

Conformational Dependence of Isotope Effects for Hyperconjugating Methyl Groups. Nonadditivity of NMR Isotope Shifts in Benzylic Ions

David A. Forsyth,* Peter Lucas, and Robert M. Burk

Contribution from the Department of Chemistry, Northeastern University, Boston, Massachusetts 02115. Received June 1, 1981

Abstract: Deuterium substitution in the methyl groups induces long-range downfield shifts in ^{13}C NMR signals of the ortho and para positions of the phenyldimethylcarbenium ion. Similar downfield isotope shifts occur in ^{19}F signals of (*p*-fluorophenyl)carbenium ions upon deuteration of α -methyl groups. These NMR isotope shifts are analogous to secondary β -deuterium isotope effects on rates and equilibria and arise from hyperconjugative interactions. The effects of substituting entire CD_3 groups for CH_3 groups are additive, but the effects of deuterium substitution within a methyl group are not additive. The nonadditive behavior is attributed to unequal populations of the possible methyl conformations for partially deuterated methyl groups, so that each C-H(D) bond is not equally involved in hyperconjugation. This interpretation is supported by the observation of an isotope effect on the vicinal ^1H - ^{19}F coupling constant in the phenylmethylfluorocarbenium ion, PhCFCH_3^+ .

In this paper we report observations of long-range, deuterium isotope effects on NMR chemical shifts in stable benzylic cations which parallel observations of secondary β -deuterium isotope effects on the rates of $\text{S}_{\text{N}}1$ solvolysis reactions. Specifically, we examine the noncumulative nature of the effects of successive deuteration at β -C-H bonds in methyl groups. These results are related to the experiments of Shiner, Murr, and Heinemann on the solvolysis of deuterated *tert*-butyl chlorides, wherein the effects of successive deuteration within a single methyl group were found to be noncumulative, while the effects of substituting entire CD_3 groups were nearly cumulative.¹ Assuming a hyperconjugative origin for the β -deuterium isotope effect, Shiner and Humphrey² drew conclusions about the angular dependence of the isotope effect which were pointed out by Sunko, Szele, and Hehre to be in contradiction with the prediction of molecular orbital theory that the hyperconjugative interaction of a freely rotating methyl group with an adjacent p orbital should be independent of conformation.³

Shiner suggested that the nonadditive isotope effect indicated a strong conformational dependence of the isotope effect and suggested that the transition state with a C-H bond aligned anti to the chloride leaving group (or parallel with the p orbital in the cation) would have a lower energy than one with a C-D bond so aligned.¹ However, the equations derived to describe the observed effects in partially deuterated methyl groups were based on a purely statistical weighting of the possible conformations.¹ This treatment led to the attribution of the conformational effect entirely to a very strong angular dependence of the isotope effect² rather than a combination of angular dependence and energy-based weighting of the conformational populations. The suggested angular dependence^{1,2} was shown by Sunko, Szele, and Hehre to be incorrect, as it requires a conformationally dependent isotope effect for a methyl- d_3 group.³

Sunko, Hehre, et al. proposed a theoretically based model for β -deuterium isotope effects. These effects were considered to arise from a $\cos^2 \theta$ dependent hyperconjugative interaction and an angularly independent inductive interaction.^{3,4} However, their model was not applied to the problem of the nonadditive effects of successive deuteration in methyl groups. Although inclusion of the inductive interaction in their model does result in nonadditivity for freely rotating methyl groups, it does not fully account for the observed nonadditivity.⁵

Nonadditivity could also occur if methyl- d_1 and $-d_2$ groups were not free rotors, that is, if there were preferred conformations for the partially deuterated methyl groups. Shiner et al. and Melander and Saunders pointed out that since a C-H bond interacts with the p orbital more strongly than does a C-D bond, a cation conformation with a C-H bond parallel to the p orbital will be of lower free energy than a conformation with a parallel C-D bond.^{1,6} Although neither set of authors stated so explicitly, the energy difference requires that the rotamers in partially deuterated, hyperconjugating methyl groups be unequally populated.

We examine here the question of conformation and isotope effects of methyl groups by using isotope effects on NMR chemical shifts as a probe. Substitution by a heavier isotope ordinarily produces an upfield shift in NMR signals,⁷⁻⁹ and this intrinsic¹⁰ isotope effect on chemical shifts is ordinarily also a short-range phenomenon. In contrast, equilibrium isotope effects¹¹⁻¹³ may affect positions considerably removed from the site of substitution.^{14,15} However, both downfield and long-range effects of an intrinsic character were observed for ^{19}F signals of methyl (*p*-fluorophenyl)carbenium ions by Timberlake, Thompson, and Taft¹⁶ and, more recently, for ^{13}C shifts of a variety of carbocations by Servis and Shue.¹⁷ The downfield isotope shifts are analogous to secondary β -deuterium isotope effects on rates and equilibria and clearly derive from hyperconjugative interactions in which a β -C-H bond behaves as though it were a better electron donor than a β -C-D bond.^{16,17}

The additivity of NMR isotope shifts associated with deuteration of methyl groups is examined for a series of (*p*-fluorophenyl)carbenium ions. The ^{19}F chemical shift provides a sensitive

(5) In ref 1, Shiner found $k_{\text{H}}/k_{\text{D}}$ per deuterium to be 1.092, 1.096, and 1.100 for the *tert*-butyl- d_1 , $-d_2$, and $-d_3$ chlorides, respectively. Using the formulas in ref 3 and making the assumption of a freely rotating methyl group, the calculated $k_{\text{H}}/k_{\text{D}}$ values per deuterium are 1.097, 1.098, and 1.100. The calculated values are derived by using the observed $k(\text{CH}_3/\text{CD}_3)$ value, eq 6 in ref 3, and eq 1-3 in ref 1.

(6) Melander, L.; Saunders, W. H., Jr. "Reaction Rates of Isotopic Molecules"; Wiley-Interscience: New York, 1980; pp 176-178.

(7) For a brief summary of recent literature, see: Riskey, J. M.; Van Etten, R. L. *J. Am. Chem. Soc.* 1980, 102, 4609-4614.

(8) Batiz-Hernandez, A.; Bernheim, R. A. *Prog. Nucl. Magn. Reson. Spectrosc.* 1967, 3, 63-85.

(9) Wehrli, F. W.; Wirthin, T. "Interpretation of Carbon-13 NMR Spectra"; Heyden: London, 1976; p 108.

(10) Saunders, M.; Kates, M. R. *J. Am. Chem. Soc.* 1977, 99, 8071-8072.

(11) Saunders, M.; Jaffe, M. H.; Vogel, P. *J. Am. Chem. Soc.* 1971, 93, 2558-2559.

(12) Saunders, M.; Vogel, P. *J. Am. Chem. Soc.* 1971, 93, 2559-2561.

(13) Saunders, M.; Vogel, P. *J. Am. Chem. Soc.* 1971, 93, 2561-2562.

(14) Anet, F. A. L.; Dekmezian, A. H. *J. Am. Chem. Soc.* 1979, 101, 5449-5451.

(15) Anet, F. A. L.; Basus, V. J.; Hewett, A. P. W.; Saunders, M. *J. Am. Chem. Soc.* 1980, 102, 3945-3946.

(16) Timberlake, J. W.; Thompson, J. A.; Taft, R. W. *J. Am. Chem. Soc.* 1971, 93, 274-276.

(17) Servis, K. L.; Shue, F.-F. *J. Am. Chem. Soc.* 1980, 102, 7233-7240.

(1) Shiner, V. J., Jr.; Murr, B. L.; Heinemann, G. *J. Am. Chem. Soc.* 1963, 85, 2413-2416.

(2) Shiner, V. J., Jr.; Humphrey, J. S., Jr. *J. Am. Chem. Soc.* 1963, 85, 2416-2419.

(3) Sunko, D. E.; Szele, I.; Hehre, W. J. *J. Am. Chem. Soc.* 1977, 99, 5000-5005.

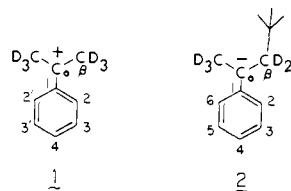
(4) DeFrees, D. J.; Hehre, W. J.; Sunko, D. E. *J. Am. Chem. Soc.* 1979, 101, 2323-2327.

Table I. ^{13}C NMR Shifts (δ_{C})^a and Isotope Shifts ($\Delta\delta_{\text{C}}$)^b for 1 and 2

positn	1		2	
	δ_{C}	$\Delta\delta_{\text{C}}^c$	δ_{C}	$\Delta\delta_{\text{C}}^c$
1	140.3	0.05	141.8	< 0.04
2,2'	141.7	-0.16	105.9	< 0.07
3,3'	132.5	< 0.06	128.1	< 0.07
4	155.4	-0.22	89.1	0.20
5			127.1	< 0.08
6			108.1	< 0.08
α	255.1	< 0.09	66.2	0.20
β -CH ₃	33.4	0.93	23.9	<i>d</i>
β -CH ₂			50.8	<i>d</i>
C(CH ₃) ₃			37.3	0.17
C(CH ₃) ₃			30.4	< 0.08

^a For undeuterated compounds, in parts per million from Me₄Si. Shifts for 1 at -60 °C were referenced to external (capillary) Me₄Si. Shifts for 2 at 0 °C were referenced to C₂ of THF (67.9 ppm). ^b $\Delta\delta_{\text{C}} = \delta_{\text{C}}(\text{undeuterated}) - \delta_{\text{C}}(\text{deuterated})$, determined from spectrum of mixture. Positive numbers are upfield shifts. ^c For each position where there was no discernible splitting of the peaks, the absolute value listed is half the line width. Error limits are ± 0.02 ppm for 1 and 0.03 ppm for 2. Both 1 and 2 were examined several times at 15 MHz and once at 67.9 MHz. ^d Signal for deuterated carbon was not detected.

probe of the effects of successive deuterium substitution within methyl groups of benzylic cations. To further demonstrate the hyperconjugative origin of the isotope effects, we also compare the ^{13}C chemical shifts in the phenyldimethylcarbenium ion 1 and the α -methyl- α -neopentylbenzyl anion 2. While the β -C-H(D)



bonds are involved in positive hyperconjugation in the cations, they should exhibit behavior associated with negative hyperconjugation in an anion.¹⁸

Results

Table I summarizes the isotope effect on ^{13}C chemical shifts caused by complete deuterium substitution at the β -positions in the dimethylphenylcarbenium ion 1, prepared¹⁹ by ionizing 2-chloro-2-phenylpropane with SbF₅ in SO₂ClF, and in the α -methyl- α -neopentylbenzyl anion 2, prepared²⁰ by the addition of *tert*-butyllithium to α -methylstyrene. The isotope effects, $\Delta\delta_{\text{C}}$, were measured in solutions containing unequal proportions of labeled and unlabeled material. Measurable peak separation due to the isotope effect was observed for the para and ortho carbons in 1, even in a 15-MHz ^{13}C spectrum (Figure 1). The peak separations were confirmed by measurement at 67.9 MHz. The long-range isotope effect was a downfield shift for both ortho and para carbons, 0.16 and 0.22 ppm, respectively. The results for 1 agree with the less precise values for 1 reported by Servis and Shue.¹⁷ In 2, the only observable long-range effect was an upfield shift of 0.20 ppm at the para carbon, again observed at both 15 and 67.9 MHz. A short-range, upfield $\Delta\delta_{\text{C}}$ was observed in both 1 and 2. The isotope effects were independent of temperature. Within experimental error, the peak separations for 1 were the same at -15 and -60 °C, and for 2 they were the same at 0 and -50 °C. The $\Delta\delta_{\text{C}}$ for 2 did not change upon the addition of excess

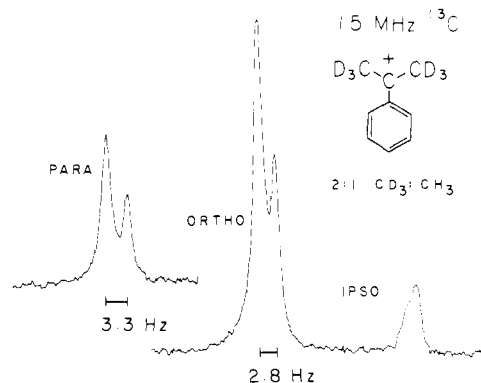


Figure 1. Partial 15.0-MHz ^{13}C NMR spectrum of 1 at -45 °C as a 2:1 mixture of the hexadeuterated and unlabeled ions. The proton-decoupled spectrum was obtained in 1000 scans at 500-Hz spectral width, using 8192 data points and 8.3-s pulse repetition rate.

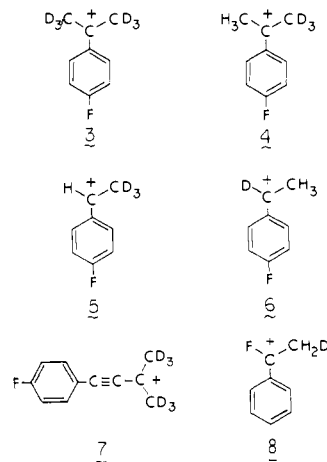
Table II. Deuterium-Induced Downfield Shifts in ^{19}F Resonances

compd	temp, °C	ϕ_{F} , ^a ppm	$\Delta\phi_{\text{F}}$ ^b	$\Delta\phi_{\text{F}}/n^c$
3	-18		0.440	0.073
3	-60	60.9	0.461	0.077
4	-15		0.226	0.075
4	-60	60.9	0.230	0.077
5	-19		0.315	0.105
5	-60	47.0	0.324	0.108
5	-121		0.335	0.112
6	-60	47.1	0.0 ^d	0.0
7	-40	77.5	0.284	0.047

^a ^{19}F chemical shifts are for the undeuterated compound in parts per million relative to CFCl₃. Shifts were measured relative to external (capillary) C₂Br₂F₄ and were converted to CFCl₃ by using $\phi_{\text{F}} = \phi_{\text{F}}(\text{obsd}) + 63.4$. Positive values are upfield from CFCl₃. ^b $\Delta\phi_{\text{F}} = \phi_{\text{F}}(\text{undeuterated}) - \phi_{\text{F}}(\text{deuterated})$; accuracy is ± 0.003 ppm. All isotope shifts are downfield. ^c Isotope shift per deuterium, where *n* is the number of deuterium atoms in the labelled ion. ^d No apparent separation in signal of 1.5-Hz line width. ^e From ref 16.

TMEDA, although the δ_{C} changed slightly.

We also prepared a series of deuterated (*p*-fluorophenyl)carbenium ions 3–6, since previous studies had demonstrated that



para- ^{19}F chemical shifts are more than 7 times more sensitive (in Hz) than are p - ^{13}C shifts to structural changes in phenylcarbenium ions.^{21,22} Isotope effects on the ^{19}F shifts in 3 and 5 were already known,¹⁶ and our results are in agreement. The ^{19}F chemical shifts and isotope effects for 3–7 are summarized in Table II. Spectra

(18) DeFrees, D. J.; Taagepera, M.; Levi, B. A.; Pollack, S. K.; Sumnerhays, K. D.; Taft, R. W.; Wolfsberg, M.; Hehre, W. J. *J. Am. Chem. Soc.* **1979**, *101*, 5532–5536.

(19) Previous preparations and reports of ^{13}C NMR data: Olah, G. A.; Porter, R. D.; Jeuell, C. L.; White, A. M. *J. Am. Chem. Soc.* **1972**, *94*, 2044–2052. Olah, G. A.; Westerman, P. W. *Ibid.* **1973**, *95*, 7530–7531.

(20) Previous preparation and report of ^{13}C data for undeuterated 2: Fraenkel, G.; Geckel, J. M. *J. Am. Chem. Soc.* **1980**, *102*, 2869–2880.

(21) Olah, G. A.; Westerman, P. W.; Forsyth, D. A. *J. Am. Chem. Soc.* **1975**, *97*, 3419–3427.

(22) Spear, R. J.; Forsyth, D. A.; Olah, G. A. *J. Am. Chem. Soc.* **1976**, *98*, 2493–2500.

Table III. ^{19}F NMR Shifts and Isotope Effects at -60°C for Different Preparations of 3

X ^a	acid ^b	ϕ_{F} , ^c ppm	$\Delta\phi_{\text{F}}$ ^d
-OH	FSO_3H	61.6	0.450
-OH	$\text{FSO}_3\text{H}/\text{SbF}_5$	62.3	0.456
-OH	SbF_5	61.1	0.443
-Cl	FSO_3H	60.9	0.461
-Cl	SbF_5	60.0	0.450

^a Indicates precursor: -OH is 2-(*p*-fluorophenyl)-2-propanol; -Cl is 2-(*p*-fluorophenyl)-2-chloropropane. ^b SO_2ClF is also present as solvent. ^c For undeuterated compound relative to CFCl_3 , as in Table II. ^d Downfield shifts due to isotope effect.

were obtained at 56.2 MHz for solutions containing unequal proportions of deuterated and undeuterated ions. In the four cases of β -deuterium substitution, 3, 4, 5, and 7, the isotope effect was a downfield shift of the ^{19}F resonance. No isotope effect was detected for α -deuterium substitution in 6.

The isotope effects on ^{19}F shifts were only slightly dependent on factors such as temperature, counterion, and concentration. The ^2H -induced shift, $\Delta\phi_{\text{F}}$, for ions 3-5 (Table II) increased slightly as temperature decreased. Varying the preparation of 3 by using either the carbinol or chloride as precursor and varying the acid used for the ionization resulted in small variations in ϕ_{F} and $\Delta\phi_{\text{F}}$ that were outside the range of experimental error, but which showed no obvious pattern or relationship (see Table III). The isotope effect for 3 in an approximately 1 M solution prepared from the chloride in $\text{FSO}_3\text{H}/\text{SO}_2\text{ClF}$ was not affected by sixfold dilution with SO_2ClF .

The additivity of isotope effects was examined in the *p*-fluorophenyl series. In Table II, it may be seen that the effect of one trideuteriomethyl group in 4 is very close to half the isotope effect observed for two trideuteriomethyl groups in 3. However, the results summarized in Table IV demonstrate that the effect of successive deuterium substitution in a particular methyl group is not additive for the long-range isotope effect. The nonadditivity is clear in the ^{19}F spectra of 4 and 5 wherein a single methyl group is labeled. In each case, spectra were obtained for solutions containing the unlabeled ion plus mono-, di-, and trideuterated ions (see spectrum for 5 in Figure 2). The β -deuterium isotope effect on the ^{19}F shift is smallest for the first deuterium introduced and is largest for the final deuterium substitution. Similar non-additivity was observed for 3, but the result is less useful because deuterium was distributed randomly between the two equivalent positions in the partially deuterated ions, so that some of the observed resonances were actually overlapping peaks from different species containing the same number of deuterium atoms.

The short-range isotope effect on the ^{13}C resonance of the methyl group is additive. Table IV gives the $\Delta\delta_{\text{C}}$ upon successive deuteration in the methyl group of (*p*-fluorophenyl)methyl-carbenium ion 5 and the neutral precursor to the ion 1-(*p*-fluorophenyl)-1-chloroethane (9). Although the isotope shift is slightly larger in the ion, each additional deuterium atom produces a constant effect in both cases, within experimental error.

It is also desirable to determine whether coupling constants involving the methyl protons are altered by isotopic substitution. Ions 3-6 exhibit coupling between the methyl protons and the para fluorine, but it is too small (~ 2 Hz) to be of use. Coupling with the α -H occurs in 5, but it could not be reliably measured in the methyl signal because of coupling of a similar magnitude to the fluorine and deuterium atoms in partially deuterated 5. However, coupling of the methyl protons with the α -F in the phenyl-methylfluorocarbenium ion 8 is large, first order, and easily measured in both the unlabeled and monodeuterated material.

The methyl ^1H NMR resonance at -60°C of unlabeled 8, PhCFCH_3^+ , is a doublet occurring at δ_{H} 3.94, with $^3J_{\text{HF}} = 22.58 \pm 0.24$ Hz. The methylene ^1H NMR resonance of $\text{PhCFCH}_2\text{D}^+$ at -60°C is a doublet of triplets at δ_{H} 3.91, with $^3J_{\text{HF}} = 21.60 \pm 0.24$ and $^2J_{\text{HD}} = 2.50$ Hz. Thus, the coupling constant is about 1 Hz smaller in the deuterated ion 8. Figure 3 shows the spectra at -20°C , where the coupling constant is the same for PhCFCH_3^+ at $^3J_{\text{HF}} = 22.58 \pm 0.24$ Hz, but it has slightly increased in

Table IV. Effect of Successive Deuteration on Chemical Shifts

(a) Long-Range Effect on Para-Fluorine Resonance					
compd	temp, $^\circ\text{C}$	$^1\Delta\phi_{\text{F}}$ ^a	$^2\Delta\phi_{\text{F}}$	$^3\Delta\phi_{\text{F}}$	$^t\Delta\phi_{\text{F}}$
4	-15	0.068	0.074	0.084	0.226
5	-19	0.090	0.108	0.116	0.315
5	-83	0.092	0.112	0.126	0.330
5	-121	0.091	0.112	0.132	0.335
(b) Short-Range Effect on Methyl Carbon Resonance					
compd	temp, $^\circ\text{C}$	$^1\Delta\delta_{\text{C}}$ ^b	$^2\Delta\delta_{\text{C}}$	$^3\Delta\delta_{\text{C}}$	$^t\Delta\delta_{\text{C}}$
5	-65	0.29	0.31	0.31	0.91
9	26	0.29	0.29	0.28	0.86

^a $^n\Delta\phi_{\text{F}}$ is the ^2H -induced downfield shift in the ^{19}F resonance (in ppm) produced by the n th deuterium, where n is the number of deuterium atoms. Where $n = t$, the total effect of a CD_3 group is given. Accuracy is ± 0.003 ppm. ^b $^n\Delta\delta_{\text{C}}$ is the ^2H -induced upfield shift (in ppm) in the methyl ^{13}C resonance, produced by the n th deuterium atom. Where $n = t$, the total effect of CD_3 is given. Accuracy is ± 0.02 ppm.

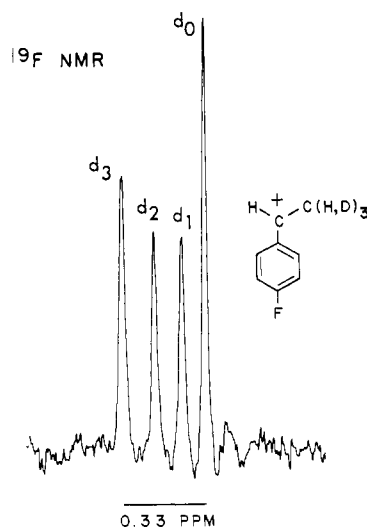


Figure 2. Proton-decoupled 56.2-MHz ^{19}F NMR spectrum of 5 at -83°C as a mixture of all the isotopomers involving deuteration at methyl. The spectrum was obtained in 20 scans at 1000-Hz spectral width, using 16384 data points and 8.3-s pulse repetition rate.

$\text{PhCFCH}_2\text{D}^+$ to $^3J_{\text{HF}} = 21.85 \pm 0.24$ Hz. The isotope effects on the chemical shift and on the coupling constant were confirmed by measuring the ^1H spectrum of the labeled and unlabeled ions in the same solutions. The ion precursors have identical couplings to fluorine: $^3J_{\text{HF}} = 18.09$ Hz for PhCF_2CH_3 and $^3J_{\text{HF}} = 18.08$ Hz for $\text{PhCF}_2\text{CH}_2\text{D}$, with $^2J_{\text{HD}} = 2.02$ Hz.

Discussion

Hyperconjugative Origin of Isotope Effects. Since the long-range isotope effects and downfield shifts reported here are unusual, it is important to establish that these are intrinsic isotope effects on chemical shifts and not equilibrium effects. It could be suggested that an isotope effect perturbing an equilibrium between free ions and ion pairs, or different ion-paired species, or some other sort of equilibrium might produce the observed chemical shift separations. The lack of any significant dependence on temperature, concentration, counterion, or acid medium effectively rules out an equilibrium in the case of the cations. For the anion 2, the isotope effect is independent of temperature and added TMEDA; thus an isotope effect on an equilibrium involving ion pairs is unlikely.

Several lines of evidence indicate that the long-range isotope effects on chemical shifts arise from the hyperconjugative interactions of the methyl groups and are transmitted via the π system. Taft et al. demonstrated that the magnitude of the isotope

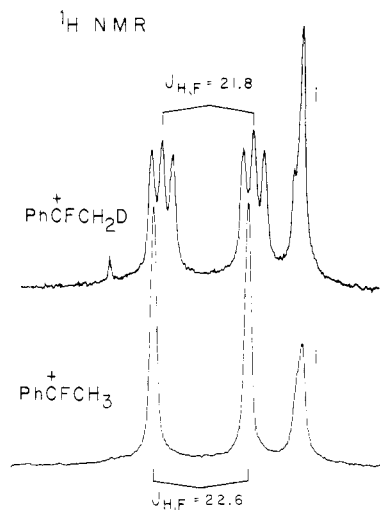


Figure 3. Partial 59.75-MHz ^1H NMR spectrum of **8** at $-20\text{ }^\circ\text{C}$ (upper) and corresponding spectrum of the unlabeled ion (lower). The spectrum was obtained in 100 scans at 1000-Hz spectral width, using 16384 data points and 8.3-s pulse repetition rate. Impurity (i) peak is due to protonated acetophenone from hydrolysis of the difluoride precursor.

effect on the ^{19}F shift in methyl(*p*-fluorophenyl)carbenium ions was related to the electron demand on the methyl group.¹⁶ For instance, the isotope effect in **4**, where two methyl groups stabilize the charge, is smaller than in **5** (see Table II), where only one methyl is present. An "inductive" origin of the isotope effect is ruled out by the lack of an isotope effect on the ^{19}F shift in **6**, where a nonhyperconjugating α -hydrogen is replaced by deuterium. A "steric" origin of the isotope effect is ruled out by the isotope effect in **7**, where a triple bond has been interposed between the sidechain and the phenyl ring.¹⁶ An isotope effect on ^{13}C chemical shifts in **1** (Table I) is observed at the ortho and para positions but not at the meta position, strongly suggesting transmission via the Π system. Finally, the long-range isotope effects for **1** and **2** are in the opposite direction: downfield isotope shifts at ortho and para carbons in the cation **1** and an upfield shift at the para carbon in the anion **2**.

Hyperconjugation is generally accepted as the major source of secondary β -deuterium isotope effects on rates of reaction involving carbocation-like transition states and on equilibria involving carbocations.²³⁻²⁵ Reduction of the vibrational force constants for β -C-H bonds is associated with hyperconjugative electron donation to a carbocation center from the C-H bonds. Because the difference in vibrational energy between C-H and C-D bonds is less in an electron-deficient species than in a neutral reactant, substitution of deuterium for hydrogen results in a slower reaction ($k_{\text{H}}/k_{\text{D}} > 1$) or a shift toward the undeuterated carbocation in an equilibrium. Similarly, secondary β -deuterium isotope effects have been observed for reactions involving negative ions and have been cited as evidence for negative hyperconjugation.^{18,26} In negative hyperconjugation, a β -C-H bond is weakened by accepting electron density.

In contrast to kinetic isotope effects, isotope effects on NMR shifts involve the properties of only a single species, not a change between ground state and transition state. Our observations of β -deuterium NMR isotope effects in the ions are indicative of differences in electron distribution produced by the isotopic substitution. In the cations, the CH_3 group "appears" to be a better electron donor than the CD_3 group. These NMR isotope effects mimic the direction of the known kinetic isotope effects as though an electronic substituent effect were responsible. However, these apparent "electronic" effects must be considered

in the context of the theory of isotope effects.

The apparent "electronic" effects are simply a reflection of the fact that observed NMR shifts are vibrationally and rotationally averaged rather than values for a fixed nuclear configuration. For isotopically substituted molecules, the C-D bonds have lower zero-point vibrational energies and smaller vibrational amplitudes than C-H bonds. If vibrations are anharmonic, the average C-D bond length will be shorter. Thus, even though the same electronic potential energy surface applies to each ion in an isotopically related series, the ions may all have different average electron distributions that fundamentally arise from the vibronic differences rather than ordinary substituent electronic effects. The kinetic isotope effects and the charge distribution differences inferred from the NMR isotope effect are both reflections of the hyperconjugative weakening of the β -C-H bond. However, it is the vibrational differences and not the charge distribution differences that are the cause of the kinetic isotope effect.

A theoretical study was recently conducted by Hehre et al. of hyperconjugation in relation to gas-phase, equilibrium β -deuterium isotope effects in positive and negative ions.¹⁸ The theoretical calculations were based on the harmonic approximation and used equilibrium geometries and force constants obtained from ab initio molecular orbital calculations. The long-range NMR isotope effects we have observed suggest that use of the harmonic approximation may be a source of difficulty in predicting kinetic equilibrium isotope effects. Although isotope effects on NMR shifts may occur even if vibrations are harmonic,²⁷ a recent theoretical treatment suggests that the chief contribution to isotope shifts comes from the anharmonic part of the expression for NMR chemical shielding.²⁸ If so, the NMR isotope shifts associated with hyperconjugating C-H bonds imply that anharmonicity may have to be accounted for in calculations of the energy differences responsible for secondary β -deuterium isotope effects on equilibria and reaction rates.

Nonadditivity of Isotope Effects for Methyl Groups. The long-range, downfield shifts induced by deuterium substitution in methyl groups of cations **1**, **3-5**, and **7** are evidence that, in effect, a C-H bond is a better hyperconjugative electron donor than a C-D bond. Two CD_3 groups in **3** produce twice the isotope shifts of the single CD_3 group in **4**; i.e., the effects of substituting entire CD_3 groups for CH_3 groups are additive. This is the expected result for two methyl groups equally involved in hyperconjugation. However, the effects of deuterium substitution within a methyl group are not additive. Each successive deuterium substitution produces a larger, long-range, downfield shift of the ^{19}F signal in methyl(*p*-fluorophenyl)carbenium ions **3-5**. The effect of a single deuterium atom in a methyl group is less than one-third the effect of three deuterium atoms. This nonadditive behavior can best be attributed to unequal populations of the possible methyl conformations for partially deuterated methyl groups, so that each C-H(D) bond is not equally involved in hyperconjugation.

A consequence of the hyperconjugative origin of β -deuterium isotope effects is that the isotope effect should exhibit a dependence on the dihedral angle between the C-H(D) bond and the vacant *p* orbital of the cation center. The angular dependence has been clearly demonstrated experimentally for kinetic isotope effects²³ and is supported by theoretical studies. Sunko, Hehre, et al. suggested a $\cos^2 \theta$ dependence for the secondary deuterium isotope effect of individual C-H(D) bonds, where θ is the dihedral angle of the C-H(D) bond with respect to the *p* orbital.³⁴ A $\cos^2 \theta$ dependence has also been used to explain the variation of $^1J_{\text{CH}}$ in groups adjacent to cationic carbons,²⁹ and it is the angular dependence that was proposed to account for ESR hyperfine splitting constants that result from the overlap of alkyl C-H bonds and a *p* orbital.³⁰

(23) Shiner, V. J., Jr. *ACS Monogr.* **1970**, No. 167, Chapter 2.

(24) Sunko, D. E.; Borcic, S. *ACS Monogr.* **1970**, No. 167, Chapter 3.

(25) Melander, L.; Saunders, W. H., Jr. "Reaction Rates of Isotopic Molecules"; Wiley: New York, 1980; Chapter 6.

(26) DeFrees, D. J.; Bartmess, J. E.; Kim, J. K.; McIver, R. T., Jr.; Hehre, W. J. *J. Am. Chem. Soc.* **1977**, *99*, 6451-6453.

(27) Maciel, G. E.; Ellis, P. D.; Hafer, D. C. *J. Phys. Chem.* **1967**, *71*, 2160-2164.

(28) Jameson, C. J. *J. Chem. Phys.* **1977**, *66*, 4983-4988.

(29) Kelly, D. P.; Underwood, G. R.; Barron, P. F. *J. Am. Chem. Soc.* **1976**, *98*, 3106-3111.

(30) Heller, C.; McConnell, H. C. *J. Chem. Phys.* **1960**, *32*, 1535-1539.

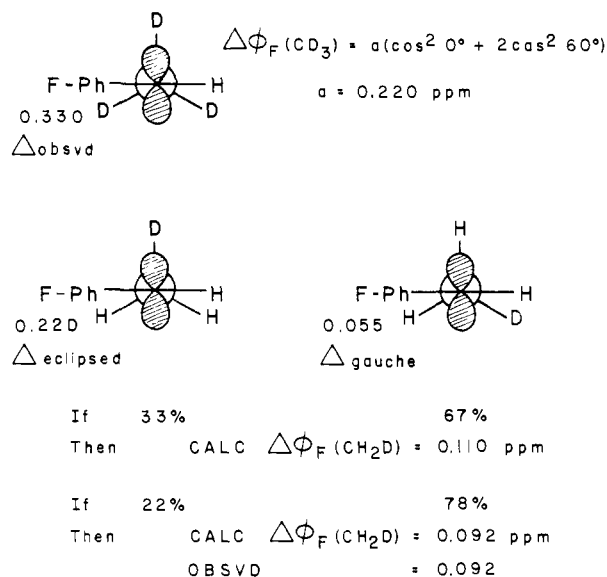


Figure 4. Scheme outlining the effect of different populations of methyl conformations on the isotope shift in monodeuterated **5**.

Sunko, Szele, and Hehre showed that the total hyperconjugative interaction of a freely rotating methyl group with the adjacent p orbital must be independent of conformation, and that this requirement is satisfied by the $\cos^2 \theta$ relationship for the three C-H(D) bonds.³ Thus, a CD_3 group should produce an isotope effect that is independent of conformation. If freely rotating CH_2D and CHD_2 groups are also assumed, this theoretical model predicts that the isotope shift, $\Delta\phi_F(\text{CH}_2\text{D})$, produced by a hyperconjugating CH_2D group should be one-third of the $\Delta\phi_F(\text{CD}_3)$, or in the case of kinetic isotope effects,³¹ $k(\text{CH}_3)/k(\text{CH}_2\text{D}) = [k(\text{CH}_3)/k(\text{CD}_3)]^{1/3}$. In fact, isotope effects on NMR chemical shifts due to *freely rotating* methyl groups should be cumulative regardless of the precise angular dependence of the hyperconjugative interactions,³² as long as the inherent capability of a C-D bond to hyperconjugate does not depend on how many deuterium atoms are present. The contradiction between the theoretical predictions and experimental observations for methyl group isotope effects can be overcome by assuming that methyl- d_1 and - d_2 groups are *not* free rotors, i.e., that there are preferred conformations for the partially deuterated methyl groups. Alternatively, the observed nonadditivity could be explained by alteration of the capability of individual C-D bonds to hyperconjugate, perhaps due to vibrational coupling, as the methyl group is successively deuterated. However, the evidence discussed below favors the first explanation.

The details of the explanation based on preferred conformations are as follows. If the angular dependence for hyperconjugation by a C-H(D) bond is assumed to be $\cos^2 \theta$, then the long-range isotope effect due to a particular C-D bond is given by eq 1, where

$$\Delta\phi_F(\text{C-D}) = a \cos^2 \theta \quad (1)$$

a is the maximum possible effect in a specific ion. From the observed isotope effect of the CD_3 group, which is the sum of the effects of three C-D bonds, the value of a can be found and the isotope effect may then be calculated for a CH_2D or CHD_2 group. Figure 4 shows these calculations for the example of the methyl(*p*-fluorophenyl)carbenium ion **5**. For the sake of convenience, a conformation is shown with one of the C-D bonds eclipsing the

p orbital (any other conformation gives the same result). The $\Delta\phi_F(\text{CD}_3)$ is due to one C-D bond with $\theta = 0^\circ$ and two C-D bonds with $\theta = 60^\circ$. At -83°C , the observed $\Delta\phi_F(\text{CD}_3)$ is 0.330 ppm, which defines a to be 0.220 ppm.

The calculated $\Delta\phi_F(\text{CH}_2\text{D})$ for an eclipsing C-D bond in the monodeuterated ion is simply a , or 0.220 ppm. The other two CH_2D conformations place the C-D bond in a gauche alignment, $\theta = 60^\circ$, with the calculated $\Delta\phi_F(\text{CH}_2\text{D})$ at 0.055 ppm. The observed $\Delta\phi_F(\text{CH}_2\text{D})$ is the weighted average, Δ_{av} (eq 2), of the

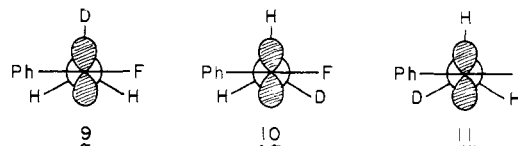
$$\Delta_{\text{av}} = p\Delta_a + (1-p)\Delta_b \quad (2)$$

expected values for the eclipsed and gauche conformers, Δ_a and Δ_b , where p is the fraction of eclipsed conformer. If these three conformers are equally populated, the weighted average gives the calculated $\Delta\phi_F(\text{CH}_2\text{D}) = 0.110$ ppm or exactly one-third the isotope effect of the CD_3 group. However, if the conformational populations are allowed to be other than the statistical distribution, then the weighted average will match the observed $\Delta\phi_F(\text{CH}_2\text{D})$ when $p = 0.22$, i.e., by having 22% of the C-D eclipsed alignment and 78% of the C-D gauche alignments.

In a similar fashion with use of eq 1 and 2, the calculated fraction of C-D eclipsed forms for dideuterated **5** is 57% at -83°C , as opposed to the statistical 67%. At -19°C , C-D eclipsed forms are calculated to be 24% for monodeuterated **5** and 59% for dideuterated **5**, thus showing the expected decrease in conformational preference with increase in temperature. The fraction of C-D eclipsed conformer for monodeuterated **4** at -15°C is calculated to be 27% and 59% for C-D eclipsed conformers in the dideuterated ion. The smaller conformation preference exhibited in monodeuterated ion **4** than in **5** is consistent with the lower demand per methyl group for hyperconjugative stabilization.

Strictly speaking, the data do not allow one to conclude that methyl conformers with C-H(D) bonds eclipsing the p orbital are at energy minima. Alternative schemes are possible in which the rotational minima occur when C-H(D) bonds eclipse bonds from the cation center or occur at various skew conformations. However, the same general conclusion would be reached in any case, that for partially deuterated methyl groups involved in hyperconjugation, the preferred conformers in the set of possible conformers are those in which C-H bonds are better aligned for hyperconjugation than C-D bonds.

Other evidence supports our explanation of the nonadditivity as being due to preferred conformations rather than an explanation based on alteration of the capability of individual C-D bonds to hyperconjugate. The strongest evidence is the observation that vicinal ^1H - ^{19}F coupling is smaller in $\text{PhCFCH}_2\text{D}^+$ (**8**) than in PhCFCH_3^+ . Assuming a rapid equilibrium between the three conformations **9**-**11**, the average ^1H - ^{19}F coupling would be the



same for CH_2D as for CH_3 if all three conformers were equally populated. If, as we propose, there is a preference for C-H to take an eclipsed position, as in **10** and **11**, rather than a gauche position, then the average coupling constant would be smaller because the C-H bonds are more often at a dihedral angle of 90° to the C-F bond. The coupling constant is expected to be at a minimum for a dihedral angle of 90° according to the Karplus relationship for vicinal ^1H - ^{19}F coupling.³³ Variation of vicinal coupling constants with variation in conformational populations is well documented,³³ but intrinsic, secondary isotope effects on coupling constants are highly unusual and have only been reported for one-bond coupling.^{34,35}

(31) Neglecting the inductive effect.³

(32) For NMR isotope shifts, the isotope effect of a CD_3 group can be represented by $\Delta_{\text{CD}_3} = \Delta_a + 2\Delta_b$, where Δ_a and Δ_b are the isotope shifts due to C-D bonds at dihedral angles of 0° and 60° , respectively. For a CH_2D group, $\Delta_{\text{CH}_2\text{D}} = (1/3)\Delta_a + (2/3)\Delta_b$. The entire effect could reside in Δ_a and additive behavior would still be observed. This is not true for kinetic isotope effects. As described in ref 1, kinetic isotope effects can be represented by $k(\text{CH}_3)/k(\text{CH}_2\text{D}) = 3ab/(b+2a)$, which will vary with the precise model chosen for angular dependence.

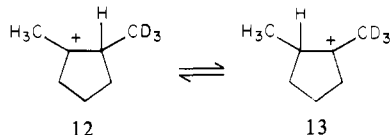
(33) Lambert, J. B.; Roberts, J. D. *J. Am. Chem. Soc.* **1965**, *87*, 3891-3895 and references therein.

(34) Murray, M. J. *Magn. Reson.* **1973**, *9*, 326-328.

(35) Friesen, K. J.; Wasylishen, R. E. *J. Magn. Reson.* **1980**, *41*, 189-191.

Another type of evidence that seems more compatible with the conformational explanation is the additive character of the one-bond isotope effect on the carbon chemical shift of the methyl group in **5**. This short-range additivity in an ion where the long-range effect is not additive suggests that alteration of the character of the C–D bond by successive deuteration is not the source of the long-range nonadditivity. Presumably either an isotope effect that would significantly alter the C–D bond strength upon the substitution of additional deuterium atoms or significant changes in vibrational coupling would show up in both the short-range and long-range NMR shifts. On the other hand, while some variation in the one-bond isotope effect with different methyl conformations might be expected because C–H(D) bonding will be somewhat dependent on hyperconjugation and the dihedral angle relative to the p orbital,^{36–38} this variation should be much smaller than the variation in the long-range isotope effect which arises completely from the angularly dependent hyperconjugation.

In essence, our conclusion is that a deuterated methyl group exerts a long-range, *intrinsic* isotope effect when it is involved in hyperconjugation but that the nonadditive character of the isotope effect is a type of *equilibrium* isotope effect. The equilibrium between the possible methyl conformations is shifted to favor those in which a C–H bond is better aligned for hyperconjugation than a C–D bond. This isotopically perturbed equilibrium is analogous to those observed for rearrangement reactions by Saunders, for instance, **12** \rightleftharpoons **13**,³⁹ in which the charge prefers to be adjacent



to the unlabeled position. In the case of methyl rotation, the perturbed equilibrium leads to a reduction in the apparent intrinsic isotope effect, whereas in a degenerate rearrangement, the perturbed equilibrium lifts the chemical shift degeneracy.

Experimental Section

NMR Spectroscopy. A JEOL FX-60Q NMR spectrometer was used to obtain ¹³C, ¹H, and ¹⁹F NMR spectra at 15.0, 59.75, and 56.2 MHz, respectively. ¹³C and ¹H spectra were obtained by using a dual C/H probe and 10-mm sample tubes. A separate ¹⁹F probe was used with 5-mm tubes. A concentric 2-mm (o.d.) capillary tube containing Me₄Si served as the reference for ¹³C and H spectra, and a 2-mm capillary tube containing 1,2-dibromotetrafluoroethane was used for ¹⁹F spectra. Field stabilization was provided by an external deuterium lock. The temperatures reported were the thermostat settings on the temperature controller, which was precalibrated to within 6 °C of actual temperature, with the exception of the reported –121 °C. Either 8192 or 16384 data points were used, with a 60° pulse. The other control parameters varied widely, depending on chemical shift range, concentration, and the nucleus being observed. For most determinations of isotope shifts, a 500-Hz spectral width was employed, with a digital resolution of 0.12 or 0.06 Hz/point. ¹³C spectra of **1** and **2** were also obtained at 67.9 MHz on the Bruker HX-270 spectrometer of the Southern New England High Field NMR Facility at Yale University. We used 16K data points, and digital resolution of 0.92 and 2.22 Hz/point were achieved for **1** and **2**, respectively.

(36) Lathan, W. A.; Hehre, W. J. Pople, J. A. *J. Am. Chem. Soc.* **1971**, *93*, 808–815.

(37) Wolf, J. F.; Devlin, J. L.; DeFrees, D. J.; Taft, R. W.; Hehre, W. J. *J. Am. Chem. Soc.* **1976**, *98*, 5097–5101.

(38) Pross, A.; Radom, L.; Riggs, N. V. *J. Am. Chem. Soc.* **1980**, *102*, 2253–2259.

(39) Saunders, M.; Telkowski, L.; Kates, M. R. *J. Am. Chem. Soc.* **1977**, *99*, 8070–8071.

Ion Precursors. Chlorides were prepared from alcohols by treatment with thionyl chloride. In a typical procedure, 2-chloro-2-phenylpropane was formed by refluxing 2-phenyl-2-propanol (5.0 g, 0.027 mol) and SOCl₂ (5.0 g, 0.042 mol) in CH₂Cl₂ for 1 h. The solution was cooled to 0 °C and K₂CO₃ (5.0 g, 0.04 mol) was added. Water (1.5 mL) was added dropwise, while the solution was stirred. Filtration, drying (Mg-SO₄), and evaporation of the solvent gave the chloride. No purification was attempted, in order to avoid elimination.

2-Phenyl-2-propanol-1,1,1,3,3,3-*d*₆ was prepared by the usual Grignard reaction of phenylmagnesium iodide and acetone-*d*₆. 2-Phenylpropene-1,1,3,3,3-*d*₅ was prepared from the *d*₆ alcohol by elimination catalyzed with potassium hydrogen sulfate.⁴⁰

2-(*p*-Fluorophenyl)-2-propanol and the corresponding *d*₆ alcohol were synthesized from (*p*-bromofluoro)benzene by lithiation with *n*-butyllithium by reaction with acetone or acetone-*d*₆. 2-(*p*-Fluorophenyl)-2-propanol-1,1,1-*d*₃ was prepared by the Grignard reaction of methylmagnesium bromide with *p*-fluoroacetophenone- α,α,α -*d*₃. The *p*-fluoroacetophenone had been deuterated to >98% by two successive K₂CO₃-catalyzed exchanges with D₂O,⁴¹ using a 2-h reflux period. *p*-Fluoroacetophenone was also obtained at 57% α deuteration by refluxing with a H₂O/D₂O mixture and K₂CO₃.

1-(*p*-Fluorophenyl)ethanol and the corresponding 2,2,2-*d*₃ and partially deuterated alcohols were obtained by NaBH₄ reduction of *p*-fluoroacetophenone or the appropriately α -deuterated ketone. 1-(*p*-Fluorophenyl)ethanol-1-*d* was synthesized by reduction of *p*-fluoroacetophenone with lithium triethylborodeuteride (Superdeuteride, Aldrich).⁴²

1,1-Difluoro-1-phenylethane and 1,1-difluoro-1-phenylethane-2-*d* were prepared from phenylethyne and phenylethyne-2-*d* by double HF addition using HF-pyridine (Aldrich).⁴³ The phenylethyne-2-*d* had been prepared by lithiation of phenylethyne with *n*-butyllithium, followed by quenching with D₂O.

Preparation of Ions. The general procedure for preparation of carbocation solutions was to add in small portions a precooled solution or suspension of about 2 mmol of the chloride or fluoride precursor in SO₂ClF (1 mL) to a vigorously stirred (vortex mixer) solution of about 10 mmol of superacid in SO₂ClF (2 mL) at –78 °C. Details of individual ions prepared in this manner are summarized as follows by the information (ion, precursor, ionizing acid): **1**, 2-chloro-2-phenylpropane-1,1,1,3,3,3-*d*₆, SbF₆[–]; **3**, 2-(*p*-fluorophenyl)-2-chloropropane-1,1,1,3,3,3-*d*₆, FSO₃H; **4**, 2-(*p*-fluorophenyl)-2-chloropropane-1,1,1-*d*₃, FSO₃H; **5**, 1-(*p*-fluorophenyl)-1-chloroethane-2,2,2-*d*₃, SbF₆[–]; **6**, 1-(*p*-fluorophenyl)-1-chloroethane-1-*d*; **8**, 1,1-difluoro-1-phenylethane-2-*d*, SbF₆[–]. The deuterated ions were prepared as 2:1 or 1:2 mixtures with the corresponding undeuterated ions in order to make certain of peak assignments and to allow accurate measurements of isotope shifts. Several ions were also prepared from the alcohols or in different acids, as reported for **3** in Table II. Ion **5** was examined as a mixture with partially deuterated and unlabeled ions by ionizing the corresponding mixture of precursors. Mixtures containing partially deuterated **3** and **4** were prepared by warming the ion solution to –15 °C, whereupon proton-deuteron exchange with the acid occurred.

The method of Fraenkel²⁰ was used to prepare (α -methyl- α -neopentylbenzyl)lithium- β -*d*₅ (**2**) in tetrahydrofuran from 2-phenylpropene-1,1,3,3,3-*d*₅, as a mixture with the corresponding unlabeled ion. The only alteration from Fraenkel's procedure was to evaporate the pentane from the *tert*-butyllithium by passing a stream of argon over the solution.

Registry No. **1**, 75296-07-0; **2**, 79663-73-3; **3**, 79663-74-4; **4**, 79680-91-4; **5**, 79663-75-5; **6**, 79663-76-6; **7**, 79663-77-7; **8**, 79663-78-8; *p*-FC₆H₄CHCHD₂⁺, 79663-79-9; *p*-FC₆H₄CHCH₂D⁺, 79663-80-2; *p*-FC₆H₄CHCH₃⁺, 31067-69-3.

(40) Horning, E. C., Ed. "Organic Syntheses Collective Volume III"; Wiley: New York, 1955; pp 204–206.

(41) Volger, H. C. *Recl. Trav. Chim. Pays-Bas* **1967**, *86*, 677–686.

(42) Brown, H. C.; Krishnamurthy, S. *J. Am. Chem. Soc.* **1973**, *95*, 1669–1671.

(43) Olah, G. A.; Nojima, M.; Kerkes, I. *Synthesis* **1973**, 779–780.