Anal. Calcd. for $C_{21}H_{25}NO_7$: C, 62.52; H, 6.25; N, 3.47. Found: C, 62.48; H, 6.26; N, 3.40.

6,11-Diacetyldihydrohaemanthidine (Ih). By the procedure cited for the preparation of If, 0.245 g. of dihydrohaemanthidine was converted to 0.200 g. of crude diacetate. The product was recrystallized from acetone–ether: m.p. 246–248°; $[\alpha]^{25}_{589}$ +39°, $[\alpha]^{25}_{436}$ +76° (c 0.51); λ^{KBr}_{max} 5.74 μ; λ^{EtOH}_{max} 238 mμ (ϵ 3900) and 289 mμ (ϵ 4100).

Anal. Calcd. for $C_{21}H_{25}NO_7$: C, 62.52; H, 6.25; N, 3.47. Found: C, 62.35; H, 6.23; N, 3.42.

Reaction of 6-Hydroxycrinamine with Nitrous Acid. To a solution of 0.300 g. of 6-hydroxycrinamine in 100 ml. of 1.5% aqueous acetic acid was added 0.300 g. of sodium nitrite. The reaction mixture was allowed to stand at room temperature for 4 hr. At this time, a negative alkaloid test was obtained with silicotungstic acid. The aqueous solution was extracted three times with chloroform, and the chloroform solution was washed with 5% sodium bicarbonate solution. Evaporation of the chloroform solution under reduced pressure gave 0.310 g. of crystalline residue which was recrystallized from ethanol–acetone: m.p. 207–208°; $[\alpha]^{25}_{589}$ +345°, $[\alpha]^{25}_{436}$ +875° (c 0.24); λ^{Nujol}_{max} 2.69 μ; λ^{EtOH}_{max} 239 mμ (ϵ 14,000) and 290 mμ (ϵ 4800). The n.m.r. spectrum in dimethyl sulfoxide showed one proton doublet at 423 c.p.s. that was removed upon treatment of the sample with deuterium oxide. This is consistent with the hemiacetal formation.

Anal. Calcd. for $C_{17}H_{18}N_2O_6$: C, 58.95; H, 5.24; N, 8.09. Found: C, 59.31; H, 5.41; N, 8.00.

N-Nitrosolactone (VI; R, R' = O). A solution of 0.310 g. of VI (R = H, R' = OH) in 80 ml. of chloroform was stirred for 6 hr. with 1.50 g. of manganese dioxide at room temperature. The manganese dioxide was removed by filtration, and the solvent was concentrated to dryness under reduced pressure to give 0.285 g. of residue which crystallized upon trituration with ether. Recrystallization from acetone–methanol–chloroform gave white prisms: m.p. 251–252°; $[\alpha]^{25}_{589}$ +360°, $[\alpha]^{25}_{436}$ +880° (c 0.15, pyridine); λ^{KBr}_{max} 5.80 and 6.19 μ; λ^{EtOH}_{max} 231 mμ (ϵ 35,000), 266 mμ (ϵ 6800), and 308 mμ (ϵ 7200). The n.m.r. spectrum (saturated in dimethyl sulfoxide) showed no benzylic protons.

Anal. Calcd. for $C_{17}H_{16}N_2O_6$: C, 59.30; H, 4.68; N, 8.14. Found: C, 59.12; H, 4.66; N, 7.91.

6-Hydroxycrinamine-6-d. A solution of 0.200 g. of 6-oxocrinamine (IV)[4] in 20 ml. of dry tetrahydrofuran was treated with 0.100 g. of lithium aluminum deuteride for 2 hr. at 0°. The excess deuteride was destroyed by water, and the inorganic salts were removed by filtration. The filtrate was concentrated under reduced pressure to provide 0.205 g. of amorphous material which crystallized upon seeding with 6-hydroxycrinamine and was recrystallized from chloroform–acetone: m.p. 209–210°; $[\alpha]^{25}_{589}$ +62°, $[\alpha]^{25}_{436}$ +167° (c 0.455). The deuterium incorporation was greater than 95% as determined by n.m.r. spectroscopy. The n.m.r. spectrum was identical with that of 6-hydroxycrinamine except for the lack of peaks at 300 and 335 c.p.s.

Fluorine-19 Magnetic Resonance Study of Secondary Deuterium Isotope Effects of the Methyl Group[1]

Daniel D. Traficante and Gary E. Maciel

Contribution from the Frank J. Seiler Research Laboratory, Office of Aerospace Research, U. S. Air Force Academy, Colorado, and the University of California, Davis, California. Received June 4, 1965

The F^{19} chemical shifts of m- and p-fluorotoluene-α,α,α-d_3 and their nondeuterated analogs were determined. No appreciable isotope effect was detected for the meta isomer; however, the chemical shift of p-fluorotoluene-α,α,α-d_3 was found to be about 0.7 c.p.s. less than that of p-fluorotoluene. In terms of Taft's correltions of F^{19} shifts for meta- and para-substituted fluorobenzenes with σ_I and σ_R^0, these results imply negligible or zero inductive isotope effects of the methyl group, but a small resonance isotope effect in the direction expected from recent results on secondary deuterium isotope effects in kinetic and equilibrium studies.

Introduction

The subject of secondary deuterium isotope effects has been of considerable interest in the past few years, both from the point of view of understanding their origin and for their application to mechanism studies.[2,3] Such effects have been observed in proton and fluorine magnetic resonance spectra[4–9] and in kinetic studies[2a] and equilibrium data.[2,3]

(2) (a) E. A. Halevi, *Progr. Phys. Org. Chem.*, 1 (1963); (b) E. A. Halevi, M. Nussin, and A. Ron, *J. Chem. Soc.*, 866 (1963).

(3) E. A. Halevi and M. Nussin, *ibid.*, 876 (1963).

(4) M. Saunders, J. Plostnieks, P. S. Wharton, and H. H. Wasserman, *J. Chem. Phys.*, 32, 317 (1960).

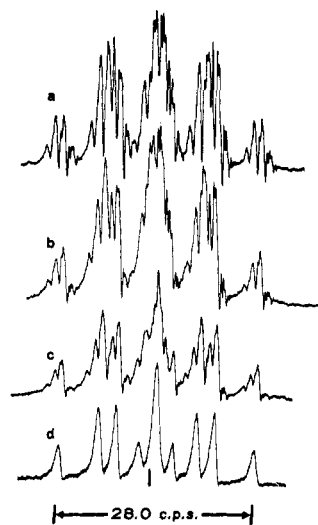(5) E. B. Whipple, W. E. Stewart, G. S. Reddy, and J. A. Goldstein, *ibid.*, 34, 2136 (1961).

Figure 1. F^{19} spectra on the same scale of chemical shift, increasing field strength from right to left: a, p-fluorotoluene; b, 2:1 mixture of p-fluorotoluene and p-fluorotoluene-α,α,α-d_3; c, 1:1:1 (v./v.) mixture of p-fluorotoluene, p-fluorotoluene-α,α,α-d_3, and carbon tetrachloride; d, 1:1 (v./v.) mixture of p-fluorotoluene-α,α,α-d_3 and carbon tetrachloride.
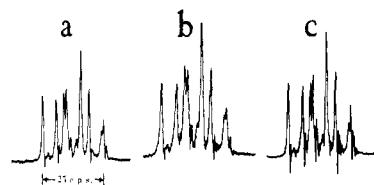

Figure 2. F^{19} spectra, increasing field sweep right to left: a, m-fluorotoluene; b, 1:1 mixture of m-fluorotoluene and m-fluorotoluene-α,α,α-d_3; c, m-fluorotoluene-α,α,α-d_3.

Attempts have been made to understand these effects in terms of the differences in vibrational zero-point energies or amplitudes which lie at their origin. With these ideas in mind, interpretations have been put forth based on an apparently greater *inductive* electron-donating tendency of D or –C–D compared to H or –C–H, and a reduced *hyperconjugative* ability of –C–D compared to –C–H. Recently Halevi has presented justification for discussion of these essentially vibronic phenomena in terms of the normal substituent characteristics of inductive and hyperconjugative tendencies, and has presented data which estimate these separate effects in particular cases.[2,3] Thus, without denying their ultimate origin, Halevi and co-workers "attempt to correlate secondary deuterium isotope effects empirically in terms of the electrical influences that have proved valuable in interpreting the effects of non-isotopic substituents."[2b] Recognizing that the electronic properties of molecules are dependent on their average electronic configurations (with respect to vibrational motion) which change slightly with isotopic substitution even in their lowest vibrational levels, "isotope effects on eminently electronic properties" were accounted for. They saw no valid objection to regarding deuterium isotope effects as due to slight but genuine differences in the ease of inductive or hyperconjugative electron release.

With these concepts in mind we have attempted to detect isotope effects on the separate inductive and resonance characteristics of the methyl group by utilizing Taft's correlation of F^{19} chemical shifts in *meta-* and *para-*substituted fluorobenzenes with σ constants.[10–14] Taft's correlations are summarized in

eq. 1 and 2, where f_H^{p-X} and f_H^{m-X} are the fluorine chemical shifts of *para-* and *meta-*substituted fluorobenzene, respectively, in p.p.m., calculated with respect to the shift of fluorobenzene, and σ_R^0 and σ_I are the separated resonance and inductive constants, respectively. These rather precise relationships are based on extensive experimental grounds,[10–14] have been justified theoretically,[15,16] and have been used to determine reactivity parameters which would have been difficult or impossible to obtain by more conventional chemical techniques.[12,13,17]

$$f_H^{p-X} - f_H^{m-X} = (-29.5)\sigma_R^0 \qquad (1)$$

$$f_H^{m-X} = -7.1\sigma_I + 0.60 \qquad (2)$$

While the general magnitude of secondary deuterium isotope effects observed in kinetic and equilibrium studies has been small, its ratio to the magnitude of ordinary substituent effects and the sensitivity of Taft's F^{19} magnetic resonance technique seemed to indicate that measurable differences in σ_R^0 and/or σ_I might be detected. We therefore prepared *p-* and *m-*fluorotoluenes, trideuterated in the methyl position, and compared their F^{19} chemical shifts with their undeuterated counterparts. Since the substitution of CD_3 for CH_3 appears to change reactivities due primarily to either inductive or resonance effects about one-fourth as much as the substitution of C_2H_5 for CH_3[2,3] and since differences of about 0.4 p.p.m. have been reported for the F^{19} shifts of *p-* (or *m-*) fluoroethylbenzene and *p-* (or *m-*) fluorotoluene,[12,13] shifts as high as 0.1 p.p.m. due to deuterium substitution might have been anticipated.

Experimental Section

N.m.r. Measurements. F^{19} magnetic resonance spectra were obtained at 56.4 Mc.p.s. using a Varian HR-60 spectrometer and associated equipment on pure compounds, mixtures, and solutions in carbon tetrachloride, in spinning 5-mm. tubes. In the dilute (7 % by volume) carbon tetrachloride solutions fluorobenzene was employed as an internal reference and chemical shifts were obtained by the standard side-band technique. The line widths in all these spectra were found to be markedly decreased by degassing; thus, the spectra shown in Figures 1 and 2 were obtained on samples through which prepurified nitrogen had been bubbled

(6) H. S. Gutowsky, *J. Chem. Phys.*, 31, 1683 (1959).
(7) T. W. Marshall, *Mol. Phys.*, 4, 61 (1961).
(8) (a) G. V. D. Tiers, *J. Am. Chem. Soc.*, 79, 5585 (1957); (b) G. V. D. Tiers, *J. Chem. Phys.*, 29, 963 (1958).
(9) H. Kusumoto, T. Itoh, K. Horota, and J. Ueda, *J. Phys. Soc. Japan*, 15, 728 (1960).
(10) R. W. Taft, *J. Am. Chem. Soc.*, 79, 1045 (1957).
(11) R. W. Taft, Jr., S. Ehrenson, I. C. Lewis, and R. E. Glick, *ibid.*, 81, 5352 (1959).

(12) R. W. Taft, Jr., E. Price, I. R. Fox, I. C. Lewis, K. K. Andersen, and G. T. Davis, *ibid.*, 85, 709 (1963).
(13) R. W. Taft, Jr., E. Price, I. R. Fox, I. C. Lewis, K. K. Andersen, and G. T. Davis, *ibid.*, 85, 3146 (1963).
(14) R. W. Taft, Jr., *J. Phys. Chem.*, 64, 1805 (1960).
(15) F. Prosser and L. Goodman, *J. Chem. Phys.*, 38, 374 (1963).
(16) R. W. Taft, F. Prosser, L. Goodman, and G. T. Davis, *ibid.*, 38, 380 (1963).
(17) G. E. Maciel, *J. Am. Chem. Soc.*, 86, 1269 (1964).

for 15 min. Proton magnetic resonance spectra were obtained with the same equipment tuned to 60 Mc.p.s. or with a Varian A-60 spectrometer.

Materials. The *m*-fluorotoluene was a redistilled sample from Penninsula Chemresearch, Inc., b.p. 116.5°. The *p*-fluorotoluene was a redistilled sample from Pierce Chemical Co., b.p. 117.0°.

Since identical procedures were used for preparing both *m*- and *p*-fluorotoluene-α,α,α-d_3, only the preparation of the *meta* isomer is reported in detail.

m-Fluorobenzyl-α,α-d_2 Alcohol. To a slurry of 0.680 g. (0.0162 mole) of lithium aluminum deuteride in 25 ml. of ether was added, with stirring, under a nitrogen atmosphere, a solution of 3.33 g. (0.0216 mole) of methyl *m*-fluorobenzoate in 25 ml. of ether. The mixture was refluxed overnight and then stirred at room temperature for 2 days. (The reaction time employed was solely for convenience, and no attempt was made to determine whether a shorter period would suffice). The mixture was then decomposed in the cold (0°) by the dropwise addition of a saturated solution of sodium potassium tartrate in water. The ether layer was separated and the aqueous phase was extracted twice with 10-ml. portions of ether. The combined extracts were dried over magnesium sulfate and distilled under reduced pressure to yield 2.61 g. (94%) of product, b.p. 85–87° (9 mm.), n^{24}D 1.5076 (lit.[18,19] b.p. 120–121° (45 mm.), n^{20}D 1.5012). For *p*-fluorobenzyl-α,α-d_2 alcohol, the yield was 2.56 g. (93%), b.p. 85–86° (9 mm.), $n^{23.5}$D 1.5064 (lit.[18,19] b.p. 122–123° (45 mm.), n^{20}D 1.5001).

α-Chloro-m-fluorotoluene-α,α-d_2. To a mixture of 3.25 g. (0.0273 mole) of thionyl chloride in 2.5 ml. of benzene containing 1 drop of pyridine was added during 30 min., with stirring, a solution of 2.63 g. (0.0206 mole) of *m*-fluorobenzyl-α,α-d_2 alcohol in 5 ml. of benzene. The mixture was refluxed for 15 min. after the addition was complete, stirred for 1 additional hr., and then distilled under reduced pressure to afford 2.68 g. (89%) of product, b.p. 55–56° (8 mm.), n^{25}D 1.5107 (lit.[18,20] b.p. 60° (10 mm.), n^{20}D 1.5126). For *α-chloro-p-fluorotoluene-α,α-d_2*, the yield obtained from 2.56 g. (0.0200 mole) of alcohol was 2.44 g. (83%), b.p. 54° (8 mm.), n^{25}D 1.5114 (lit.[18,20] b.p. 62° (10 mm.), n^{20}D 1.5230).

m-Fluorotoluene-α,α,α-d_3. The apparatus consisted of a semimicro reflux condenser fitted to a 25-ml. reaction flask, which was connected by means of a side arm and a short piece of tygon tubing to a 50-ml. flask. The complete apparatus was flushed with nitrogen while being flamed with a microburner. After cooling under a nitrogen atmosphere, 1.330 g. (0.055 g.-atom) of previously dried magnesium turnings and a magnetic stirrer were placed in the reaction flask, and *ca.* 2 g. of P_2O_5 and a magnetic stirrer were placed in the 50-ml. flask. From a dry pipet, 20 ml. of ether was run down through the condenser into the reaction flask and stirred with the magnesium for 5 min. The apparatus was then tipped so that the ether flowed into the flask containing the P_2O_5, and stirred for 5 min. The ether was distilled back into the reaction flask, stirred with the

magnesium again, poured back into and stirred with the P_2O_5 once more, and 10–12 ml. was redistilled for the final time. To this mixture 2.433 g. (0.0166 mole) of freshly distilled *α-chloro-m-fluorotoluene-α,α-d_2* was added through the tygon tubing, dropwise and with stirring under a nitrogen atmosphere, from a dry hypodermic syringe at such a rate that the ether refluxed gently. After stirring for 1 hr. after the addition was complete, deuterium oxide (99.75%) was added through the tygon tubing, dropwise and with cooling under a nitrogen atmosphere, from a previously dried hypodermic syringe. After the decomposition was complete, the ether layer was separated and the aqueous phase was extracted twice with 5-ml. portions of ether. The combined extracts were concentrated, with a 50–60° bath, through an 8 in. × 6 mm. micro spinning-band column. The relatively pure product was obtained from the residue by collecting from a gas chromatography column.[21] The collected material, weighing 1.354 g. (72%), was dried over magnesium sulfate and distilled to afford 1.028 g. (55%) of pure product, b.p. 106° (589 mm.) (lit.[18,22] b.p. 114–115° (758 mm.)), n^{25}D 1.4670 (lit.[18,23] n^{20}D 1.4691). For *p*-fluorotoluene-α,α,α-d_3 the collected material obtained from 2.086 g. (0.0142 mole) of *α-chloro-p-fluorotoluene-α,α-d_2* weighed 0.846 g. (53%), and was dried and distilled to afford 0.423 g. (26%) of pure product, b.p. 107° (594 mm.) (lit.[18,24] b.p. 116° (756 mm.)), n^{27}D 1.4664 (lit.[18,23] n^{15}D 1.4705). The proton magnetic resonance spectra of *p*- and *m*-fluorotoluene-α,α,α-d_3 are consistent with their structures and indicated that the methyl groups were at least 99.5% trideuterated. Analyses by gas chromatography showed no impurities.

Results

The high-resolution F^{19} magnetic resonance spectrum of *p*-fluorotoluene has been obtained previously by Schaefer[25] at a measuring frequency of 29.9 Mc.p.s. Our spectrum, obtained at 56.4 Mc.p.s., is shown in Figure 1a. It has more precisely defined fine structure but the same general form as the typical A_2B_2X pattern (where A and B represent the protons *ortho* and *meta*, respectively, to the fluorine nucleus X) reported by Schaefer, for the case of small chemical shift between *ortho* and *meta* hydrogens, and splitting constants between the latter and the fluorine nucleus of 8.7 and 5.8 c.p.s., respectively.[26] The basic A_2B_2X pattern is complicated by long-range coupling with the methyl group protons which Schaefer has estimated to be 0.9 c.p.s. in this case. The chemical shift was determined to be 5.41 p.p.m. with respect to fluorobenzene (in 7% solution in CCl_4), in good agreement with the value obtained by Taft and co-workers.[18] The F^{19} spectrum of *p*-fluorotoluene-α,α,α-d_3 as shown in Figure 1d has broader peaks, presumably due to the reduced and hence unresolved splittings of the CD_3 group as compared with the CH_3 group. It closely resembles the typical A_2B_2X patterns reported by

(18) The physical constants are for the nondeuterated compounds.
(19) L. A. Brooks, *J. Am. Chem. Soc.*, 66, 1295 (1944).
(20) S. Jerumanis and A. Bruylants, *Bull. soc. chim. Belges*, 69, 312 (1960).

(21) A 4 ft. × $^1/_8$ in. column packed with silicone gum rubber (methyl) GE SE-30 (10%) suspended on 60–80 mesh Diatoport W at 80° was employed.
(22) G. Schiemann, *Ber.*, 62, 1794 (1929).
(23) F. Swarts, *J. chim. phys.*, 20, 30 (1923).
(24) G. Balz and G. Schiemann, *Ber.*, 60, 1186 (1927).
(25) T. Schaefer, *Can. J. Chem.*, 37, 882 (1959).
(26) T. Schaefer and W. G. Schneider, *ibid.*, 37, 2078 (1959).

Aruldhas and Venkateswarlu[27,28] for *para*-substituted fluorobenzenes. A solution containing two parts of *p*-fluorotoluene to one part (by volume) of *p*-fluorotoluene-α,α,α-d_3 as well as one containing these components and carbon tetrachloride in the volume ratio 1:1:1 gave patterns showing some asymmetry. The spectra of these solutions are shown in Figures 1b and 1c. By considering changes in the relative intensities of peaks due to *p*-fluorotoluene as its volume per cent in solution with respect to the trideuterio isomer changes from 100 to $66^2/_3$ to 50 to 0% in Figures 1a, 1b, 1c, and 1d, respectively, one can conclude that the center of the pattern due to *p*-fluorotoluene-α,α,α-d_3 occurs slightly downfield from that of *p*-fluorotoluene itself. Thus, by choosing spectra showing the smallest nonlinearity in field sweep rate and photographically enlarging them to the same scale of c.p.s./cm. we have aligned them as to corresponding peaks as shown in Figure 1, attempting to account for the overlapping patterns in the most consistent manner. By this analysis we conclude that the chemical shift of *p*-fluorotoluene-α,α,α-d_3 is about 0.7 ± 0.2 c.p.s. (about 0.01 p.p.m.) less than that of its undeuterated analog. The 0.2-c.p.s. range is based on our estimate of the uncertainty resulting from residual nonlinearity in sweep rates and the asymmetries due to line-shape distortions present in the spectra of the pure compounds.

The samples of *m*-fluorotoluene and its trideuteriomethyl analog gave complex F^{19} spectra as shown in Figures 2a and 2c, respectively. These spectra are virtually identical in form, with the only observable difference being in the relative sharpness of the lines. The apparently narrower peak widths of *m*-fluorotoluene-α,α,α-d_3 spectrum may reflect a diminished broading due to splitting by the CD_3 deuterons as compared with the CH_3 protons. Figure 2b shows a spectrum of a 1:1 mixture of the trideuterated and undeuterated *m*-fluorotoluenes. Within the limits of experimental determination it is identical in basic form with the spectrum of either component, with no apparent distortions in line shape such as new shoulders, and with line widths not significantly greater than those of *m*-fluorotoluene itself. This indicates essentially no chemical shift difference between the components, within the limits of about ±0.2 c.p.s.

Discussion

The essentially zero isotope effect on the chemical shift of *m*-fluorotoluene seems to imply in terms of eq. 2 that there is no difference between the inductive constant σ_I for the groups CH_3 and CD_3; the precision of our experiments would seem to place a maximum limit of about 5×10^{-4} for $\Delta\sigma_I$ in this case. The approximately 0.7-c.p.s. effect of methyl deuteration on $f_H^{p\text{-}CH_3}$ implies, when interpreted in terms of eq. 1 and the result with the *meta* compounds, a small but measurable effect of deuteration on the resonance (*i.e.*, hyperconjugative) characteristics of the methyl group. This corresponds to $\Delta\sigma_R^0$ between CH_3 and CD_3 of about -4×10^{-4}. Naturally, this difference is much smaller than the precision claimed for correlation of σ constants. However, for the sake of discussion, if one thinks of σ_I and σ_R^0 as being alterna-

tively defined by Taft's F^{19} chemical shift correlations, then these numbers reflect the isotope effect on inductive and resonance characteristics of the methyl group as manifested in F^{19} shifts. These results clearly represent an example of the failure of isotope effects on n.m.r. chemical shifts to be transmitted through an aromatic system, although ample evidence exists to demonstrate transmission through one or two saturated atoms.[4-9] Such behavior is not uncommon in reactivity studies such as aromatic substitution.[29,30]

Crude estimates can be made for the magnitudes which might have been expected for $\Delta\sigma_I$ and $\Delta\sigma_R^0$ and for the isotope effect on the F^{19} shifts themselves if one employs published data from various investigations (not all of which are mutually consistent). Halevi and co-workers,[2b] in their study of the inductive contribution to the isotope effect in a methyl group, found a ΔpK_a of 0.026 upon deuteration of the methyl group of acetic acid, about one-fourth of the difference between the pK_a values of propionic and acetic acids, 0.114. On the basis of Halevi's assumption of a dominant role of induction in determining these pK_a values[31] one might predict the rough relationship

$$(\sigma_I)_{CH_3} - (\sigma_I)_{CD_3} \cong 0.25\{(\sigma_I)_{CH_3} - (\sigma_I)_{C_2H_5}\} \quad (3)$$

The bracketted difference has been determined by Taft and co-workers[12] using eq. 2 to be -0.05. Thus a magnitude of 1×10^{-2} might have been expected for $\Delta\sigma_I$ with deuteration of the methyl group, corresponding to a predicted chemical shift difference of 4 c.p.s.[32] Halevi and Nussin[3] found a 7% difference between the equilibrium constants for the association of chloranil with toluene and its α-trideuterio analog, compared to a 28% change in the association constant when substituting ethylbenzene for toluene. These results were interpreted by Halevi and Nussin[3] primarily in terms of the hyperconjugative abilities of CH_3, CD_3, and C_2H_5, although they also mentioned possible contributions due to inductive effects and to the steric requirements of C_2H_5. About the same relative effects of changing from methyl to trideuteriomethyl as opposed to ethyl have been observed in kinetic studies of the solvolyses of *p*-alkylphenyldimethylcarbinyl chlorides[33] and *p*-alkylphenylmonomethylcarbinyl chlorides.[34] If one is willing to take these chemical data as rough measures of the relative hyperconjugative abilities of C_2H_5, CD_3, and CH_3, knowingly neglecting complications due to steric and/or inductive effects, then a rough *a priori* prediction of $(\sigma_R^0)_{CH_3} - (\sigma_R^0)_{CD_3}$ can be made (eq. 4) (since log 1.07/log

(27) G. Aruldhas and P. Venkateswarlu, *Mol. Phys.*, 7, 65 (1964).
(28) G. Aruldhas and P. Venkateswarlu, *ibid.*, 7, 77 (1964).

(29) C. G. Swain, T. E. C. Knee, and A. J. Kresge, *J. Am. Chem. Soc.*, 79, 505 (1957).
(30) This casts some doubt on the validity of choosing in the following paragraph the ionization of aliphatic carboxylic acids in estimating $\Delta\sigma_I$ for alkyl groups.
(31) For a more complete discussion of this point see R. W. Taft, Jr., in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956.
(32) This prediction does not rest on indisputable grounds, since the σ_I values quoted for C_2H_5 and CH_3 imply that CH_3 is a stronger inductive electron donor than C_2H_5,[12] whereas the relative sensitivity factor of one-fourth above[2b] was based on ΔpK_a values which seem to require the opposite conclusion, and since a discrepancy between the acetic acid isotope effects determined by Halevi and by Streitwieser remains unresolved.[2b]
(33) H. C. Brown and Y. Okamoto, *J. Am. Chem. Soc.*, 79, 1913 (1957).
(34) E. S. Lewis and G. M. Coppinger, *ibid.*, 76, 4495 (1954).

$(\sigma_R{}^0)_{CH_3} - (\sigma_R{}^0)_{CD_3} \cong 0.28\{(\sigma_R{}^0)_{CH_3} - (\sigma_R{}^0)_{C_2H_5}\}$ (4)

1.28 = 0.28). Then, if one uses the value -0.01 for $(\sigma_R{}^0)_{CH_3} - (\sigma_R{}^0)_{C_2H_5}$ reported by Taft[13] from reactivity measurements, the result $\Delta\sigma_R{}^0 = -2.8 \times 10^{-3}$ is obtained, about seven times the value determined in this investigation. Furthermore if one assumed *a priori* that the relative sensitivity of the solvolysis rates to change in the inductive and resonance influences which accompany changing the *p*-alkyl substituent in the above-mentioned halides is approximately reflected in the F^{19} shifts of the corresponding *p*-alkylfluorobenzenes, then a chemical shift difference of about one-fourth the 0.40-p.p.m. difference between the shifts reported for *p*-fluorotoluene and *p*-fluoroethylbenzene[13] (about 6 c.p.s.) might have been expected. Of course, these estimates are based on a suspicious web of assumptions[35] and are only useful in that they provide a magnitude to be compared with the present results.

The experimental results reported and referred to in this communication appear to constitute a paradox: on one hand there is a substantial body of evidence indicating that secondary deuterium isotope effects can be considered quite properly in terms of differences in inductive and hyperconjugative characteristics[2,3]; on the other hand, our present application of Taft's well-established and apparently self-consistent F^{19} chemical shift correlations shows virtually no inductive isotope effect and a smaller resonance isotope effect than one might have anticipated from kinetic and thermodynamic studies.

(35) It is interesting to note that if the right side of eq. 4 is expressed in terms of F^{19} chemical shifts by means of eq. 1, and if Taft's chemical shift data[12,13] are employed, the computed $\Delta\sigma_R{}^0$ is -4×10^{-4}, exactly the result obtained from our experiments. This may be viewed as a demonstration of the self-consistency of Taft's relationships (eq. 1 and 2) and may indicate some validity for employing the factor 0.28 in eq. 4.

While the values of σ_I and $\sigma_R{}^0$ computed for arbitrary substituents by Taft's relationship are not identical in many cases with those derived by kinetic and/or equilibrium measurements,[12,13] the correlations of f_H^{m-X} and f_H^{p-X} with the electronic properties of substituents X seem to rest on a sound basis of extensive experimental data and critical theoretical considerations.[15,16] These relationships should be particularly useful when applied to a set of closely related compounds, where average electronic excitation energies, etc., remain essentially constant.[15,16] The compounds studied in this investigation should constitute such a set. Thus, the above-mentioned paradox suggests a need for more critical consideration of the applicability of the language of ordinary substituent effects in discussions of secondary deuterium isotope effects. Perhaps the solution is related to the argument[36] that the largest secondary deuterium isotope effects may be expected when the carbon atom involved in a reaction acquires a positive charge and/or a change in hybridization.[36] This would render a significant change in vibrational force constants in nonreacting C–H and C–D bonds and corresponding changes in vibrational frequencies which are at the foundations of kinetic and thermodynamic isotope effects.[36,37] The F^{19} chemical shift technique would not be expected to reflect the special requirements of particular reactions, and this may be responsible for the results obtained in this study, as well as the small discrepancies which do exist between σ_I and $\sigma_R{}^0$ values determined by F^{19} magnetic resonance and chemical techniques for ordinary substituents.

(36) K. B. Wiberg, "Physical Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1964, p. 360.
(37) These reaction characteristics are not to be considered necessary and/or sufficient conditions for significant secondary deuterium isotope effects.[29]