

JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

© Copyright 1986 by the American Chemical Society

VOLUME 108, NUMBER 11

MAY 28, 1986

NMR Isotope Shift and Perturbational MO Study of Conformation and Hyperconjugation in Cyclopentyl Cations

James H. Botkin,^{1a} David A. Forsyth,^{*1a} and Dennis J. Sardella^{1b}

Contribution from the Departments of Chemistry, Northeastern University, Boston, Massachusetts 02115, and Boston College, Chestnut Hill, Massachusetts 02167.

Received July 22, 1985

Abstract: The 1-methylcyclopentyl cation is shown to have the twist conformation through the additivity characteristics of the NMR isotope shifts at C⁺ induced by β -deuteration. The *trans*-2,5-*d*₂ isotopomer has an isotope shift that is smaller than expected on the basis of additivity. This small isotope shift is due to an isotope effect on the conformational equilibrium that is only possible in the twist conformation. The 1-(4-fluorophenyl)cyclopentyl cation also exists in the twist conformation. The ratio of β -CD₂ to β -CD₃ effects in these and other cations indicates that hyperconjugation is stronger for endocyclic methylene bonds than for exocyclic methyl bonds. A theoretical model, based on MINDO/3 calculations and a perturbational approach, provides a possible explanation for the relative magnitude of these isotope shifts.

Deuterium substitution at carbon atoms adjacent to the cation center in classical tertiary alkylcarbenium ions induces a downfield shift of the ¹³C NMR signal of the carbenium carbon.² Similar long-range, downfield NMR isotope shifts due to deuterium substitution at a carbon atom adjacent to the cation center in phenyldialkylcarbenium ions have been documented.³⁻⁷ These NMR isotope shifts due to β -deuteration have been postulated to be related to the hyperconjugative interaction and in this sense are analogous to β -deuterium kinetic isotope effects.²⁻⁷ In an effect fundamentally arising from vibrational differences, the C-D bond behaves as a poorer electron donor than a C-H bond in cationic hyperconjugation, resulting in decreased electron density in the π system of the cation and hence NMR deshielding.

Typical NMR isotope shifts are additive.^{8,9} However, non-additivity of NMR isotope shifts in carbocations may occur when C-H(D) bonds are involved in hyperconjugation and are also conformationally mobile, because of the imposition of an equilibrium isotope effect on the population of conformers that may have different intrinsic NMR isotope shifts. For instance, the nonadditivity of the ⁷ΔF(D) NMR isotope shifts¹⁰ at ¹⁹F for

successive deuteration in the methyl groups of the 2-(4-fluorophenyl)-2-propyl cation, **1**, has been attributed to an unequal population of rotamers for partially deuterated methyl groups, with preferential placement of C-D bonds out of alignment with the p-orbital at the cation center.⁴ In a recent communication we reported the determination of the conformation of the 1-(4-fluorophenyl)cyclopentyl cation, **2**, based on the additivity properties of the isotope shifts at ¹⁹F due to β -deuteration.⁶

In the present paper we report the determination of the conformation of the 1-methylcyclopentyl cation, **3**, by use of the additivity characteristics of the ²ΔC⁺(D) NMR isotope shifts at C⁺ due to β -deuteration. Cation **3** should be free of steric interactions between the C₁ substituent and the cyclopentyl ring that might influence the conformation of the ring system in **2**.

In addition to the empirical use of isotope shifts as a probe of conformation, we examine the question of exocyclic vs. endocyclic hyperconjugation through the relative magnitude of isotope shifts in **3** and in other cations. Furthermore, a theoretical model is developed that provides a possible explanation for the relative magnitude of isotope shifts in **3**, based on MINDO/3 MO calculations and a perturbational approach.

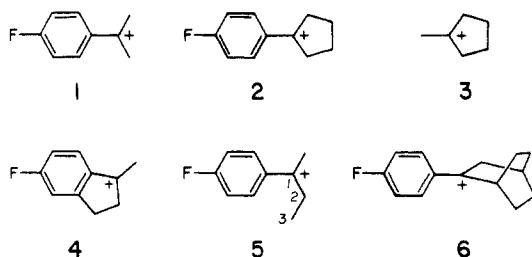
Results

The 1-methylcyclopentyl cations were prepared¹¹ by ionizing appropriately labeled 1-chloro-1-methylcyclopentanes with

- (1) (a) Northeastern University. (b) Boston College.
- (2) Servis, K. L.; Shue, F.-F. *J. Am. Chem. Soc.* **1980**, *102*, 7233.
- (3) Timberlake, J. W.; Thompson, J. A.; Taft, R. W. *J. Am. Chem. Soc.* **1971**, *93*, 274.
- (4) Forsyth, D. A.; Lucas, P.; Burk, R. M. *J. Am. Chem. Soc.* **1982**, *104*, 240.
- (5) Forsyth, D. A.; MacConnell, M. M. *J. Am. Chem. Soc.* **1983**, *105*, 5920.
- (6) Forsyth, D. A.; Botkin, J. H. *J. Am. Chem. Soc.* **1984**, *106*, 4296.
- (7) Forsyth, D. A.; Botkin, J. H.; Osterman, V. M. *J. Am. Chem. Soc.* **1984**, *106*, 7663.
- (8) Hansen, P. E. *Annu. Rep. NMR Spectrosc.* **1983**, *15*, 106.
- (9) Forsyth, D. A. *Isot. Org. Chem.* **1984**, *6*, 1.

(10) The notation ⁿΔX(Y) indicates the incremental change in the chemical shift of nucleus X induced by substitution by the heavy nucleus Y at a distance of *n* bonds from X.⁸ However, since the usual sign conventions for the fluorine and carbon chemical shift scales are opposite, to avoid confusion about the direction of effects in this paper, the ⁿΔX(Y) are defined so that all downfield isotope shifts are positive and upfield isotope shifts are negative.

(11) Olah, G. A.; Bollinger, J. M.; Cupas, C. A.; Lukas, J. *J. Am. Chem. Soc.* **1967**, *89*, 2692.



$\text{FSO}_3\text{H}/\text{SbF}_5$ in SO_2ClF at -117°C (liquid nitrogen/ethanol slush temperature) or SbF_5 in SO_2ClF at -78°C (dry ice/acetone slush temperature). The ^{13}C chemical shifts of unlabeled **3** were in agreement with those previously reported.^{2,12}

Table I summarizes the isotope effect on the C^+ chemical shift caused by deuterium substitution at the β -positions in **3** and also the isotope shifts at fluorine in **2**, which we reported in an earlier communication.⁶ The isotope shifts $^2\Delta\text{C}^+(\text{D})$ were measured in solutions containing unequal proportions of labeled and unlabeled **3**. Mixtures containing various proportions of labeled and unlabeled **3** were examined to make certain the peak assignments. The isotope shift for **3-methyl- d_3** is in good agreement with the value reported by Servis and Shue.² However, the isotope shift for **3-2,2,5,5- d_4** of 2.34 ppm is much larger than the value of 0.5 ppm reported by Servis and Shue.² Their lower value is apparently due to observation of a $\beta\text{-}d_1,\gamma\text{-}d_3$ cation produced by deuterium scrambling in the ring.

Preparation of ring-labeled methylcyclopentyl cations at -78°C results in scrambling of deuterium about the ring, which presumably occurs by a series of 1,2-hydride shifts.¹³ This scrambling was largely avoided by carefully preparing **3-2,2,5,5- d_4** at -117°C and immediately recording NMR spectra at -110°C . A mixture of **3** and **3-2,2,5,5- d_4** prepared and measured in this way provided the isotope shift of 2.34 ppm in Table I. Warming to -80°C causes scrambling which is slow on the NMR time scale but progresses to a large extent within 75 min.^{12c} The exchange process has been measured through line shape changes in ^1H spectra at higher temperatures.¹³ The scrambling was observed in the ^{13}C spectra through the appearance of additional peaks in the C^+ region which correspond to various d_4 isotopomers and in signals for $\text{C}_{2,5}$ and $\text{C}_{3,4}$ where the multiplicity due to C-D coupling depends on the pattern of labeling. These isotopomers have C^+ chemical shifts that depend primarily on the β -deuterium content, because the isotope shifts due to γ -deuteration are very small, as shown by comparison with the completely ring-deuterated d_8 cation. Eventually the scrambling in the **3- d_4** cations leads to a predominantly $\beta\text{-}d_1,\gamma\text{-}d_3$ cation, which is consistent with an equilibrium isotope effect that favors placement of deuterium in nonhyperconjugating positions. Another rearrangement with a higher energy barrier involving an equilibrium between **3** and the cyclohexyl cation¹³ was not observed when the cations were prepared at -110 or -78°C , as shown by the retention of methyl deuterium in **3-methyl- d_3** and the retention of ring deuterium in **3-2,2,3,3,4,4,5,5- d_8** .

Figure 1 shows the C^+ region of two of the ^1H -decoupled 15.0-MHz ^{13}C spectra obtained from two mixtures of labeled and unlabeled **3** prepared at -117°C . Figure 1a is a spectrum of partially labeled **3** mixed with unlabeled **3**. In this sample, the deuterium had been introduced by random exchange, so the deuterated species should be present in about 1:1:1 proportions of geminal, cis, and trans patterns of labeling. Indeed, the peak corresponding to **trans-3-2,5- d_2** is about one-half the size of the single peak corresponding to **3-2,2- d_2** and **cis-3-2,5- d_2** . Figure 1b is from a mixture enriched in **trans-3-2,5- d_2** and allows clear identification of which of the d_2 peaks corresponds to the trans-labeled isotopomer.

Table I. NMR Isotope Shifts^a at C^+ in **3** and Fluorine in **2**, **4**, and **5**

isotopomer	$^2\Delta\text{C}^+(\text{D})$	$^7\Delta\text{F}(\text{D})$		
	3	2	4	5^b
d_0	0.00	0.000		
$2\text{-}d_1$	0.42	0.138		0.085
trans 2,5- d_2	0.65	0.258		
cis 2,5- d_2	1.14	0.299		
2,2- d_2	1.14	0.299	0.286	0.180
2,2,5- d_3	1.59	0.440		
2,2,5,5- d_4	2.34	0.603		
3,3,4,4- d_4	(0.11) ^c	-0.065		
2,2,3,3,4,4,5,5- d_8	2.45	(0.538) ^c		
methyl- d_3	0.39		0.156	0.228
d_5^d			(0.442) ^c	0.402

^a In ppm, ± 0.02 ppm for ^{13}C and ± 0.005 ppm for ^{19}F . Positive sign indicates downfield shift in the deuterated compound. Measurement temperatures for **3**, **2**, **4**, and **5** were -110 , -75 , -93 , and -60°C , respectively. ^b Side chain numbered as shown with structure. ^c Derived from other listed results by assuming additivity. ^d Labeled as $\text{CD}_3\text{-C}^+$ and at C_2 .

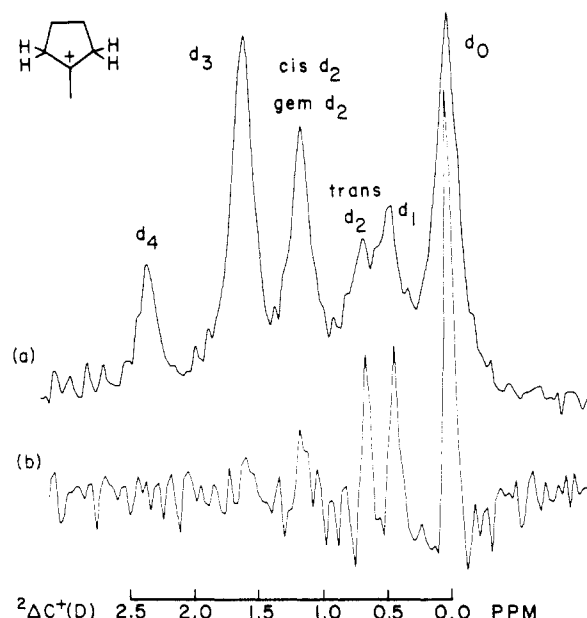


Figure 1. Downfield region of proton-decoupled 15.0-MHz ^{13}C NMR spectra at -110°C of the 1-methylcyclopentyl cation. The most upfield peak corresponds to the unlabeled cation at δ_c 336.9. The upper spectrum is of a mixture of the unlabeled and partially labeled ions. The lower spectrum is of another mixture enriched in the trans dilabeled cation; a resolution-enhancing weighting function was applied to the FID before Fourier transformation in generating this spectrum.

Isotope shifts at ^{19}F due to β -deuteration were determined for two additional ions, the 5-fluoro-1-methyl-1-indanyl cation, **4**, and the 2-(4-fluorophenyl)-2-butyl cation, **5**,¹⁴ which were prepared by ionization of the corresponding alcohols with $\text{FSO}_3\text{H-SbF}_5$ in SO_2ClF at -78°C . These isotope shifts are also listed in Table I.

Discussion

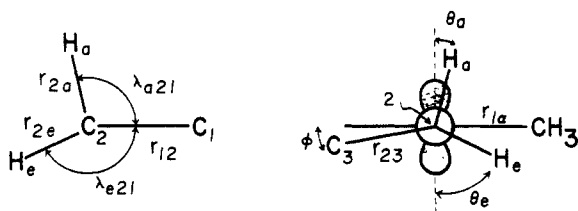
Conformation of Cyclopentyl Cations. A cyclopentyl cation could adopt a planar, envelope, or twist conformation. For either the envelope or the twist there would be two equivalent conformers, with a low-barrier, rapid interconversion between equivalent conformers.¹⁵ However, the degeneracy of the equilibrium between conformers could be removed by appropriate β -deuterium substitution. An equilibrium isotope effect would then result in

(12) (a) Our results, δ_c (ppm): 26.4, $\text{C}_{3,4}$; 36.7, CH_3 ; 63.3, $\text{C}_{2,5}$; 336.9, C_1 . (b) Kelly, D. P.; Brown, H. C. *Aust. J. Chem.* **1976**, *29*, 957. (c) Kelly, D. P.; Underwood, G. R.; Barron, P. F. *J. Am. Chem. Soc.* **1976**, *98*, 3106. (13) (a) Saunders, M.; Rosenfeld, J. J. *Am. Chem. Soc.* **1969**, *91*, 7756. (b) Brouwer, D. M.; Hogeveen, H. *Prog. Phys. Org. Chem.* **1972**, *9*, 179.

(14) Side chain numbered as shown for convenience of comparison in Table I.

(15) Lambert, J. B.; Papay, J. J.; Khan, S. A.; Kappauf, K. A.; Magyar, E. S. *J. Am. Chem. Soc.* **1974**, *96*, 6112.

Scheme III



of the methyl- d_3 isotopomer (k_H/k_D is 1.31 for the methylene and 1.26 for the methyl).¹⁶

The isotope shift evidence suggests that the hyperconjugative interaction of a C–H bond with the empty p-orbital of a cation center is stronger in the case of an endocyclic methylene bond than a methyl bond. The $\cos^2 \theta$ model of hyperconjugation is not sufficient to account for this phenomenon, even with the inclusion of an inverse inductive effect. It appears to be a matter of endocyclic vs. exocyclic interaction rather than interior vs. terminal positions, since the CD_2 effect is not larger than expected in **5**. The CD_3 effect is nearly the same in **1** and **5** at 0.230 and 0.228 ppm, respectively, but is reduced to 0.156 ppm in competition with the endocyclic methylene in **4**. The endocyclic methylene effect is very similar in **2**, **4**, and **6**. The $\Delta(CD_2)/\Delta(CD_3)$ ratio is largest in ion **3**, which has the strongest electron demand for hyperconjugative stabilization.

Theoretical Model. To further explore possible reasons for the unusually large ratio of CD_2 to CD_3 isotope effects in cyclopentyl cations, we introduce here a perturbational approach to the simulation of isotope effects. In this approach, a molecular orbital calculation is first performed on a particular structure to obtain the charge distribution and then a second calculation is performed with a shorter C–H bond. The perturbation by bond shortening is an attempt to model the isotope effect on the vibrationally averaged geometry which is associated with anharmonicity of the stretching vibration.^{9,18} The average geometries differ because isotopic substitution changes the frequencies and amplitudes of vibrational motions within anharmonic energy surfaces. These shorter “C–D” bonds¹⁹ are poorer electron donors to an adjacent cation center than normal C–H bonds and thus simulate the isotope effect on charge distribution which is assumed to be the origin of the downfield NMR isotope shifts. The difference in charge, Δq , at the C^+ atom between the perturbed structure and the reference structure gives the predicted isotope effect on C^+ charge arising from vibrational differences between isotopomers.

MINDO/3 MO calculations^{20,21} were carried out on 1-methylcyclopentyl cation in conjunction with various constraints on the geometry so as to create different conformations.²² Complete geometry optimization of cation **3** results in an envelope geometry in which the carbon framework is only slightly bent, with an angle between the approximate planes containing C_2 – C_1 – C_5 – CH_3 and C_2 – C_3 – C_4 – C_5 of about 3° . However, the methylene hydrogens at C_2 and C_5 are distinctly different. The cis pair of pseudoaxial C–H bonds are at a dihedral angle (θ) of 30° with respect to the p-orbital and $\theta = 40^\circ$ for the cis pair of pseudoequatorial C–H bonds. Key geometric features of this conformer and others are given in Scheme III and Table II.

Table II. Key Features of MINDO/3 Geometries for 1-Methylcyclopentyl Cation Conformers^a

	optimum envelope	planar ^b	slight twist	strong twist	bridged twist
distances, Å					
r_{12}	1.499	1.499	1.499	1.491	1.491
r_{23}	1.530	1.530	1.529	1.540	1.536
r_{34}	1.526	1.526	1.526	1.531	1.532
r_{1a}	1.460	1.461	1.460	1.464	1.467
r_{2a}	1.117	1.116	1.118	1.131	1.138
r_{2e}	1.115	1.116	1.114	1.105	1.104
r_{1e}	2.124	2.132	2.108	1.978	1.875
r_{1e}	2.147	2.140	2.133	2.247	2.260
bond angles, deg					
λ_{a21}	108	108	108	97	90
λ_{e21}	110	109	110	119	120
dihedral angles, deg					
θ_a	30	34	30	0	0
θ_e	40	35	40	63	66
ϕ	2	0	2	9	8

^a See text for qualitative descriptions of conformers. Geometries are fully optimized except for the constraints described. Definitions of distances and angles are indicated in Scheme III. ^b The carbon skeleton is planar, but the conformation of the methyl group prevents this plane from being a plane of symmetry.

The MINDO/3 energy surface for **3** is rather flat regarding mild deviations of the carbon skeleton from planarity. Restriction to planarity raises the energy by only 0.1 kcal/mol. A carbon skeleton with a slight twist was created by restricting the C_2 and C_5 methylene hydrogens to the same θ as in the optimized envelope structure but with one of the methylenes rotated in the opposite sense; this structure is only 0.2 kcal/mol higher in energy than the optimized structure.

As discussed below, no indication of greater methylene than methyl hyperconjugation was found in the planar or mildly nonplanar conformations, so further geometric distortion within the twist conformation was explored. A more strongly twisted geometry was created in the MINDO/3 calculations by restricting two trans C_2 – H_{ax} and C_5 – H_{ax} bonds to $\theta = 0^\circ$ (90° with respect to the C_1 – CH_3 bond) while still allowing all other structural parameters to optimize. The strong twist lies 10.0 kcal/mol higher than the fully optimized geometry, but it has some interesting features. First, electron donation to the cation center is better in this conformer, with a significantly higher electron density at C_1 than in the other three conformers (Table III). Second, the trans, axial C_2 – H , and C_5 – H bonds show strongly both hyperconjugative lengthening and a tendency toward bridging: the H_{ax} – C bond length is 1.131 Å and the angle H_{ax} – C_2 – $C_1 = 97^\circ$, while the H_{eq} – C_2 bond length is 1.104 Å and the angle H_{eq} – C_2 – $C_1 = 119^\circ$.

A partly H-bridged geometry in the twist form was created by restricting two trans C–H bonds to $\theta = 0^\circ$ as above for the strong twist but also setting the H_{ax} – C_2 – C_1 angle to 90° . This had the effect of further reducing the positive charge at the cation center and raising the energy slightly, to 10.8 kcal/mol above the fully optimized geometry. The bridging is highly unsymmetrical, with the C_2 – H_{ax} bond distance of 1.138 Å and the distance from this bridging hydrogen to C_1 of 1.876 Å.

To simulate the effect of a particular pattern of deuterium substitution in any particular cyclopentyl conformer, a MINDO/3 calculation was carried out with the appropriate C–H bond or bonds arbitrarily shortened by 0.02 Å while the rest of the geometric features were held constant. The charge at C^+ in the perturbed structure was then compared to the charge at C^+ in the reference structure. This perturbational model is somewhat crude and arbitrary,²³ but it is reasonable to expect at least a qualitative relationship between these charge perturbations and isotope effects on NMR chemical shifts at a cation center. The shorter “C–D” bonds are intended to simulate an isotope effect

(18) (a) Jameson, C. J. *J. Chem. Phys.* **1977**, *66*, 4983. (b) Osten, H. J.; Jameson, C. J. *J. Chem. Phys.* **1984**, *81*, 4288.

(19) Shorter C–D bonds have been demonstrated experimentally: (a) Bartell, L. S.; Kachitsu, K.; DeNeui, R. J. *J. Chem. Phys.* **1961**, *35*, 1211. (b) Richardson, E. H.; Brodersen, S.; Krause, L.; Welsh, H. L. *J. Mol. Spectrosc.* **1962**, *8*, 406. (c) Pawley, G. S.; Yeats, E. A. *Acta Cryst.* **1969**, *25B*, 2009.

(20) Bingham, R. C.; Dewar, M. J. S.; Lo, D. H. *J. Am. Chem. Soc.* **1975**, *97*, 1294, 1302, 1307.

(21) Stewart, J. J. P. Quantum Chemistry Program Exchange, Program No. 455.

(22) The MINDO/3 method is not particularly good for finding minimum energy ring conformations, but it has proven useful in calculations of carbocations: (a) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 4907. (b) Dewar, M. J. S.; Haddon, R. C.; Komornicki, A.; Rzepa, H. *J. Am. Chem. Soc.* **1977**, *99*, 377.

(23) The shortening of 0.02 Å, while more than double experimental values,^{18,19} was chosen so that round-off errors in charge densities would be relatively small.

Table III. Changes in MINDO/3 Charge at C⁺ in 3 Induced by 0.02 Å Bond Shortening in Simulation of Deuterium Substitution^a

isotopomer	$\Delta q \times 10^4$				
	optimum envelope	planar	slight twist	strong twist	bridged twist
d_0	0 (0.3945)	0 (0.3952)	0 (0.3942)	0 (0.3794)	0 (0.3617)
trans- 2,5- d_2^b	7	6	8,5	13, -1	15, -2
cis 2,5- d_2^b	7,6	6	7	6	7
2,2- d_2	7	6	6	6	7
2,2,5,5- d_4	13	12	13	12	14
CH ₂ D ^c	6	5	6	5	
CHD ₂ ^c	0	0	0	0	
CD ₃	6	5	6	4	3

^a Change in charge, Δq , is for total charge at C⁺. The initial fractional charge is given in parentheses for the d_0 compound. Positive sign indicates an increase in positive charge. ^b When two entries are given, there are two nonequivalent isotopomers. The first entry is for the diaxial pair and the second is for the diequatorial pair of shortened bonds. ^c CH₂D has C–D aligned with the C⁺ p-orbital; CHD₂ has C–D bonds out of alignment ($\theta \approx 63^\circ$).

on the vibrationally averaged geometry,^{18,19} and thus the model does not imply a breakdown of the Born–Oppenheimer approximation of electronic structure.

The results of the perturbational calculations are summarized in Table III. Some general features should be noted: (1) The effects of the bond-shortening perturbation on charge are additive. In any fixed conformation, the sum of the effects of partial “deuteration” of a group equals the effect of complete “deuteration”. (2) The calculated results correspond qualitatively to the pattern of effects which was anticipated and used as the basis for conformational analysis (vide supra). For example, in the twist conformers, the pair of trans pseudoaxial “C–D” bonds at C₂ and C₅ have a larger effect on C⁺ charge than either the trans pseudoequatorial pair or the cis axial–equatorial pair. (3) The bond perturbation effects on total charge at C⁺ do not follow a $\cos^2 \theta$ relationship, although the largest effects are seen when $\theta = 0^\circ$. The effect is essentially nil or slightly negative for “C–D” bonds with $\theta = 60^\circ$, in both methyl and strongly twisted methylene groups, but does not become any more negative for a “C–D” bond at $\theta = 90^\circ$ in a separate calculation which used an appropriately rotated methyl group. However, simulated isotope effects on the p-orbital electron density (not given here) do follow the $\cos^2 \theta$ function fairly well until bridging becomes significant in the partly bridged twist form.

On the basis of this perturbational approach, the greater endocyclic CD₂ effect on the C⁺ chemical shift compared to the exocyclic CD₃ effect may be related to the extent of H-bridging. As seen in Table III, the predicted CD₂ and CD₃ effects are nearly equal, $\Delta q(\text{CD}_2)/\Delta q(\text{CD}_3) = 1.0\text{--}1.2$, in the planar or mildly nonplanar forms where little bridging occurs. As the distortion toward H-bridging is included in the strong twist and partly bridged twist conformers, the CD₃ effect declines and the CD₂ effect increases slightly. In the partly bridged twist form, the ratio $\Delta q(\text{CD}_2)/\Delta q(\text{CD}_3)$ is calculated to be 2.3, which is approaching the experimental ratio ${}^2\Delta C^+(\text{CD}_2)/\Delta C^+(\text{CD}_3) = 2.9$ for the 1-methylcyclopentyl cation. Since the MINDO/3 method underestimates bridging compared to some ab initio methods,²⁴ it is quite reasonable that a weakly H-bridged twist structure could be the true minimum energy configuration for 3. The importance of both bridging and hyperconjugation would be expected to be reduced in less electron demanding ions, which is consistent with the lowered ratio of methylene to methyl isotope effects in the series of resonance stabilized ions 1, 2, 4, and 5. Clearly, this suggestion of partial H-bridging should be explored further in higher level calculations which would properly predict a twist structure as the minimum energy conformation for cyclopentyl cations.

Experimental Section

NMR Spectroscopy. A JEOL FX-60Q NMR spectrometer equipped with a dual ¹³C/¹H probe was used to obtain ¹H-decoupled ¹³C NMR spectra at 15.0 MHz. A 5-mm ¹⁹F probe was used to obtain ¹H-decoupled ¹⁹F NMR spectra at 56.2 MHz. The probe temperature was measured with an Omega 450AET Thermocouple Thermometer Type E. A concentric 2-mm (o.d.) capillary tube containing Me₄Si served as a

reference for some spectra. Isotope shifts were determined by using either a 2000-Hz spectral width and 8192 data points or a 4000-Hz spectral width and 16384 data points. Routine ¹H spectra were run on a Varian EM-360 spectrometer.

Preparation of Ions. A precooled solution of ca. 2 mmol of the appropriate alcohol or chloride precursor in SO₂ClF (0.5 mL) was added dropwise to a vigorously stirred (vortex mixer) solution of ca. 10 mmol 1:1 SbF₅/FSO₃H in SO₂ClF (1 mL) at either -117°C (liquid nitrogen/ethanol slush temperature) or -78°C (dry ice/acetone slush temperature). Some ions were prepared by ionizing the chloride precursor with SbF₅ in SO₂ClF at -78°C . Sulfuryl chloride fluoride was prepared from sulfuryl chloride and ammonium fluoride by the method of Woy-ski²⁵ and was distilled from SbF₅ before use. ¹³C NMR data have been reported previously for unlabeled 1,⁴ 2,²⁶ 3,^{2,14} and 5.²⁷ ¹³C NMR shifts (ppm) and J_{CF} values (Hz, in parentheses) for 4 at -86°C are as follows: C₁, 246.3 (6.1); C₂, 48.5; C₃, 23.8; C_{3a}, 184.5 (18.3); C₄ or C₆, 116.0 (23.2); C₆ or C₄, 121.2 (24.4); C₅, 179.2 (291); C₇, 138.8 (15.8); C_{7a}, 141.7; and CH₃, 34.7.

Ion Precursors. The labeled 1-chloro-1-methylcyclopentanes were prepared from labeled cyclopentanones by a two-step sequence involving reaction with methylmagnesium iodide followed by chlorination of the resulting alcohol with either thionyl chloride⁴ or concentrated aqueous HCl.²⁸ The labeled 5-fluoro-1-methyl-1-indanols and 2-(4-fluorophenyl)-2-butanols were prepared by reaction of either 5-fluoro-1-indanone or 1-(4-fluorophenyl)-1-propanone with methylmagnesium iodide, with the label in either the ketone or the Grignard reagent.

Preparation of 5-fluoro-1-indanone-2,2- d_2 was accomplished by exchange in refluxing dioxane/D₂O catalyzed by K₂CO₃. Similar exchange gave labeled 1-(4-fluorophenyl)-1-propanone.

Cyclopentanone randomly labeled at C₂ and C₅ to ca. 70% deuteration was prepared by exchange in D₂O/H₂O catalyzed by K₂CO₃. Cyclopentanone-2,2,5,5- d_4 was prepared by two exchanges in D₂O catalyzed by K₂CO₃. Cyclopentanone enriched in the trans 2,5- d_2 isotopomer was prepared by exchange in D₂O catalyzed by (1R,2S,3R,4R)-3-((dimethylamino)methyl)-1,7,7-trimethyl-2-norbornanamine.²⁹ Cyclopentanone-2,2,3,3,4,4,5,5- d_8 was prepared by the sequence of steps outlined below.

1,4-Dibromobutane-2,2,3,3- d_4 . A modification of the method of Della and Patney³⁰ was used. To a cold (ice-water bath) solution of concentrated sulfuric acid (14.5 mL) in 48% hydrobromic acid (67 mL) was added 1,4-butanediol-2,2,3,3- d_4 ^{30,31} (21 g, 0.22 mol), followed by concentrated sulfuric acid (24 mL). The mixture was heated to reflux for 3 h and then after cooling poured into 100 mL of ice water. The organic phase was removed and the aqueous layer was extracted with hexane (3 × 50 mL). The combined organic solutions were washed with water (100 mL), saturated NaHCO₃ (2 × 50 mL), and water (100 mL) and then dried (MgSO₄), filtered, and evaporated. The crude product was distilled (bp 55–58 °C (2.5 mm Hg)), giving 40.65 g (84%) of 1,4-dibromobutane-2,2,3,3- d_4 . ¹H NMR (CDCl₃) 3.42 ppm (s).

Cyclopentanone-3,3,4,4- d_4 . A slurry of 24% potassium hydride in mineral oil (41.0 g, 9.8 g KH, 0.25 mol) was washed with hexane (3 × 50 mL) to remove most of the oil, and 300 mL of THF added. The

(25) Woy-ski, M. M. *J. Am. Chem. Soc.* **1950**, 72, 919.

(26) Brown, H. C.; Kelly, D. P.; Periasamy, M. *Proc. Natl. Acad. Sci. U.S.A.* **1980**, 77, 6956.

(27) Brown, H. C.; Periasamy, M.; Liu, K.-T. *J. Org. Chem.* **1981**, 46, 1646.

(28) Norris, J. F.; Olmsted, A. W. *Org. Synth.* **1941**, Collect. Vol. 1, 144.

(29) Hine, J.; Li, W.-S.; Ziegler, J. P. *J. Am. Chem. Soc.* **1980**, 102, 4403.

(30) Della, E. W.; Patney, H. K. *J. Labelled Compd.* **1973**, 9, 651.

(31) Humski, K.; Malojcic, R.; Borcic, S.; Sunko, D. E. *J. Am. Chem. Soc.* **1970**, 92, 6534.

(24) Goddard, J. D.; Osamura, Y.; Schaeffer, H. F., III *J. Am. Chem. Soc.* **1982**, 104, 3258.

suspension was cooled (salt-ice bath) and then methyl methylsulfanyl-methyl sulfide^{32,33} (11.3 g, 0.091 mol) was added dropwise. After the mixture was stirred for 1 h, 1,4-dibromobutane-2,2,3,3-*d*₄ (20.0 g, 0.091 mol) was added dropwise. The mixture was stirred for 1.5 h with cooling and 20 h at room temperature and then quenched by adding 6 mL of 25% NH₄Cl. The mixture was filtered and evaporated and then taken up in 150 mL of diethyl ether, and 0.4 mL of 9 N sulfuric acid was added. The solution was stirred for 30 h and then poured into 20 mL of saturated NaHCO₃ solution. The aqueous phase was washed with diethyl ether (3 × 10 mL). The combined ethereal solutions were dried (MgSO₄), filtered, and evaporated to ca. 25 mL. The solution was stirred with a saturated solution of 15 g of NaHSO₃ for 30 min. The aqueous layer was removed and the ether phase stirred with a saturated solution of 5 g of NaHSO₃ for 30 min. The combined aqueous phases were treated

with 20% NaOH (50 mL) and extracted with diethyl ether. The combined ether extracts were dried (MgSO₄), filtered, and evaporated to give 4.45 g of cyclopentanone-3,3,4,4-*d*₄ (56%). ¹³C NMR (CDCl₃) 220.0, 37.7, 21.9 ppm (5 lines, *J*_{CD} = 20 Hz).

Cyclopentanone-2,2,3,3,4,4,5,5-*d*₈. A mixture of cyclopentanone-3,3,4,4-*d*₄ (4.0 g), D₂O (25 mL), and K₂CO₃ (0.4 g) was stirred for 19 h. The mixture was extracted with diethyl ether (4 × 10 mL). The combined ether extracts were evaporated and the exchange repeated as above. Workup as above followed by distillation (bp 126–129 °C) gave 1.80 g of a clear liquid. ¹³C NMR (CDCl₃) 220.2, 37.1 (p, *J*_{CD} = 20 Hz), 21.7 ppm (p, *J*_{CD} = 20 Hz).

Acknowledgment. We acknowledge support by the National Science Foundation (CHE-8211125) and helpful comments by Dr. Hans-Ullrich Siehl.

Registry No. 2, 51804-49-0; 3, 17106-22-8; 1,4-dibromobutane-2,2,3,3-*d*₄, 52089-63-1; cyclopentanone-3,3,4,4-*d*₄, 36219-23-5; cyclopentanone-2,2,3,3,4,4,5,5-*d*₈, 4477-17-2.

(32) Ogura, K.; Yamashita, M.; Furukawa, S.; Suzuki, M.; Tsuchihashi, G. *Tetrahedron Lett.* **1975**, 2767.

(33) Sing, L. Y.; Lindley, M.; Sundaraman, P.; Barth, G.; Djerassi, C. *Tetrahedron* **1981**, 37 (Supplement No. 1), 181.

Cation Effects on One Bond P–H Coupling Constants in Phosphinate Ion (Hypophosphite Ion). Experimental Evidence for the Effect of Association with Metal Cations on the Structure of Tetracoordinate Phosphorus Anions in Solution

Francis R. Spitz, José Cabral, and Paul Haake*

Contribution from the Departments of Chemistry and Molecular Biology and Biochemistry, Wesleyan University, Middletown, Connecticut 06457. Received July 22, 1985

Abstract: In order to test the proposal that metal ion association affects bond angles in phosphate anions, the effect of metal ions on the one bond P–H coupling constant, ¹*J*_{PH}, in phosphinate ion (hypophosphite ion), H₂PO₂[−], has been observed by studying couplings over a range of metal ion concentrations and extrapolating to complete association. Ions with small ionic radii, Li⁺, Mg²⁺, and Zn²⁺, have large effects, increasing ¹*J*_{PH} by 14, 18, and 26 Hz (Table I). Ba²⁺ has a small effect on ¹*J*_{PH}, and Sr²⁺ and Ca²⁺ have successively larger effects. Guanidinium ion has almost no effect. The pattern of these effects is consistent with increases in ¹*J*_{PH} due to bidentate coordination causing a decrease in the O–P–O bond angle. The result for Li⁺ indicates inner sphere coordination.

The association of cations with phosphate anions appears to have important functional consequences in binding to enzymes, enzymic catalysis, nucleic acids, and expression of genetic information.^{1–3} The structural effect on phosphates due to association with cations could be significant. On the basis of ³¹P NMR chemical shifts,^{4–8} it has been proposed that the O–P–O bond angle in phosphate anions is altered by the presence of small divalent metal cations due to electrostatic attractive forces. In this paper, we report experimental results which give information about the effects on O–P–O bond angles due to complexation with metal ions. The experimental method utilizes one bond P–H coupling constants (¹*J*_{PH}) for H₂PO₂[−].

Moedritzer et al.⁵ reported the ³¹P NMR spectra of over 200 phosphorus compounds including a few one bond P–H couplings. Van Wazer et al. studied the chemical shifts of phosphate esters and interpreted the results in terms of a quantum mechanically

derived relationship which involved the electronegativity of the phosphoryl oxygens, the degree of occupation of the d-orbitals, and the O–P–O bond angle.⁶ Gorenstein,^{7,8} after examining the ³¹P chemical shifts of various phosphate esters, proposed an empirical correlation between O–P–O bond angles and ³¹P chemical shifts. Citing disagreement between his data and Van Wazer's approach, he has concluded that the effects of d-orbital participation and phosphoryl oxygen electronegativity are minor. Prigodich used ³¹P NMR chemical shifts (relative to trimethylphosphate as a standard) to determine association constants of various mono- and dications with mono- and dianion phosphate esters.⁴ The association of small metal dications causes upfield chemical shifts in phosphate ester anions consistent with decreases in the O–P–O bond angle whereas monocations and large dications cause downfield chemical shifts consistent with predominance of electrostatic deshielding.

Hypophosphite anion (H₂PO₂[−]) is structurally similar to a phosphate anion but contains two P–H bonds. As is true for C–H couplings, the ¹*J*_{PH} is predominantly sensitive to the hybridization of the P–H bond.⁹ If the O–P–O angle decreases due to bidentate coordination to a metal ion, the p-orbital contribution from phosphorus in the P–O σ bonds will increase. This will cause increased s-orbital contribution from phosphorus in the P–H bonds

- (1) Pezzano, H.; Poso, F. *Chem. Rev.* **1980**, 80, 365.
- (2) Cooperman, B. S. *Met. Ions Biol. Syst.* **1976**, 5, 79.
- (3) Melchior, N. C. *J. Biol. Chem.* **1954**, 208, 615.
- (4) Haake, P.; Prigodich, R. V. *Inorg. Chem.* **1984**, 23, 457.
- (5) Groeneweghe, L. C. D.; Mair, L.; Moedritzer, K. *J. Phys. Chem.* **1962**, 66, 901.
- (6) Costello, A. J. R.; Glonek, T.; Van Wazer, J. R. *Inorg. Chem.* **1976**, 15, 972. Letcher, J. H.; Van Wazer, J. R. *J. Chem. Phys.* **1966**, 44, 815. *J. Chem. Phys.* **1966**, 45, 2915, 2926.
- (7) Gorenstein, D. G. *J. Am. Chem. Soc.* **1975**, 97, 898.
- (8) Gorenstein, D. G. *J. Am. Chem. Soc.* **1977**, 99, 2254.

- (9) (a) Pople, J. A.; McIver, J. W.; Ostlund, N. S. *J. Chem. Phys.* **1968**, 49, 2965. (b) Muller, N.; Pritchard, D. *J. Chem. Phys.* **1959**, 31, 768.