the axial conformer of fluorocyclohexane was observed to be about 20 ppm upfield of the signal for the equatorial conformer at low temperature,[9] and the ^{13}C shift of the methyl group of the axial conformer of methylcyclohexane was observed about 6 ppm upfield of the shift for the equatorial methyl group at $-110°$.[12] In principle, ^{31}P NMR should be useful for performing both of the methods of conformational analysis. Low-temperature ^{31}P NMR has been generally neglected in the study of dynamic behavior of molecules containing phosphorus. This laboratory recently showed the power of this technique in the investigation of the conformational equilibrium of phosphorinanes. Thus, for 1-methylphosphorinane, ring inversion was slowed down at 143 K and ^{31}P signals separated by 3.1 ppm were observed for the two conformers.[2] In the present paper, low-temperature ^{31}P NMR spectroscopy will be seen to be quite useful for conformational study of some of the cyclohexyl derivatives.

Results and Discussion

Synthesis. The cyclohexylphosphorus compounds utilized in this study (Table I) were prepared by the reactions outlined in Scheme I. All of the reactions were based on conventional methods that have recently been surveyed.[14]

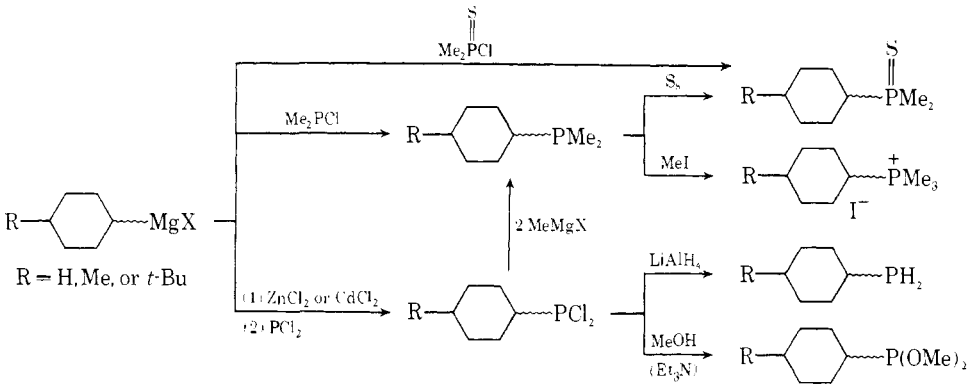
The Grignard reagent prepared from *cis*-4-*tert*-butylcyclohexyl chloride reacted with dimethylphosphinous chloride to give the cis (**9**) and trans (**10**) isomers of the tertiary phosphine in a ratio of about 1 to 9. Nearly the same isomer ratio was obtained for the tertiary phosphine sulfides (**15, 16**) that were produced by the reaction of the same Grignard reagent with dimethylthiophosphinyl chloride. The great preference for equatorial attack on this Grignard reagent was not unexpected, from the report[15] that trimethy-

Table I. Compounds Prepared and ^{31}P Shifts at 300 K[a]

P	 Compd	δ ^{31}P, ppm	 Compd	δ ^{31}P, ppm	 Compd	δ ^{31}P, ppm	 Compd	δ ^{31}P, ppm	 Compd	δ ^{31}P, ppm
PH_2	1	−111.8	7	−131.3	8	−111.6	19	−122.5	20	−111.8
PMe_2	2	−42.7	9	−54.8	10	−42.5	21	−49.0	22	−42.5
PCl_2	3	+195.0	11	+208.9	12	+194.6	23	+199.8	24	+194.9
$P(OMe)_2$	4	+189.7	13	+192.6	14	+190.0	25	+191.0	26	+189.9
$P(S)Me_2$	5	+42.9	15	+43.3	16	+42.5	27	+42.7	28	+42.7
$P^+Me_3(I^-)$	6	+29.6	17	+30.8	18	+29.6	29	+30.0	30	+29.8

[a] ^{31}P spectra were obtained on neat samples of the trivalent phosphorus compounds and $CDCl_3$ solutions of the tetravalent compounds. Negative shifts are upfield from the reference (external 85% H_3PO_4).

Scheme I



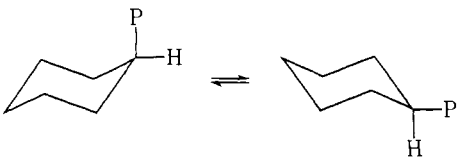
tin chloride attacks it to give greater than 95% *trans*-4-*tert*-butylcyclohexyltrimethyltin.

Preparation of the phosphonous dichlorides was carried out by first converting the Grignard reagent to the less reactive zinc[16] or cadmium derivatives.[17] Attack by phosphorus trichloride on these organometallics was of low stereoselectivity, resulting in a cis (**11**), trans (**12**) ratio of about 1:1 and 1:1.8, respectively. Fractional distillation gave partial separation, yielding a first fraction rich in the cis isomer (80%) and a final cut rich in the trans isomer (88%). Reduction, esterification, or methylation of a mixture of the phosphonous dichlorides **11** and **12** proceeded with no change of configuration at the carbon bearing the phosphorus function, giving products with a cis, trans isomer composition close to that of the starting materials. The same was true of quaternization or sulfurization of a tertiary phosphine mixture (**9** and **10**).

The 4-methylcyclohexylphosphorus compounds were prepared in a set of reactions completely analogous to those yielding the 4-*tert*-butyl compounds. The Grignard reagent from predominantly *cis*-4-methylcyclohexyl chloride reacted with dimethylphosphinous chloride or dimethylthiophosphinyl chloride to give products that were again enriched in the trans isomer (90% or higher). The zinc and cadmium reagents reacted with phosphorus trichloride to give a mixture (about 1:1) of cis (**23**) and trans (**24**) phosphonous dichlorides. No attempt at separation of **23** and **24** was made.

The assignment of cis and trans structure to the 4-*tert*-butylcyclohexylphosphorus compound was achieved readily by ^{13}C NMR spectroscopy. Signals for C-3,5 of the ring were used for this purpose; it is a well-established fact that these carbons will have signals several ppm upfield in isomers with axial 1-substituents relative to isomers with equatorial 1-substituents.[18] These carbon signals were readily detected in the spectra of our enriched isomer mixtures, and the shift differences (2.7–6.7 ppm) between isomers were of the magnitude and direction expected. Thus, the isomer formed in great predominance by reaction of dimethylphosphinous chloride with 4-*tert*-butylcyclohexylmagnesium chloride would be expected[15] to have trans structure **10**, and indeed its C-3,5 signal (δ 28.0) was downfield of that for the minor isomer (**9**, δ 23.5). The trans isomer of the phosphonous dichloride (**12**) as assigned from the C-3,5 relation, on conversion to the other phosphorus functions, always gave the isomer with the more downfield C-3,5 signal. Full details of the ^{13}C NMR spectra of these compounds will be published elsewhere.[19] The structural assignments were tested by ^{31}P NMR spectral properties as will be described later in the present paper. Cis, trans assignment to the 4-methyl series of compounds followed readily from the spectral properties established for the 4-*tert*-butyl series.

Steric Effects on ^{31}P Shifts of Cyclohexylphosphorus Compounds. The parent cyclohexyl compounds **1–6** exist as a pair of rapidly interconverting axial and equatorial conformers.



The observed ^{31}P NMR signal (Table I; note the use of the sign convention of negative shifts being upfield of the standard H_3PO_4) will be determined by the relative concentrations of the conformers at equilibrium. Placement of a 4-*tert*-butyl group on the ring will lead to isomers with fixed axial (cis) or equatorial (trans) phosphorus functions, and by analogy to ^{13}C NMR effects these would be expected to have quite different ^{31}P shifts. Thus, it is known[18] that axial CH_3 gives a ^{13}C signal several ppm upfield of that from equatorial CH_3. This effect and the upfield shift also experienced at ring carbons 3 and 5 are said to have a common origin from steric compression of the C–H bonds and resultant displacement of electron density to carbon.[20] For some other substituents, however, additional effects may be operative,[21] and cases are even known where steric compression causes deshielding of involved carbons.[22] From the data in Table I, it may be seen that the PH_2 and PMe_2 functions follow the relationship of $^{13}CH_3$; the isomers with the axial

group (**7** and **9**) are upfield of those with the equatorial group (**8** and **10**) by 19.7 and 12.3 ppm, respectively. However, the opposite is true for all other functions studied. The reversal of the effect is most striking for the PCl_2 group, where equatorial is upfield of axial by 14.3 ppm.

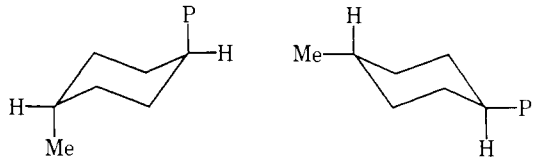
The surprising result for the phosphonous dichlorides called into question the assignments of cis, trans structure, and prompted additional experiments to confirm their correctness. A mixture containing the downfield-upfield signals in 80:20 ratio was treated with methylmagnesium iodide; this gave a mixture of the tertiary phosphines where the downfield-upfield ratio was reversed (21:79), which clearly supports the assigned structures. Furthermore, when the ^{31}P spectrum of a mixture of dichlorides **11** and **12** was recorded without proton decoupling, the peak at +194.6 ppm appeared as a broad doublet with peak separation of about 13 Hz, while the peak at +208.9 had a much larger half-bandwidth and a more complex coupling pattern. While $^2J_{PH}$ would be similar (about 15 Hz[23]) for both isomers, $^3J_{PH}$ has been shown to follow a Karplus-type relationship in several classes of organophosphorus compounds.[24] In the present case, for the trans isomer both P_{eq}-C_1-C_2-H_{eq} and P_{eq}-C_1-C_2-H_{ax} dihedral angles will be about 60° and hence relatively small coupling is expected. In the cis isomer, the dihedral angle for P_{ax}-C_1-C_2-H_{ax} will be 180° and this leads to a larger coupling. The observed spectra are in accord with these relations.

Phosphonites **13** and **14** had ^{31}P shifts that differed by only 2.6 ppm, again with the cis isomer downfield of trans. In the systems with tetravalent phosphorus, the ^{31}P shift differences between isomers became even smaller (1.2 ppm for the salts, 0.8 ppm for the sulfides). Consideration of the possibility that some distortion of the chair structure is present in the cis isomers is made later.

Our results require an altered view of the impact of steric environment on ^{31}P NMR shifts. There is no doubt that steric structure about phosphorus is important in establishing the shift, but it is now obvious that the simple assumption that sterically compressed groups attached to phosphorus will always cause net *shielding* of this atom is not adequate. Just as is the case for ^{13}C NMR, we are not yet able to specify the complete nature of the γ interaction in ^{31}P NMR. In the noncyclic compounds we have discussed elsewhere,[4] all γ effects were shielding but consideration of the γ constants derived in these studies in the light of our new knowledge from cyclic compounds reveals that a definite relationship exists. In the noncyclic compounds, the largest γ constants were obtained for the PH_2 and PR_2 functions (−7 and −4 ppm, respectively), while much smaller constants (−0.6 to −1.5) were obtained for PCl_2, $P(OMe)_2$, P^+R_3, and $P(S)R_2$. The latter group of functions, of course, is that which exhibited net deshielding in the axial disposition in cyclohexane. The effect which acts on these functions to cause the diminished γ-shielding constants relative to those for the nonpolar phosphines apparently is more pronounced in the cyclic compounds and tips the balance in favor of deshielding.

Examination of the ^{31}P shifts for the parent cyclohexyl compounds (Table I) results in the important observation that they resemble closely the shifts of the *trans*-4-*tert*-butyl compounds (e.g., cyclohexylphosphine (**1**) −111.8; the 4-*tert*-butyl derivative (**8**) −111.6). This clearly indicates that the equilibrium for the conformationally mobile parent compounds must be biased very strongly toward the equatorial form, a point which will be placed on a quantitative basis in the next section.

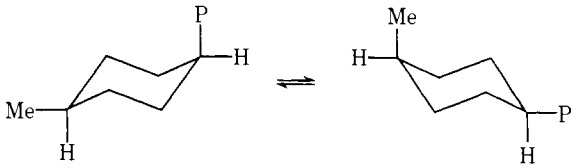
The ^{31}P shifts for the *cis*- and *trans*-4-methylcyclohexyl compounds **19–30** are also found in Table I. Although the 4-methyl group does not prevent chair-chair interconversion as does the 4-*tert*-butyl group, the trans isomer will nevertheless exist almost entirely as the diequatorial conformer, since the diaxial conformer would be highly unfavored energetically, especially if the phosphorus groups proved to be sterically large. The *trans*-4-methyl compound



diax dieq

20 (P = PH_2) has a shift of −111.8, which closely resembles the shift for the corresponding *trans*-4-*tert*-butyl compound **8** (−111.6). In fact the deviation of ^{31}P shifts between each monosubstituted compound (**1–6**) and its *trans*-4-*tert*-butyl or *trans*-4-methyl derivative is never greater than ±0.4 ppm and is usually less. These data show that a *trans*-4-alkyl group has only a very small effect, if any, on the ^{31}P shift of the equatorial phosphorus group at the opposite position of the ring.

In the case of the *cis*-4-methyl compounds, significant populations of both conformers (eq Me-ax P and ax Me-eq P) are expected to be present in equilibrium.



eq Me-ax P ax Me-eq P

The ^{31}P shift of a *cis*-4-methyl compound at room temperature is observed as a single time-averaged signal whose position is determined by the relative populations of the two conformers. Thus the shift observed for *cis*-4-methylcyclohexylphosphine (**19**) at −122.5 ppm is in between the shifts found for the isomers of 4-*tert*-butylcyclohexylphosphine with the phosphine group axial (**7**, −131.3) and equatorial (**8**, −111.6).

***A* Values for Phosphorus Functions by the Chemical Shift Method.** The equation developed by Eliel for proton NMR[7] can be applied to ^{31}P NMR shifts to calculate K_{equil} for the conformational equilibrium of the *cis*-4-methylcyclohexylphosphorus compounds.

$$K_{equil} = \frac{\delta_{ax\ P} - \delta_{cis\text{-}4\text{-}Me\text{-}P}}{\delta_{cis\text{-}4\text{-}Me\text{-}P} - \delta_{eq\ P}}$$

Here $\delta_{ax\ P}$ and $\delta_{eq\ P}$ are the shifts of the *cis*- and *trans*-4-*tert*-butyl derivatives, respectively, and $\delta_{cis\text{-}4\text{-}Me\text{-}P}$ is the time-averaged shift for the mobile *cis*-4-methyl compound. In principle, the conformational equilibrium constants for the monosubstituted compounds **1–6** are also derivable from this approach, but the time-averaged shifts for these compounds are too similar to the shifts of the *trans*-4-*tert*-butyl derivatives. The equilibrium constants and the free energies $\Delta G^\circ_{cis\text{-}4\text{-}Me}$ at 300 K for the *cis*-4-methylcyclohexyl systems with *trivalent* phosphorus groups are reported in Table II. It is immediately observed that in all four systems K_{equil} is near unity, indicating that the methyl group and the trivalent phosphorus groups have similar preference for the equatorial position. Assuming that free energy differences are additive in this system,[25] and using a value for ΔG°_{Me} of −1.7 kcal/mol,[26] the conformational free energies for phosphorus functions can be calculated from the equation

$$\Delta G^\circ_P = \Delta G^\circ_{cis\text{-}4\text{-}Me} + \Delta G^\circ_{Me}$$

Table II. Thermodynamic Values

Group	Chemical shift method (300 K)[a]			Low-temperature method (183 K)[b]		
	K_{equil}	$\Delta G°_{cis\text{-}4\text{-}Me}$	A	K_{equil}	$\Delta G°_{cis\text{-}4\text{-}Me}$	A
$-PH_2$	0.81	+0.13	1.6	0.68	+0.14	1.6
$-PMe_2$	0.89	+0.07	1.6	0.54	+0.22	1.5
$-PCl_2$	1.75	−0.33	2.0	1.72	−0.20	1.9
$-P(OMe)_2$	1.50	−0.24	1.9	0.56	+0.21	1.5

[a] Neat samples. [b] Vinyl chloride solutions.

The results are presented as A values ($A_P = -\Delta G°_P$) in Table II.

The accuracy of these values depends heavily on the validity of the assumption of additivity[27] of free energy differences in the *cis*-4-methylcyclohexyl systems. The cases in which the additivity principle has been found to be invalid are those in which both of the 1,4-substituents are highly polar groups; here attractive electrostatic interactions can occur across the ring.[28] The present compounds would be free of this complication. Also of great concern in assessing the accuracy of the A values determined by the chemical shift method is the validity of the assumption that the *cis*- and *trans*-4-*tert*-butyl model compounds give ^{31}P shifts that represent true values for axial and equatorial phosphorus groups. It has been shown in the preceding section that the room-temperature ^{31}P shifts of the *trans*-4-alkylcyclohexyl and monosubstituted cyclohexyl phosphorus compounds are very similar, indicating that the equatorial 4-substituent has no appreciable effect on an equatorial phosphorus group. A slightly larger effect seems to exist for axial groups, as is seen from comparison of the room-temperature ^{31}P shifts of the *cis*-4-*tert*-butyl model compounds (Table I) with the shifts found at 183 K for the *cis*-4-methyl conformers with axial phosphorus groups (Table III; these low-temperature results are discussed in the next section). The shifts for the conformer with axial phosphorus in the *cis*-4-methyl compounds **19, 21,** and **23** are downfield by 1.5–2.5 ppm from the shifts of the corresponding *cis*-4-*tert*-butyl compounds **7, 9,** and **11.** Since, however, the ^{31}P shift differences between axial and equatorial phosphorus groups given by the *cis*- and *trans*-4-*tert*-butyl PH_2, PMe_2, and PCl_2 compounds are quite large (12.3 to 19.7 ppm), an uncertainty of 1–2 ppm in the true shift of an axial phosphorus group leads to an uncertainty of only ±0.1 kcal/mol in the A values of PH_2, PCl_2, and PMe_2 as determined by the chemical shift method.

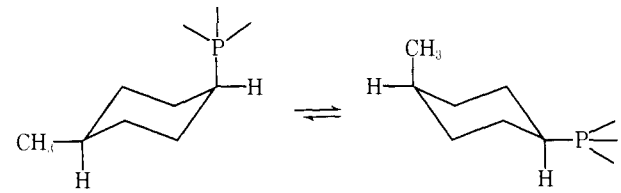
More serious difficulties were present in the case of the $P(OMe)_2$ group. First, the ^{31}P shifts for the *cis*- and *trans*-4-*tert*-butyl model compounds **13** and **14** differed by only 2.6 ppm. More importantly, the shifts for both the *cis*- and *trans*-4-*tert*-butyl compounds and the *cis* and *trans*-4-methyl compounds **25** and **26** were found to have a unique and sizable temperature dependence; it may be presumed that rotational phenomena about the P–O–C bonds are involved, but this point requires further investigation. Thus the uncertainty of the A value for $P(OMe)_2$ determined by the chemical shift method may be as large as ±0.3.

A values for the tetravalent phosphorus functions $P(S)Me_2$ and $P^+Me_3(I^-)$ could not be reasonably calculated from the chemical shift data in Table I, since the differences for the *cis*- and *trans*-4-*tert*-butyl model compounds were very small (0.8 and 1.2 ppm). In fact, there was no apparent difference in the shifts of the conformationally mobile *cis*-4-methyl sulfide **27** and the *trans* isomer **28,** while in the quaternary salts **29** and **30** the shift difference was only 0.2 ppm. This may suggest identity of the steric environment about P in the cis and trans forms, which would imply that in the case of the tetravalent phosphorus functions, the equilibrium for the *cis*-4-methyl compounds is largely controlled by the bulky phosphorus group:

Table III. ^{31}P Shifts for 4-Methylcyclohexylphosphorus Compounds at 183 K[a]

Conformer	P substituent			
	$-PH_2$	$-PMe_2$	$-PCl_2$	$-P(OMe)_2$
trans-eq P, eq Me	−111.0	−43.7	+194.6	+183.6
cis-eq P, ax Me	−110.2	−44.2	+194.1	+182.3
cis-ax P, eq Me	−133.4	−57.2	+210.4	+187.8

[a] Cis–trans mixtures, 25% in vinyl chloride solution.



Indeed, $P(S)Me_2$ or $P^+Me_3(I^-)$ may approach the size of the $C(CH_3)_3$ group (A value ≥4);[26] this point seems more conveniently examined by ^{13}C NMR spectroscopy, a study now in progress.[19] This raises the question of whether nonchair forms contribute to the structure of the *cis*-4-*tert*-butyl compounds **15** or **17,** as proposed for *cis*-1,4-di-*tert*-butylcyclohexane.[29] Since **15** and **17** are solids, this possibility can be explored by x ray analysis, which we plan to do in the future.

Direct Measurement of Conformer Population at Low Temperatures. Early in this study we found that the ^{31}P signal for only the equatorial conformer of monosubstituted cyclohexylphosphorus compounds **1, 2,** and **3** could be observed from 300 to 183 K. In the case of **1,** no reproducible signals for an axial conformer could be detected even when the more sensitive Fourier mode was employed. Likewise, the proton NMR signal for the PMe_2 doublet of **2** and the low-field half of the signal for PH_2 in **1** were identical at 183 K with those found at room temperature. The signal-to-noise ratio of the spectra obtained for **1, 2,** and **3** at 183 K was excellent, in some cases about 100:1. These results were consistent with the strong equatorial preference already noted, and pointed to the desirability of using the *cis*-4-methyl compounds for low-temperature studies. As noted previously, the presence of the *cis*-4-methyl groups results in a more balanced equilibrium (ca. 1:1). Results for the tertiary phosphine system are typical. The proton-decoupled ^{31}P spectrum at 300 K of a neat 43:57 mixture of **21** and **22** showed two peaks (Figure 1). The trans isomer (**22**), almost totally composed of the diequatorial conformer, absorbed at −42.5 ppm, while the time-averaged signal for the two cis (**21**) conformers appeared at −49.0. As the temperature was lowered, the signal for the trans isomer remained sharp and in the same position, while the signal for cis gradually broadened until at about 240 K it appeared to vanish in the baseline. Use of vinyl chloride as a solvent for the phosphines allowed spectra to be obtained at lower temperatures (Figure 1). Between 240 and 220 K, the cis signal re-

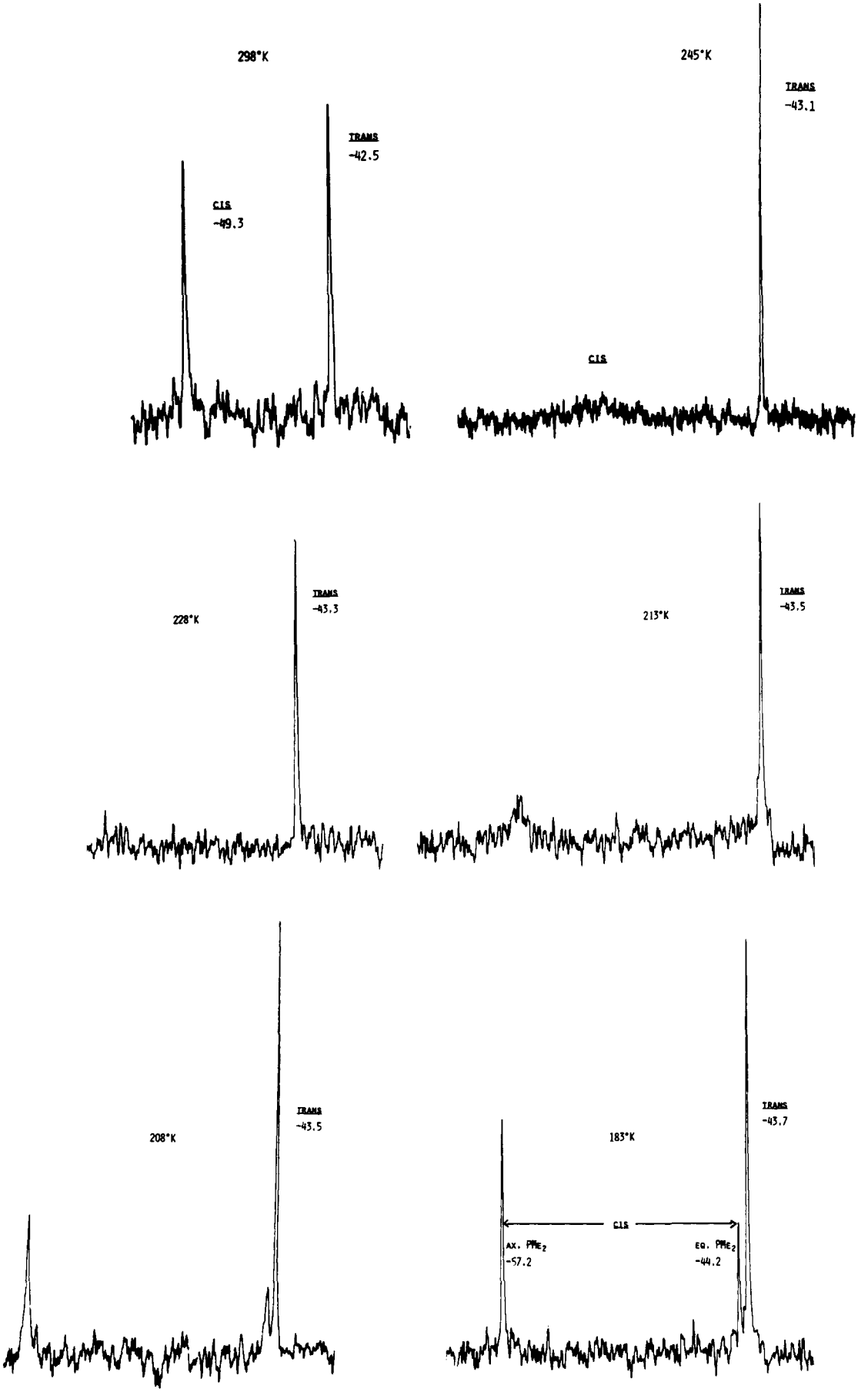


Figure 1. ^{31}P NMR spectra of *cis*- and *trans*-4-methylcyclohexyldimethylphosphine over the temperature range 183 to 298 K.

mained in the baseline, while the trans signal remained sharp. At 208 K, two new signals could be distinguished in the spectrum (Figure 1). As the temperature was lowered further, these two signals rapidly became sharper, and the final measurement at 183 K showed three equally sharp peaks. The new peak at −44.2, close to the trans diequatorial signal (−43.7), was assigned to the cis conformer with equatorial PMe_2. The peak for the conformer with axial PMe_2 appeared at −57.2, which is near the shift (−54.8) for the axial PMe_2 of the *cis*-4-*tert*-butyl model compound **9**. Similar variable-temperature spectra were obtained for the other *cis*-4-methylcyclohexyl trivalent phosphorus compounds **19, 23,** and **25.**

In all cases the coalescence temperature (T_c) for the temperature-dependent signals was 215 ± 4 K. From T_c and the ^{31}P peak separation ($\Delta\nu$ in Hz) between the two signals at the low-temperature limit (183 K) a free energy of activation ($\Delta G_{T_c}^{\ddagger}$) of 9.6 ± 0.4 kcal/mol was calculated from the approximate Gutowsky-Holm formula.[30] This value confirms that the phenomenon being observed is the reversal of the cyclohexane ring, derivatives of which have $\Delta G^{\ddagger}$ in the range 9.5 to 12 kcal/mol.[31]

The disappearance of the ^{31}P signal for one isomer near the coalescence temperature is a phenomenon of some interest. It is a consequence of the considerable shift range encompassed by the signals for the two equilibrating conformers. Without any other information, it allowed unequivocal assignment of cis structure to the isomer. This assignment is the same as reached by several other lines of evidence, as already mentioned.

As seen in Table III, the axial or equatorial disposition of the 4-methyl group has a small effect (0.5-0.8 ppm) on the ^{31}P shift of an equatorial PH_2, PMe_2, or PCl_2 group. The direction of this effect is not consistent, however; in the PMe_2 and PCl_2 cases an axial 4-methyl group results in a slight shielding (0.5 ppm) of equatorial phosphorus, while it results in deshielding (0.8 ppm) in the PH_2 case.

Equilibrium constants (eq P/ax P) at 183 K were determined for the four trivalent phosphorus groups in the *cis*-4-methylcyclohexyl series usually by peak height ratios for the two cis conformers. Use of peak area measurements gave ratios that differed negligibly, and A values were within ±0.05 units. The A values at 183 K, again calculated from the additivity of free energy differences, are presented in Table II. The two NMR methods gave values that are quite consistent for the PH_2, PMe_2, and PCl_2 groups. Since $\Delta S°$ between axial and equatorial conformers of monosubstituted cyclohexanes is generally between 0 and 1 eu, A values obtained at low temperature are expected to be within 0.1 kcal/mol of room-temperature values.[32]

As previously stated, the accuracy of the determination of the A value for the $P(OMe)_2$ group by the chemical shift method at 300 K (1.9 ± 0.3) suffered from the fact that the *cis*- and *trans*-4-*tert*-butyl model compounds had ^{31}P shifts that differed by only 2.6 ppm. The A value found at low temperature (1.5 ± 0.1) should be more representative for $P(OMe)_2$, since this method uses only peak areas to determine conformer populations in the *cis*-4-methylcyclohexyl system.

Jensen and coworkers have maintained in ^1H NMR spectroscopy that the low-temperature peak area method is more direct and accurate than the chemical shift method, since the former method eliminates the use of 4-*tert*-butyl model compounds and the assumptions inherent in their use.[6,32] As pointed out in a recent review,[33] the two methods do often give results that are in the same range (±0.1 to 0.2 kcal/mol), and this is seen in the present study. The low-temperature method is not without its own sources of error, however. Thus, differential saturation may influence signal size and give erroneous equilibrium constants; Jensen and coworkers[32] showed that the signals due to the less-populated conformer will saturate less readily than those of the more stable conformer. However, this problem should not have introduced significant error into the measurements of the present study, since low radio frequency observing powers were carefully chosen to avoid saturation and the two *cis*-4-methyl conformers were of relatively equal stability and population. Another problem is related to the determination of the low-temperature ^{31}P spectra under conditions of proton noise decoupling; the possibility existed that a differential nuclear Overhauser effect prevailed for the ^{31}P signals for the axial and equatorial phosphorus functions. However, this was ruled out by demonstrating that the same conformer ratios were obtained from the undecoupled and the proton-decoupled spectra.

Trends in *A* Values. The four trivalent phosphorus functions studied here are seen to have quite large A values. In part, the sizable free energy difference between conformers may be associated with destabilization of the axial conformer through interaction with the axial 3,5-hydrogens; to the extent that they reflect steric compression, the relatively upfield ^{13}C NMR shifts for C-3,5 in the *cis*-4-*tert*-butyl model compounds[19] point this out. However, other steric interactions must also be considered; Wertz and Allinger[34] focus attention on gauche H-H interactions, and Katritzky and coworkers[35] in studying amine functions consider also the interaction with the 2,6-hydrogens. The measured A value is a manifestation of the complex interplay among several molecular features, with relief of strain where possible by changes in bond and torsion angles, and we cannot at this time fully account for the magnitude of the A values we have observed. A recent discussion of structural effects on A values[6] suggests that lengthening of the bond attaching the substituent to the ring might be expected to diminish the A value, but this is clearly not seen in our data. This is particularly obvious from comparing A values for PH_2 to NH_2 (Table IV). Indeed, a comparison of similar oxygen and sulfur functions (Table IV) shows the same to be true here also. Since the reverse is known for the halogens,[6] the presence of hydrogen may be important in establishing the destabilizing interactions for the group 5 and 6 elements.

We recognize a similarity in our A value trends for phosphines to those established for amines.[35] On replacement of hydrogen on nitrogen by methyl, the A value becomes smaller (1.2 vs. 1.0), an effect attributed to a significant interaction between the methyl of equatorial NHMe with the 2,6-hydrogens. Development of such an interaction in PMe_2, when equatorial, might counterbalance any increase in the axial PMe_2 interaction with the axial 3,5-hydrogens, thus accounting for the lack of difference in its A value from PH_2. An extension of this thinking may account for the larger A value of PCl_2 relative to PMe_2; destablization of the equatorial form is not experienced, since the P-Cl bond is not as able as PC-H to interact with the 2,6-hydrogens, and there is no compensation for the increased interaction of axial PCl_2 with the 3,5-hydrogens. Examination of the data for comparable oxygen and sulfur functions (Table IV) reveals that this effect of methylation is present here also.

It has been pointed out[34] that moving to the right in a row of elements in the periodic system is accompanied by a decrease in A value. Certainly the values for CH_3, NH_2, OH, and F follow this trend. In the next row of the system, insufficient data have been available up to the present to confirm this relation. We can now add the value for PH_2 to those for SH and Cl, and indeed we see that the trend is again being followed. By this logic, one would expect the A value for SiH_3 to be as large or larger than PH_2, and con-

Table IV. Comparative A Values

Group 5 elements		Group 6 elements	
Function	A value[a]	Function	A value
$-NH_2$	1.2[b] (1.08)	$-OH$	0.6[d]–0.97[e]
$-NHMe$	1.0[b] (0.96)	$-OCD_3$	0.547[e]
$-NMe_2$	c (0.87)		
$-PH_2$	1.6	$-SH$	1.20[e]
$-PMe_2$	1.5–1.6	$-SCD_3$	1.07[e]
$-PCl_2$	1.9–2.0		
$-P(OMe)_2$	1.5–1.9		

[a] Values in parentheses are calculated; others are experimental. [b] See ref 35. [c] No reliable value yet available; see reference in footnote b. [d] E. L. Eliel and M. H. Gianni, *Tetrahedron Lett.*, 97 (1962). [e] See ref 6.

ceivably as large as that for CH_3. The only silicon function for which an A value has been experimentally obtained is $SiCl_3$, where 0.459 has been reported.[32] However, recent theoretical considerations of conformational aspects of silicon chemistry predict considerably larger values for SiH_3 (1.26[36] and 1.47[37]), approaching the range we might expect from the periodic system trend. Experimental attempts to define this value[36] have been unsuccessful, but it is possible that techniques involving ^{29}Si NMR as employed in the present paper for ^{31}P might be useful.

Experimental Section

General. Boiling points are uncorrected; melting points were taken on a Mel-Temp apparatus and are corrected. ^1H NMR spectra were obtained on JEOL MH-100 or Varian T-60 spectrometers using neat samples or $CDCl_3$ solutions, with tetramethylsilane as an internal reference. Room-temperature (300 K) ^{31}P NMR spectra (Table I) were obtained on a Bruker HFX-10 spectrometer at 36.43 MHz on neat samples or $CDCl_3$ solutions, and are referenced to external 85% H_3PO_4 with negative values upfield and positive downfield. Proton noise decoupling was generally employed. A 1-mm coaxial capillary containing hexafluorobenzene, trichlorofluoromethane, or 1,2-dibromotetrafluoroethane served as an external heteronuclear lock. Proton noise-decoupled Fourier transform ^{13}C NMR spectra were obtained at 22.62 MHz on neat liquids or $CDCl_3$ solutions utilizing C_6F_6 in a 3-mm coaxial capillary as an external heteronuclear lock; chemical shifts are referenced to internal TMS. Complete ^{13}C spectral details will be published elsewhere.[19] Diethyl ether and tetrahydrofuran were dried by distilling from lithium aluminum hydride. Dimethylthiophosphinyl chloride, bp 80–83° (16 mm) [lit.[38] 72–75° (12 mm)], and dimethylphosphinous chloride, bp 72–73° [lit.[38] 72–75°], were prepared by the procedure of Maier.[38] *trans*-4-*tert*-Butylcyclohexanol was prepared from a cis, trans mixture of the alcohol (Aldrich Chemical Co.) by the equilibration procedure of Eliel,[39] mp 75–78° [lit.[40] mp 75–78°]. 4-Methylcyclohexanol (80% trans, 20% cis) was prepared by the method of Noyce and Denney,[41] bp 85–88° (23 mm) [lit.[41] 89–91° (40 mm)]. *cis*-4-*tert*-Butylcyclohexyl chloride, bp 101–105° (21 mm) [lit.[42] bp 125° (49 mm)], and 4-methylcyclohexyl chloride (92% cis, 8% trans), bp 59.5–60° (23 mm) [lit. [43] cis bp 34–36° (4 mm)], were prepared from the above alcohols by treatment with triphenylphosphine[44] in refluxing CCl_4. Grignard reagents were prepared from the above chlorides by the general procedure of Gilman and Zoellner.[45] Cyclohexylphosphine (**1**) was obtained from Aldrich Chemical Co. and was used as received. Since all of the following preparations of cyclohexylphosphorus compounds are based on recently summarized general procedures,[14] complete experimental details are not included. Most of the 4-alkylcyclohexylphosphorus compounds were studied as cis, trans mixtures; compositions were determined by ^{31}P NMR. Because of their air sensitivity, analyses were generally not performed on trivalent compounds.

Preparation of Phosphonous Dichlorides. The reaction of PCl_3 with the appropriate alkylzinc chloride[16] (method A) or dialkylcadmium reagent[17] (method B) gave the following compounds.

***cis*- (23) and *trans*- (24) -4-Methylcyclohexylphosphonous Dichloride.** Method A gave **23** (45%)-**24** (55%) in 51% overall yield, bp 59–62° (0.2 mm); ^1H NMR (neat) δ 0.8–1.0 (complex, CH_3), 1.0–2.8 (complex, cyclohexyl). Method B gave **23** (41%)-**24** (59%) in 56% overall yield, bp 86–92° (3 mm), 1.0–2.8 (complex, cyclohexyl).

***cis*- (11) and *trans*- (12) -4-*tert*-Butylcyclohexylphosphonous Dichloride.** Method A gave **11** (53%)-**12** (47%) in 52% overall yield, bp 85.5–87° (0.35 mm); ^1H NMR (neat) δ 0.88 (s, $C(CH_3)_3$), 0.9–2.5 (complex, cyclohexyl); partial ^{13}C NMR (neat) δ 23.8 (d, $^3J_{PC}$ = 9 Hz, C-3,5 for **11**), δ 27.1 (d, $^3J_{PC}$ = 11 Hz, C-3,5 for **12**). Another run gave a 37% yield of **11** (52%)-**12** (48%). Fractionation through a 12-in. glass helices packed column gave an initial cut, bp 65–65.5° (0.07 mm), composed of 80% (**11**)-20% (**12**). Method B gave a mixture of **11** (36%) and **12** (64%) in 56% overall yield. Fractionation gave a final cut, bp 65–66° (0.02 mm), composed of 12% **11** and 88% **12**.

Preparation of Primary Phosphines. Reduction of the above cyclohexylphosphonous dichlorides with $LiAlH_4$[14] provided the following compounds.

***cis*- (19) and *trans*- (20) -4-Methylcyclohexylphosphine.** A mixture of **23** (41%) and **24** (59%) gave **19** (40%)-**20** (60%) in 33% overall yield, bp 61–62° (20 mm); ^1H NMR (neat) δ 0.8–1.0 (complex, CH_3), 1.0–2.6 (complex, cyclohexyl), 4.23 (d, $^3J_{HH}$ = 4 Hz, downfield half of PH_2 for **20**), 4.30 (d, $^3J_{HH}$ = 7 Hz, downfield half of PH_2 for **19**).

***cis*- (7) and *trans*- (8) -4-*tert*-Butylcyclohexylphosphine.** A mixture of **11** (45%) and **12** (55%) gave **7** (51%)-**8** (49%) in 64% overall yield, bp 108–109° (20 mm); ^1H NMR (neat) δ 0.87 (s, $C(CH_3)_3$), 0.95–2.50 (complex, cyclohexyl), 3.57 (d, $^3J_{HH}$ = 6 Hz, downfield half of PH_2 for **8**), 3.67 (d, $^3J_{HH}$ = 8 Hz, downfield half of PH_2 for **7**); partial ^{13}C NMR (neat) δ 21.8 (d, $^3J_{PC}$ = 2 Hz, C-3,5 for **7**), 28.5 (d, $^3J_{PC}$ = 9 Hz, C-3,5 for **8**). Another run with a mixture of **11** (15%) and **12** (85%) gave a 50% yield of **7** (15%)-**8** (85%), bp 105–105.5° (16 mm).

Preparation of Tertiary Phosphines. The reaction of the appropriate cyclohexyl Grignard reagent with dimethylphosphinous chloride[14] (method A), and of the appropriate cyclohexylphosphorus dichloride with methylmagnesium iodide[14] (Method B), gave the following compounds.

Cyclohexyldimethylphosphine (2). Method A gave **2** in 26% yield, bp 94–98° (51 mm); ^1H NMR (neat) δ 0.91 (d, $^2J_{PH}$ = 3 Hz, $P(CH_3)_2$), 1.0–2.3 (complex, cyclohexyl). Method B gave **2** in 31% yield, bp 71–76° (16 mm).

***cis*- (21) and *trans*- (22) -4-Methylcyclohexyldimethylphosphine.** Method A gave a mixture of **21** (10%) and **22** (90%) in 58% overall yield, bp 28.5–30.5° (0.05 mm); ^1H NMR (neat) δ 0.8–1.0 (complex, CH_3), 0.97 (d, $^2J_{PH}$ = 2.3 Hz, $P(CH_3)_2$), 1.0–2.5 (complex, cyclohexyl). From a mixture of **23** (45%) and **24** (55%), method B gave **21** (43%)-**22** (57%) in 51% overall yield, bp 39.5–41° (0.4 mm).

***cis*- (9) and *trans*- (10) -4-*tert*-Butylcyclohexyldimethylphosphine.** Method A gave a mixture of **9** (15%) and **10** (85%) in 52% overall yield, bp 65–66° (0.07 mm); ^1H NMR ($CDCl_3$) δ 0.87 (s, $C(CH_3)_3$), 0.96 (d, $^2J_{PH}$ = 2.7 Hz, $P(CH_3)_2$), 1.0–2.1 (complex, cyclohexyl); partial ^{13}C NMR ($CDCl_3$) δ 23.5 (d, $^3J_{PC}$ = 8 Hz, C-3,5 for **9**), 28.0 (d, $^3J_{PC}$ = 11 Hz, C-3,5 for **10**). Another run gave a mixture of **9** (5%) and **10** (95%). From a mixture of **11** (80%) and **12** (20%) method B gave **9** (79%)-**10** (21%) in 29% overall yield, bp 64–66° (0.2 mm).

Preparation of Phosphonites. The reaction of the appropriate cyclohexylphosphonous dichloride with methanol in the presence of triethylamine[14] gave the following compounds.

Dimethyl cyclohexylphosphonite (4)[46] was prepared in 43% yield, bp 87–90° (8 mm); ^1H NMR (neat) δ 1.0–2.0 (complex, cyclohexyl), 3.62 (d, $^3J_{PH}$ = 11 Hz, O-CH_3).

Dimethyl *cis*- (25) and *trans*- (26) -4-Methylcyclohexylphosphonite. A mixture of **23** (41%) and **24** (59%) gave **25** (49%)-**26** (51%) in 32% overall yield, bp 58–60° (0.5 mm); ^1H NMR (neat) δ 0.8–1.0 (complex, C-CH_3), 1.0–2.0 (complex, cyclohexyl), 3.51 (d, $^3J_{PH}$ = 11 Hz, $P(OCH_3)_2$ for **26**), 3.52 (d, $^3J_{PH}$ = 11 Hz, $P(OCH_3)_2$ for **25**).

Anal. Calcd for $C_9H_{19}O_2P$: C, 56.82; H, 10.07; P, 16.28. Found: C, 56.68; H, 10.18; P, 16.32.

Dimethyl *cis*- (13) and *trans*- (14) -4-*tert*-Butylcyclohexylphosphonite. A mixture of **11** (45%) and **12** (55%) gave **13** (51%)-**14** (49%) in 31% overall yield, bp 84–85° (0.35 mm); ^1H NMR (neat) δ 0.86 (s, $C(CH_3)_3$), 0.9–2.2 (complex, cyclohexyl), 3.56 (d, $^3J_{PH}$

= 11 Hz, $P(OCH_3)_2$ for **14**), 3.58 (d, $^3J_{PH}$ = 11 Hz, $P(OCH_3)_2$ for **13**); partial ^{13}C NMR (neat) δ 24.5 (d, $^3J_{PC}$ = 7 Hz, C-3,5 for **13**), 27.4 (d, $^3J_{PC}$ = 9 Hz, C-3,5 for **14**).

Anal. Calcd for $C_{12}H_{25}O_2P$: C, 62.04; H, 10.85; P, 13.33. Found: C, 61.96; H, 10.88; P, 13. 22.

Another run with a mixture of **11** (28%) and **12** (72%) gave **13** (21%)-**14** (79%) in 43% overall yield, bp 85-87° (0.3 mm).

Preparation of Tertiary Phosphine Sulfides. The reaction of the appropriate cyclohexyl Grignard reagent with dimethylthiophosphinyl chloride[14] (method A), and the reaction of the appropriate tertiary phosphine with sulfur[14] (method B), were used to prepare the following compounds.

Cyclohexyldimethylphosphine Sulfide (5). The reaction of **2** with sulfur gave **5** in 50% yield, mp 113-113.5°; ^1H NMR ($CDCl_3$) δ 1.1-2.2 (complex, cyclohexyl), 1.66 (d, $^2J_{PH}$ = 13 Hz, $P(CH_3)_2$).

Anal. Calcd for $C_8H_{17}PS$: C, 54.51; H, 9.72; P, 17.57. Found: C, 54.38; H, 9.74; P, 17.43.

***cis*- (27) and *trans*- (28) -4-Methylcyclohexyldimethylphosphine Sulfide.** Method A gave **27** (less than 4%) and **28** (greater than 96%) in low overall yield, mp 104-104.5°; ^1H NMR ($CDCl_3$) for **28** δ 0.92 (d, $^3J_{HH}$ = 6 Hz, C-CH_3), 1.0-2.3 (complex, cyclohexyl), 1.68 (d, $^2J_{PH}$ = 12.5 Hz, $P(CH_3)_2$).

Anal. Calcd for $C_9H_{19}PS$: C, 56.81; H, 10.06; P, 16.28. Found: C, 57.04; H, 9.83; P, 16.55.

From a mixture of **21** (40%) and **22** (60%) method B gave **27** (40%)-**28** (60%) in 58% overall yield, mp 125.5-136°; ^1H NMR δ 0.92 (d, $^3J_{HH}$ = 6 Hz, C-CH_3 for **28**), 0.98 (d, $^3J_{HH}$ = 6 Hz, C-CH_3 for **27**), 1.0-2.3 (complex, cyclohexyl), 1.67 (d, $^2J_{PH}$ = 12 Hz, $P(CH_3)_2$ for **27** and **28**).

***cis*- (15) and *trans*- (16) -4-*tert*-Butylcyclohexyldimethylphosphine Sulfide.** Method A gave **15** (less than 5%)-**16** (greater than 95%) in 29% overall yield, mp 217.5-219.5° (sealed tube); ^1H NMR ($CDCl_3$) δ 0.86 (s, $C(CH_3)_3$), 0.9-2.2 (complex, cyclohexyl), 1.87 (d, $^2J_{PH}$ = 12.5 Hz, $P(CH_3)_2$ for **16**), 1.74 (d, $^2J_{PH}$ = 12 Hz, $P(CH_3)_2$ for **15**); partial ^{13}C NMR ($CDCl_3$) δ 23.2 (d, $^3J_{PC}$ = 4 Hz, C-3,5 for **15**), 27.3 (d, $^3J_{PC}$ = 13 Hz, C-3,5 for **16**).

Anal. Calcd for $C_{12}H_{25}PS$: C, 62.03; H, 10.85; P, 13.33. Found: C, 62.12; H, 10.83; P, 13.14.

From a mixture of **9** (15%) and **10** (85%) method B gave **15** (4%)-**16** (96%) in 61% overall yield, mp 220-223°; from a mixture of **9** (68%) and **10** (32%) method B gave **15** (50%)-**16** (50%) in 43% overall yield, mp 182-197°.

Preparation of Phosphonium Iodides. The quaternization of the appropriate tertiary phosphine with methyl iodide[14] gave the following compounds.

Cyclohexyltrimethylphosphonium Iodide (6). The quaternization of **2** gave **6** in 39% yield, mp 293-295° dec.

Anal. Calcd for $C_9H_{20}IP$: C, 37.78; H, 7.04; P, 10.82. Found: C, 37.58; H, 6.75; P, 10.53.

***cis*- (29) and *trans*- (30) -4-Methylcyclohexyltrimethylphosphonium Iodide.** From a mixture of **21** (10%) and **22** (90%) was obtained **29** (less than 5%)-**30** (greater than 95%), mp 210-213° dec; ^1H NMR ($CDCl_3$) δ 0.93 (d, $^3J_{HH}$ = 6 Hz, C-CH_3 for **30**), 1.01 (d, $^3J_{HH}$ = 7 Hz, C-CH_3 for **29**), 1.1-3.0 (complex, cyclohexyl), 2.19 (d, $^2J_{PH}$ = 14 Hz, $P(CH_3)_3$ for **30**), 2.20 (d, $^2J_{PH}$ = 14 Hz, $P(CH_3)_3$ for **29**).

Anal. Calcd for $C_{10}H_{22}IP$: C, 40.01; H, 7.40; P, 10.32. Found: C, 39.84; H, 7.40; P, 10.66.

From a mixture of **21** (43%) and **22** (57%) was obtained **29** (46%)-**30** (54%), mp 205-208° dec.

***cis*- (17) and *trans*- (18) -4-*tert*-Butylcyclohexyltrimethylphosphonium Iodide.** A mixture of **9** (less than 5%) and **10** (greater than 95%) gave **17** (less than 5%)-**18** (greater than 95%), mp 253-254° dec; ^1H NMR ($CDCl_3$) δ 0.85 (s, $C(CH_3)_3$), 0.9-2.8 (complex, cyclohexyl), 2.18 (d, $^2J_{PH}$ = 14 Hz, $P(CH_3)_3$ for **18**), 2.25 (d, $^2J_{PH}$ = 14 Hz, $P(CH_3)_3$ for **17**); partial ^{13}C NMR ($CDCl_3$) δ 23.8 (d, $^3J_{PC}$ = 4 Hz, C-3,5 for **17**), 26.5 (d, $^3J_{PC}$ = 15 Hz, C-3,5 for **18**).

Anal. Calcd for $C_{13}H_{28}IP$: C, 45.61; H, 8.26; P, 9.05. Found: C, 45.80; H, 8.32; P, 9.27.

A mixture of **9** (79%) and **10** (21%) gave **17** (79%)-**18** (21%), mp 206-208.5°.

Variable Temperature ^{31}P NMR Spectra. The instrumentation and some of the general technique have been outlined elsewhere.[2] Temperatures were measured with a copper-constantan thermocouple and were calibrated to 193 K by the method employing proton NMR signals of methanol. The freezing of $(CF_2Br)_2$ in the coaxial insert caused loss of the ^{19}F signal and provided a low-temperature (163 K) calibration point. Temperatures are probably accurate to ±2° at moderately low ranges (210 K) and ±4° at lower values (173 K). The variable temperature ^{31}P NMR spectra were obtained in the CW mode under conditions of proton noise decoupling. Cyclohexylphosphine (**1**) was also studied in the Fourier mode. The following compounds were run as vinyl chloride solutions at the given concentrations: **2** (50% v/v); **3** (50%); **19-20** mixture (25%); **21-22** mixture (25%); **23-24** mixture (25%); and **25-26** mixture (25%). The **21-22** mixture was also studied as a neat liquid. The primary phosphine **1** was studied as a 50% solution in trichlorofluoromethane or 1,2-dibromotetrafluoroethane; samples of **1** were degassed using several freeze-thaw cycles and sealed under vacuum. The fluorocarbon solvent served as an internal heteronuclear lock. For all other experiments $CFCl_3$ or CF_2BrCF_2Br was used as external heteronuclear locks.

Constants were determined at 183 K for the conformational equilibrium of the *cis*-4-methylcyclohexyl compounds **19, 21, 23,** and **25** by finding the peak height ratio for the two cis conformers; the measurements from three to eight scans were averaged, yielding a typical average deviation of ±0.05 for K_{equil}. In using this procedure it was first demonstrated that peak heights were proportional to peak areas. The observing radio frequency power was carefully controlled in order to avoid saturation of either conformer. The peak height ratio obtained from the proton-decoupled spectrum was shown to be equivalent to the peak area ratio from the undecoupled spectrum.

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A New Approach to Empirical Intermolecular and Conformational Potential Energy Functions. III. Application of EPEN to the Conformational Analysis of 1,2-Disubstituted Ethanes[1]

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Abstract: An empirical potential using electrons and nuclei (EPEN) is described briefly and used to study the conformational properties of a set of 1,2-disubstituted ethanes, $X{\cdot}CH_2{\cdot}CH_2{\cdot}Y$ where X,Y = CH_3, NH_2, or OH. Minimum-energy conformations and dipole moments predicted by the EPEN calculations are in reasonable agreement with available experimental data. The EPEN method provides a computationally rapid yet reliable tool for obtaining dihedral angles, relative energies, and dipole moments of local minimum-energy conformations, as well as the dihedral angles and heights of internal rotational barriers between local energy minima, for alkanes, amines, and alcohols.

One important aspect of chemistry and biochemistry is the elucidation and understanding of the conformational properties of small and large molecules. Considerable progress has been made in the development and implementation of conformational analysis of organic molecules using a wide range of experimental and theoretical techniques. The present report is concerned with a new approach to empirical conformational energy calculations,[3] developed from the concept that molecules should exhibit conformational properties expected from the interactive properties of their constituent electrons and nuclei. This approach makes use of an empirical potential using electrons and nuclei (EPEN).[4,5]

A brief description of EPEN has appeared earlier,[4] and initial tests[5] showed that this approach could reproduce the conformational characteristics of several alkanes, alcohols, amines, and carbohydrates without the need to resort to special add-on energy terms such as intrinsic torsional potentials[6] to treat interactions between atoms across a bond (1-4 interactions), or to special energy functions to treat interactions between atoms participating in a hydrogen bond.[6] It was also possible to compute the lattice constants and lattice binding energies of crystals with EPEN, using the same parameters;[4,5] by considering the lone-pair electrons explicitly, EPEN was found to account for both directionality and hydrogen-bond strength in the crystals studied to date.[4,5] In the present study, EPEN is used to calculate the dipole moments and all zero-gradient points on the conformational energy surfaces of several 1,2-disubstituted ethanes. Where possible, the results are compared to experimental data and to the results of recent ab initio molecular orbital calculations[7] on the same molecules.

Rigid geometry (fixed bond lengths and bond angles) has been used; the only degrees of freedom allowed are the dihedral angles for rotations about bonds. This approximation makes it possible to treat large molecules in a reasonable amount of computer time without significant losses of accuracy; there is experimental and theoretical evidence that bond lengths and bond angles in noncyclic molecules remain remarkably constant in different intermolecular environments and in different minimum-energy conformations.[6,8-16]

In the earlier papers,[4,5] we derived the EPEN parameters for C, N, and O fragments with approximately tetrahedral geometry about the heavy atom, and used these fragments and parameters to study the properties of some saturated molecules. We apply them here to some 1,2-disubstituted ethanes. Work is presently in progress to derive EPEN parameters for other molecular fragments that will be useful for the study of unsaturated molecules such as acids, esters, ketones, aldehydes, polypeptides, and proteins.

Empirical Potential Using Electrons and Nuclei (EPEN)

The derivation and parameterization of EPEN, based on the transferability of molecular fragments from one molecule to another, has been reported previously,[4] and only a brief description will be presented here. In the present formulation, each molecule is constructed from molecular fragments consisting of a single heavy atom (nonhydrogen) nucleus, any hydrogen atom nuclei bonded to this nucleus, and point charges representing the bonding and lone-pair electrons associated with this heavy-atom fragment.

The operational procedure for assembling a molecule