J. Org. Chem. 1980, 45, 3476–3483

Table IV. Visible Absorption of 4-Phenyl-1,2,4-triazoline-3,5-dione

solvent	λ_{max}, nm	ϵ_{max}
dichloromethane	546	160.0
1,2-dichloromethane	544.5	183.0
benzene	543.5	240.7
nitrobenzene	538	178.8
ethyl acetate	531	170.8
tetrahydrofuran	528	171.9

be almost pure **13** (purity >95%).

The filtrate was concentrated, and the yellow oil was purified by column chromatography on silica gel with chloroform and 5% methanol in chloroform as eluents. The main fractions were combined and concentrated. The almost colorless oil was dissolved in benzene, and hexane was added. From this solution, 1.89 g (38.3%) of white needlelike crystals were obtained. These crystals consisted of 75% of **14** and 25% of **13**. For **13**: mp 77–78 °C dec; NMR ($CDCl_3$) δ 0.93 (t, 3), 1.51 (hextet, 2), 2.06 (t, 2), 3.10 (s, 3), 4.13 (s, 2), 5.04 (s, 2), 8.44 (br s, 1). For **14**: mp 51.53 °C dec; NMR ($CDCl_3$) δ 1.00 (t, 3), 1.65 (s, 3), 2.10 (q, 2), 3.08 (s, 3), 4.06 (s, 2), 5.48 (t, 1), 8.4 (br s, 1).

1-(Methylenepentyl)-2-acetyl-4-methyl-1,2,5-triazolidine-3,5-dione (15) and 1-(2-Methyl-2-pentenyl)-2-acetyl-4-methyl-1,2,4-triazolidine-3,5-dione (16). Compound **13** was treated with acetic anhydride,[6] and **15** was obtained as a colorless oil after chromatographic purification. Compound **16** was also synthesized from **14**.

Reaction of 16 with 1a. A 370-mg (1.54 mmol) sample of **16** and 245 mg (1.40 mmol) of **1a** were dissolved in 30 mL of DCE, and the mixture was left at room temperature. After 3 days, DCE was removed on a rotary evaporator, and the residue was purified by column chromatography (silica gel). The main fractions were combined and concentrated. After two recrystallizations from benzene–hexane, 433 mg (74.6%) of a mixture of **19** and **20** was obtained. The ratio of **19** to **20** was found to be 3:2 from ^1H NMR analysis.

The data for the mixture of **19** and **20** are as follows: mp 166.5–167.5 dec; NMR ($CDCl_3$) δ 0.93 (t), 0.97 (t), 1.90 (quintet), 1.97 (s), 2.53 (s), 2.58 (s), 3.10 (s), 3.13 (s), 4.45 (t), 4.6 (s), 5.33 (d), 5.98 (s), 7.48 (s). Anal. Calcd for $C_{19}H_{22}N_6O_5$: C, 55.06; H, 5.35; N, 20.98. Found: C, 54.54; H, 5.37; N, 20.12.

1-Propyl-4-phenyl-1,2,4-triazolidine-3,5-dione (21). To 5.26 g of potassium hydroxide (85% purity, 0.080 mol) in 200 mL of ethanol was added 14.16 g (0.08 mol) of 4-phenylurazole. To this solution, which was heated to 60–65 °C, was added 41.0 g (0.24 mol) of 1-iodopropane. The mixture was kept at 70 °C for 3 h, during which the salts precipitated. The mixture was left at room temperature overnight. After filtration, ethanol and excess of 1-iodopropane were removed on a rotary evaporator. The resulting yellow oil was dissolved in ethyl acetate, and the ethyl acetate solution was washed with water and then dried over anhydrous sodium sulfate. The slightly yellow solid residue, after evaporation of the ethyl acetate, was purified by column chromatography (silica gel). After concentration and recrystallization from benzene–hexane, 8.78 g (50.7%) of pure **21** was obtained: mp 98–99 °C dec; NMR ($CDCl_3$) δ 0.90 (t, 3), 1.66 (six peaks, 2), 3.56 (t, 2), 7.49 (s, 5), 8.6 (br s, 1). Anal. Calcd for $C_{11}H_{13}N_3O_2$: C, 60.26; H, 5.98; N, 19.17. Found: C, 60.90; H, 6.17; N, 19.30.

1-Propyl-2-acetyl-4-phenyl-1,2,4-triazolidine-3,5-dione (22). Compound **21** was acetylated by using acetic anhydride: mp 107–108 °C; NMR ($CDCl_3$) δ 0.93 (t, 3), 1.64 (six peaks, 2), 2.65 (s, 3), 4.04 (t, 2), 7.50 (s, 5).

1-Methyl-4-phenyl-1,2,4-triazolidine-3,5-dione (24). The potassium salt of 4-phenylurazole was permitted to react with methyl iodide in ethanol to give, after purification, **24**: mp 158–160 °C; NMR (acetone-d_6) δ 3.23 (s, 3), 7.48 (m, 5).

Reaction of 21 with 1a. To 2.00 g (0.1 mmol) of **21** in 150 mL of DCE was added 1.59 g (9.1 mmol) of PhTD at 60 °C. After 1 day, the red color was completely discharged, and a large amount of white crystals was formed. The crystals were collected by filtration and washed with dichloromethane to give 2.79 g (77.8%) of **25**. The filtrate was concentrated, and the residue was washed with benzene to give 0.28 g (7.8%) of **25**: mp 193–195 °C dec; NMR (Me_2SO-d_6) δ 1.03 (t, 3), 2.23 (quintet, 2), 5.63 (t, 1), 7.45 (s, 10). Anal. Calcd for $C_{19}H_{18}N_6O_4$: C, 57.86; H, 4.60; N, 21.31. Found: C, 57.72; H, 4.64; N, 21.29.

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Registry No. **1a**, 4233-33-4; **1b**, 13274-43-6; **1c**, 13274-44-7; **1d**, 13274-75-4; **2**, 592-41-6; **3**, 763-29-1; **4**, 4050-45-7; **5**, 13269-52-8; **6**, 513-35-9; **8**, 110-83-8; **9**, 591-49-1; **13**, 74113-08-9; **14**, 74113-09-0; **15**, 74113-10-3; **16**, 74113-11-4; **19**, 74113-12-5; **20**, 74113-13-6; **21**, 74113-14-7; **22**, 74113-15-8; **24**, 28538-67-2; **25**, 74113-16-9; 1-iodopropane, 107-08-4.

Fluorine Magnetic Resonance Spectra of Monofluoro- and Difluoro-Substituted Hydrocarbons

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Fluorine chemical shifts have been measured for some simple mono- and difluorides. Substituent effects analogous to those in carbon NMR have been developed for aliphatic, phenyl, and fluorine substituents. The substituent parameters for individual compounds are interpreted in terms of conformational effects, and the general parameters are compared with those of other nuclei.

Fluorine NMR, although indispensable to the fluorine chemist,[1,2] is not as useful as it might be in distinguishing between alternative structures. In part, this problem has arisen because, in contrast to carbon NMR,[3,4] the basic rules governing fluorine chemical shifts, as would be determined from simple compounds, have never been elucidated. Carbon chemical shifts have been correlated with substituent parameters derived from rigid molecules and rotamer populations derived from regression analyses. This ideal approach is more feasible for carbon than for

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[1] J. W. Emsley, J. Feeney, and L. H. Sutcliffe, "Progress in NMR Spectroscopy", Vol. 7, Pergamon Press, Elmsford, NY, 1971.

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[3] D. M. Grant and E. G. Paul, *J. Am. Chem. Soc.*, **86**, 2984 (1964).

[4] (a) L. P. Lindeman and J. Q. Adams, *Anal. Chem.*, **43**, 1245 (1971); (b) H. Beierbeck and J. K. Saunders *Can. J. Chem.*, **55**, 771 (1977).

Table I. NMR Data for Primary Fluorides

fluoride	method	$-\delta_F$[c]	$N(\beta)$	$N(\gamma)$	$N(\delta)$	J(HF)[b]
methyl	*a*	267.9	0	0	0	
ethyl	C	211.5	1	0	0	48.5 (t), 27 (d)
propyl	C	218.6	1	1	0	48.5 (t), 24.5 (d), m
butyl	C	218.6	1	1	1	48.2 (t), 25 (t)
3-methylbutyl	C	218.6	1	1	2	
2-methylpropyl	C	220.3	1	2	0	48 (t), 17 (d)
2-methylpentyl	C	222.7	1	2	1	49 (t), 19 (d)
2,2-dimethylpropyl	A	222.8	1	3	0	
2-ethylbutyl	C	226.4	1	2	2	
3,3-dimethylbutyl	C	217.3	1	1	3	47 (t), 26 (t)
allyl	C	216.0				48 (t)
propargyl	C	217.5				48 (t), 6.5 (d)
2-methoxyethyl	C	223.1				49 (t), 31 (t)
trans-2-butenyl	C	209.7				

[a] I. Ruppert, *Angew. Chem., Int. Ed. Engl.*, **18**, 880 (1979). [b] Values given in hertz with multiplicities in parentheses. [c] In parts per million.

fluorine NMR because of the larger data base available.[4b] Fluorine spectroscopists have previously chosen perfluorocarbons as their "simple" model compounds.[5,6] Unfortunately, this corresponds closely to choosing poly(tetramethylethylene) instead of polyethylene as the unsubstituted standard to which substituents would be compared in carbon NMR. Correlations could be developed, but at least in carbon NMR, pairwise interactions have been shown to dominate in this situation.

Because fluorine chemical shifts are "large",[7] workers have been less careful than they might be in standardizing solvents and reference materials. While the chemical shifts of fluorine bonded to nitrogen vs. fluorine bonded to carbon are large,[5,6] this effect is generally not the sort of information the chemist seeks. Conformational and long-range substituent effects are the same order of magnitude as medium effects, and the latter must be controlled if reliable structural conclusions are to be drawn.

Correlations of *m*- and *p*-fluorine chemical shifts in aromatic systems with Hammett substituent parameters have been extremely useful,[8] but similar correlations for aliphatic and alicyclic compounds have not been developed. The effects of polar substituents on fluorine shifts in substituted ethanes have been explained in terms of electric field effects,[9] but the extension of this work to structure determination has not been pursued.

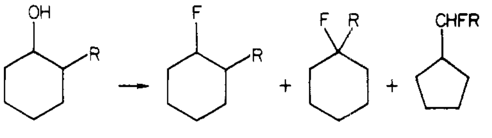
The fluorine chemical shifts of some continuous-chain primary fluorides have been measured,[10] as have those of a few secondary fluorides such as cyclohexyl[11,12] and *exo*-2-norbornyl[13] and tertiary fluorides such as *tert*-butyl[14] and 1-adamantyl.[15] Detailed studies of the effect of methyl substitution on 1,1-difluorocyclohexanes[16] and 2,2-difluoronorbornanes[17] have demonstrated the possibility of using these effects in conformational analysis, but, in general, the basic data needed to efficiently use fluorine NMR to distinguish subtle structural alternatives is not available.

In this paper, the fluorine chemical shifts of some aliphatic and phenyl-substituted hydrocarbons in which one or two of the protons have been replaced with fluorine are presented, and the substituent effects are discussed in terms of conformational effects.

Syntheses

Conventional methods of replacing hydroxyl with fluoride or carbonyl with difluoride substituents were used.[18,19] The products were not isolated but were characterized solely by their fluorine NMR spectra. The structures were confirmed by the proton–fluorine spin–spin coupling and the patterns of the fluorine shifts which became apparent during this work. Rearrangements and aberrant reactions were quite easy to detect by multiplet patterns and shifts which were not consistent with the expected reaction products.

Attempts to prepare secondary fluorides adjacent to tertiary or quaternary centers generally gave products derived from a more stable, rearranged carbenium ion. For example, 2-methylcyclohexanol gave two products (see eq 1) with multiplets at −172.7 and −152.3 ppm. (In this paper negative shifts are to high field of the reference standard.) The latter resonance was identified as 1-fluoro-1-methylcyclohexane by independent synthesis from 1-methylcyclohexanol. The chemical shift of the former is consistent with either the desired substitution product or one in which the ring has contracted to give cyclopentylfluoroethane. 2-Phenylcyclohexanol gave two resonances at −171.1 and −171.8 ppm. The former had a splitting pattern consistent with that expected for a 1-fluoro-2-phenylcyclohexane and a chemical shift consistent with an equatorial fluorine. The latter was a doublet of doublets (J = 48, 16 Hz) which is consistent with the ring-contracted cyclopentylphenylfluoroethane. Neither *cis*-2-phenyl-1-fluorocyclohexane nor phenyl migration was observed.



(1)

R = Ph, CH_3

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(18) W. J. Middleton, *J. Org. Chem.*, **40**, 574 (1975).

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Table II. NMR Data for Secondary Fluorides

fluoride	method	$-\delta_{\mathrm{F}}$[h]	$N(\beta)$	$N(\gamma)$	$N(\delta)$
2-propyl	C	165.2	2	0	0
2-butyl	C	173.2	2	1	0
2-pentyl	C	172.8	2	1	1
3-pentyl	C	182.7	2	2	0
3-octyl	C	181.3	2	2	1
4-methyl-2-pentyl	C	173.0	2	1	2
2-methyl-3-pentyl	C	188.9	2	3	0
cyclohexyl (a)[f]	*a*	186.0	2	2	1
cyclohexyl (e)[g]	*a*	165.5	2	0	1
cis-3-methylcyclohexyl	C	182.4	2	2	2
trans-3-methylcyclohexyl	C	165.7	2	0	2
cis-4-methylcyclohexyl	C	168.1	2	0	1
trans-4-methylcyclohexyl	C	184.8	2	2	1
trans-2-phenylcyclohexyl	C	171.1			
1-buten-3-yl	*b*	171.6			
1-penten-4-yl	C	172.4			
cyclohex-1-en-4-yl	*c*	175.4			
1-indanyl	C	159.9			
exo-norbornyl	*d*	158.9			
cyclooctyl	*e*	179.6, 159.2, 150.6			

[a] References 11 and 12. [b] Reference 18. [c] By the Diels-Alder reaction of vinyl fluoride and butadiene: D. M. McQueen, U.S. Patent 2 904 598 (1959). [d] Reference 13. [e] At −170 °C in propene. A full description of the variable-temperature NMR spectra has been accepted for publication in *J. Org. Chem.* [f] Axial fluorine. [g] Equatorial fluorine. [h] In parts per million.

Table III. NMR Data for Tertiary Fluorides

fluoride	method	$-\delta_{\mathrm{F}}$[c]	$N(\beta)$	$N(\gamma)$	$N(\delta)$
2-methyl-2-propyl	C	130.8	3	0	0
2-methyl-2-butyl	*a*	139.2	3	1	0
3-methyl-3-pentyl	C	149.1	3	2	0
3-ethyl-3-pentyl	C	156.2	3	3	0
2,3-dimethyl-2-butyl	C	139.9	3	1	0
2,3,3-trimethyl-2-butyl	C	147.8	3	2	0
2-methyl-2-pentyl	C	137.1	3	1	1
1-methyl-1-cyclohexyl	C	152.3	3	2	1
1-adamantyl	*b*	130.0	3	0	3
3,3-dimethylpropargyl	*a*	129.3			

[a] Reference 18. [b] Reference 15. Although there are formally three γ carbons, all three are rigidly trans. The δ parameter to the other tertiary carbons averages +2.6 ppm in this system. [c] In parts per million.

Attempts to prepare 2-fluoro-3,3-dimethylbutane gave the Wagner–Meerwein rearrangement product 2-fluoro-2,3-dimethylbutane. 2,2-Diphenylethanol gave 1,2-diphenylfluoroethane and no resonance above −200 ppm as would be expected for the simple substitution product. The fluorination of benzoin gave initially 1-phenyl-1-fluoroacetophenone with a chemical shift at −175.4 ppm and J(HF) = 48 Hz. Fluorination of the ketone to give the trifluoride occurred more slowly. In spite of these exceptions, most substitutions proceeded normally to give the expected products.

Results

The chemical shifts for the various alkyl fluorides are given in Tables I–V, and those for the phenyl-substituted compounds are presented in Table VI. For clarity, primary, secondary, and tertiary monofluorides are listed separately as are the difluorides derived from aldehydes and ketones. The results of a Grant and Paul[3] analysis with three adjustable parameters for each of the five classes of compounds are given in Table VII. In all cases, the δ parameter was not statistically significant. The data for the mono- and difluorides were also analyzed by using an equation of the form discussed by Lindeman and Adams,[4] and the results are given in Table VIII along with the corresponding carbon, nitrogen, and oxygen parameters taken or calculated from literature data. Chemical shifts of 1,2-difluorides and the effect of introducing the γ-

Table IV. NMR Data for Primary Difluorides

fluoride	method	$-\delta_{\mathrm{F}}$[f]	$N(\beta)$	$N(\gamma)$	$N(\delta)$	J(HF)[e]
methylene	*a*	143.6	0	0	0	
ethylidine	*b*	110	1	0	0	
propylidine	B	120.0	1	1	0	57 (d), 17.5 (t)
butylidine	B	116.8	1	1	1	57 (d), 17 (t)
pentylidine	B	118.5	1	1	1	57 (d), 17.5 (t)
hexylidine	B	118.0	1	1	1	57 (d), 17 (t)
3-methylbutylidine	B	115.5	1	1	2	57 (d), 17.2 (t)
3-methylpentylidine	B	117.3	1	1	2	57 (d), 17.5 (t)
2-ethylbutylidine	B	123.3	1	2	2	57 (d), 15 (t)
2-methylpropylidine	B	126.7	1	2	0	57.5 (d), 14.5 (d), 0.7 (m)
2-methylbutylidine[c]	B	124.0	1	2	1	(m)
2-ethylhexylidine	B	123.6	1	2	2	57 (d), 16 (d)
2,2-dimethylpropylidine	B	128.6	1	3	0	57 (d), 1.2 (m)
cyclohexylmethylene	*d*	126.3	1	2	2	57 (d), 13 (d)

[a] Reference 8b. [b] Reference 8c. [c] Average of nonequivalent fluorines. The shift difference is 2.17 ppm; J(FF) = 281 Hz. [d] Reference 18. [e] Values given in hertz with multiplicities in parentheses. [f] In parts per million.

Table V. NMR Data for Secondary Difluorides

fluoride[f]	method	$-\delta_F$[g]	$N(\beta)$	$N(\gamma)$	$N(\delta)$	J(HF)[e]
propylidine	B	84.5	2	0	0	18 (s)
butylidine	B	93.3	2	1	0	15.5 (t), 18.5 (q)
2-pentylidine	B	91.0	2	1	1	(m)
3-pentylidine	B	102.4	2	2	0	21.5 (p)
2,2-dimethylbutylidine	B	102.2	2	2	0	20 (q)
4-methyl-2-pentylidine	B	87.7	2	1	2	
4-heptylidine	*a*	98.6	2	2	2	(m)
3-methyl-2-pentylidine	B	95.1	2	2	1	
2-phenylcyclohexylidine (a)	B	113.2				
2-phenylcyclohexylidine (e)	B	93.0				
cyclohexylidine (a)	*a*	104	2	2	1	
cyclohexylidine (e)	*a*	88	2	0	1	
exo-norbornylidine	*c*	86				
endo-norbornylidine	*c*	109				
2-methylcyclohexylidine (a)	*d*	117.1				
2-methylcyclohexylidine (e)	*d*	97.9				
3-methylcyclohexylidine (a)	*d*	102.0				
3-methylcyclohexylidine (e)	*d*	90.2				
4-methylcyclohexylidine (a)	*d*	102.9				
4-methylcyclohexylidine (e)	*d*	91.2				

[a] Reference 18. [b] References 11 and 12. [c] Reference 17. [d] Reference 16. [e] See footnote *e* in Table IV. [f] An a or e in parentheses indicates whether the fluorine is axial or equatorial, respectively. [g] In parts per million.

Table VI. Fluorine Chemical Shifts of Phenyl-Substituted Compounds

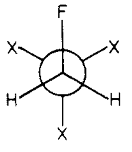
compd	$-\delta_F$	J(HF)[e]
$PhCH_2CH_2F$	216.0	47 (t), 29 (t)
$PhCH_2F$	206.3	49 (t)
$PhCH_2CHFCH_2Ph$	178.3	24 (p)
PhCHFEt	175.4	44 (d), 25 (d), 19 (d)
$PhCH_2CHFPh$	173.1	48 (d), 23 (d), 19 (d)
$PhCH_2CHFMe$	171.3	48 (d), 24 (t), 20 (q)
t-2-Ph-cyclohexyl	171.1	
Ph_2CHF	167.4	48 (d)
PhCHFMe	166.8	48 (d), 24 (q)
$PhCFMe_2$	137.3	22 (h)
Ph_2CFMe	135.0	23 (q)
Ph_3CF[a]	126.7	
Ph_2CHCHF_2	118.6	57 (d), 16 (d)
$PhCH_2CHF_2$	115.0	57 (d), 12 (t)
2-Ph-cyclohexylidine (a)	113.2	236[d]
$PhCHF_2$	111.2	57 (d)
$PhCF_2Et$	97.9	
$PhCH_2CF_2CH_2Ph$	95.9	17 (p)
$PhCH_2CF_2Ph$	94.9	21 (t)
2-Ph-cyclohexylidine (e)	93.0	236[d]
$PhCH_2CF_2Me$	89.6	18 (q), 16 (t)
Ph_2CF_2	88.5	
$PhCF_2Me$[b]	87.7	18 (q)
$PhCF_3$[c]	64	

[a] A. L. Johnson, private communication. [b] W. J. Middleton, private communication. [c] Reference 1. [d] J(FF) value. [e] See footnote *e* of Table IV.

fluoride are given in Table IX.

Discussion

Statistics. Ultimately, the simple statistical analyses pioneered for carbon NMR by Grant and Paul[3] and by Lindeman and Adams[4] break down because they do not take into account conformational differences. For example, if the gauche and trans γ effects are different, 2,2-dimethyl-1-fluoropropane has two gauche effects and one trans methyl effect, not three "γ" effects (see structure I).



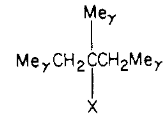
I, X = H, Me

Table VII. Substituent Parameters for Mono- and Difluoroalkanes

compd type	substituent effect,[a] ppm				std error, ppm
	β	γ	δ[b]	N[c]	
CH_2F	59.4	−4.2	−1.0	10	2.22
CHF	53.2	−8.3	−0.1	15	1.75
CF	47.1	−7.7	−0.3	11	4.4
CHF_2	32.0	−6.5	0.4	15	1.6
CF_2	28.5	−6.3	1.0	11	3.5

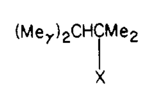
[a] Positive values are shifts to lower field. [b] These values are not statistically significant. [c] Number of observations.

Statistical methods of correlating carbon chemical shifts and structural parameters fail for highly branched systems unless "branching parameters" are introduced. For example, the shifts of the methyls in hydrocarbons **1a** and **2a** are both predicted to be at 26.3 ppm because each has one α, three β, and two γ carbons. The actual shifts bracket the calculated shift, and the difference between them of 0.7 ppm is within the expected error of the calculation. Fluorine shifts are larger than carbon shifts, and the corresponding fluorides **1b** and **2b** differ by 9 ppm, also with the more highly branched compound at lower field. A similar effect occurs in 3-ethyl-3-fluoropentane and 2,3,3-trimethyl-2-fluorobutane, with the more highly branched compound being 8 ppm to low field although again the formal numbers of β and γ effects are identical. In these types of analyses, special cases, which are not explained by the limited number of parameters available, always appear, and ad hoc additions to the parameter sets proliferate.



$Me_\gamma CH_2C(Me_\gamma)(X)CH_2Me_\gamma$

1



$(Me_\gamma)_2CHC(X)Me_2$

2

	1	2
a, X = CH_3	25.6	27.0
b, X = F	−149.1	−139.9

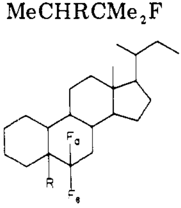
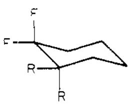
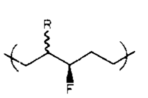
If the structural types included in the data bases are similar, changes in the substituent parameters reflect nuclear properties and can give insights into how substituent effects are transmitted and received. The ratios $B3/B2$ and $B4/B3$ in Table VIII are essentially independent of

Table VIII. Comparison of Alkyl Substituent Parameters of Various Nuclei[a]

nucleus	$B2^c$	$B3^c$	$B4^c$	γ^c	δ^c	N	std error[c]	RSQ	ref
carbon	9.6	17.8	25.4	−3.0	−0.5	59			3
nitrogen	23.3	41.1	55.5	−4.6[b]	−0.2[b]	11			32, 33
oxygen	44.7	78.6	102.3	−4.5	6.8	13	3.5	0.994	from 21, 22
oxygen	43.5	73.2	97.5	−4.3		16	4.0	0.985	from 23
monofluorides	59.1	101.4	136.7	−7.3	−0.5[b]	39	3.0	0.993	
difluorides	31.7	57.4		−6.5	0.6[b]	24	2.5	0.980	

[a] Positive values are shifts to lower field. [b] These values are not statistically significant. [c] In parts per million.

Table IX. γ Effect of Fluorine on Fluorine

compd	$-\delta_F$ (R = F)	shift diff[c]	ref
RCH_2CH_2F	225.9	14.4	18
$MeCHRCMe_2F$	152.0	12.8	18
 F_a	106.9	−0.5 (=*t*)	*a*
F_e	106.9	13.8 (=*g*)	
 F_a	122	19.5 (=*g*)	26
F_e	127	1.5 (=*t*)	
PhCHRCHFMe, erythro	193.5	22.2	*b*
threo	186.8	15.5	
MeCHRCHFPh, erythro	182.5	7.1	*b*
threo	183.8	8.4	
 *d,l*	191.1	10.9	31
meso	196.1	15.9	
$PhCHRCF_2Ph$	106.2	11.3	this work
	109.8	17.9	
$PhCR_2CHFPh$	191.7	18.6	this work

[a] G. A. Boswell, private communication. [b] R. F. Merritt *J. Am. Chem. Soc.*, **89**, 609 (1967). [c] Vicinal cis or gauche difluorides are upfield from monofluorides. In parts per million; calculated by subtracting shift when R = F from that when R = H.

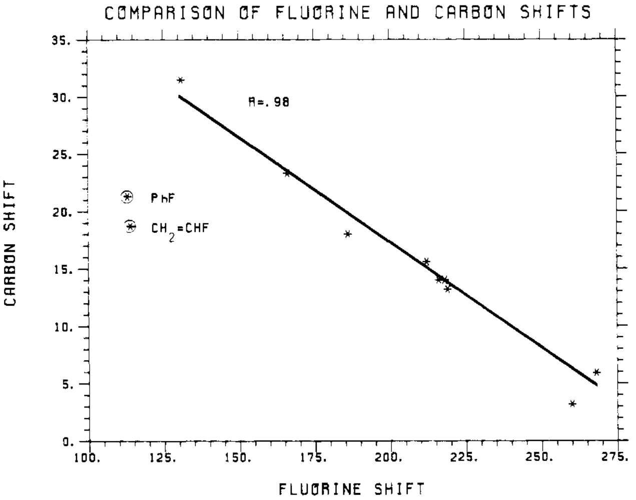
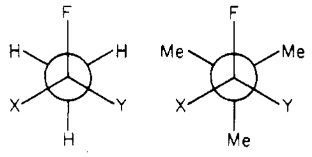


Figure 1. Comparison of fluorine and carbon chemical shifts.

the nuclei being observed, although the values of the β parameters do depend on the nuclei and appear to increase with an "effective nuclear charge" or Slater exponent.[20] The correlation is equally good for Z^2 and Z^3 over this narrow range of nuclei. The γ effect varies less than the β effect, but an increase with the atomic number of the nucleus is observed for both. For carbon NMR, the β and γ effects are comparable; the β effect dominates fluorine NMR so that there is little overlap in the resonances of primary, secondary, and tertiary fluorides. The entries for oxygen,[21,23] illustrate how the parameters can change as different compounds are included in the data bases. The γ-fluorine parameters are also still sensitive to the introduction of new highly branched molecules because the γ count is statistical rather than conformational.

Stereospecific γ Effect of Carbon on Fluorine. In carbon NMR, the γ parameter has two components from independent gauche and trans interactions. The gauche parameter is large; the trans parameter is essentially zero.[24] The same relationship holds for the γ interaction of carbon substituents on fluorine shifts.[17] The difference between two gauche and two trans effects accounts for the differences between the axial and equatorial shift differences in mono- and difluorocyclohexanes. Two gauche effects and one trans effect are the differences between compounds **3** and **4**. Solving the five equations in two unknowns (leaving out the apparently anomalous result for **3a** and **4a**) gives a gauche γ interaction of −9 ppm and an essentially zero trans γ interaction. This can be compared to the cis γ interaction of −10 ppm found in the norbornyl system.[17] As in carbon NMR, the cis and gauche γ effects are comparable.



3 **4**

	X	Y	$-\delta_F$ (3)	$-\delta_F$ (4)	Δ, ppm
a	H	H	211.5	222.8	11.3
b	H	Me	165.2		
c	Me	Me	130.8	147.8	17.0
d	F	Me	84.5	102.2	17.7
e	F	H	110	128.6	18.6

Long-Range Effects. The assumption commonly made in carbon NMR, that long-range effects can be neglected, is probably not valid for either carbon or fluorine NMR.[25] The long-range effects may be highly stereospecific so that in aliphatic cases they will average to a small value. They show up dramatically, however, in alicyclic systems. For example, adding a 4-methyl group (ϵ) to 1,1-difluorocyclohexane shifts the equatorial fluorine upfield by 4.6 ppm while the axial fluorine remains nearly unchanged.[26] Similar effects are seen in the monofluorides. The as-

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(24) J. B. Stothers, "Carbon-13 NMR Spectroscopy", Academic Press, New York, 1972.

(25) S. H. Grover, J. P. Guthrie, J. B. Stothers, and C. T. Tan, *J. Magn. Reson.*, **10**, 227 (1973).

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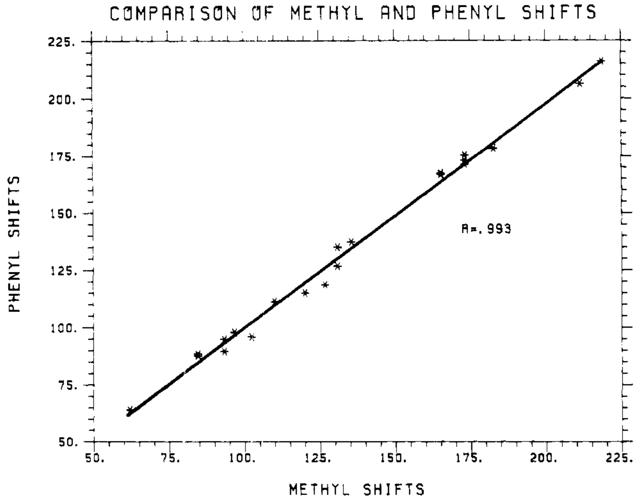

Figure 2. Comparison of fluorine chemical shifts in methyl- and phenyl-substituted compounds.

sumption that the difference between axial and equatorial fluorocyclohexanes arises from two or zero γ effects may be in error because of the differing geometry of the two δ effects. Nevertheless, because of the averaging effects in aliphatic systems, the measured δ effects are generally not significant, and conformation can be profitably discussed in terms of the dominant γ effect.

Other Substituent Effects. Propyl, allyl, and propargyl fluorides have similar shifts, showing that, as in carbon NMR, unsaturation in the β position has little effect on chemical shifts. The analogy cannot be extended to directly bonded conjugation as shown in Figure 1. The downfield shift from fluoroethane (−211 ppm) to fluoroethene (−114 ppm)[1] is not paralleled by the methyl carbon shifts in propane (15.6 ppm) and propene (18.7 ppm).[24] The methyl shift in propyne (3.1 ppm) does correlate with the fluorine shift in fluoroacetylene (−260 ppm).[27] The downfield shifts in fluorobenzene and fluoroethene may correlate with resonance forms such as $^-CH_2CH{=}F^+$ as discussed for oxygen NMR by Crandall.[23] The shift to high field in both acetylenes may arise from the diamagnetic anisotropy of the triple bond.

Phenyl Effect. The fluorine chemical shifts of the phenylalkyl fluorides and difluorides given in Table VIII are to a first approximation equivalent to the shifts in the related compounds in which the phenyl group is replaced by a methyl as shown in Figure 2. The standard error of 3.7 ppm is about as good as that derived for the alkyl parameters by direct measurement.

β-Fluorine Effect. From the differences between mono- and difluorides, we can comment on the β-fluorine effect. As has been discussed for carbon shifts,[28] this effect can be looked at in two different ways. The fluorine can replace a hydrogen (Table X) or a methyl group (Table XI). The 21 examples in Table X consist of one with $R_1 = R_2 = H$, eight with $R_1 = H$ and R_2 = carbon, and 12 with $R_1 = R_2$ = carbon. The β-fluorine effect is 128 ppm from methyl to methylene fluoride and averages 98 ± 3.7 ppm for the secondary and 79 ± 2.7 ppm for the tertiary examples. Likewise from Table XI, the three β effects are 68 ppm for primary, 55 ± 1.2 ppm for secondary, and 47 ± 1.7 ppm for tertiary monofluorides. Just as there is no single β-methyl effect, so also the β-fluorine effect depends on the degree of substitution at both the α- and β-carbons.

Table X. β-Fluorine Substituent Effects by Replacing Hydrogen with Fluorine, R_1R_2CHF vs. $R_1R_2CF_2$

R_1	R_2	shift diff[a]	R_1	R_2	shift diff[a]
H	H	128.4	Me	Ph	79.1
H	Me	101.5	Ph	Ph	78.9
H	Et	98.6	$PhCH_2$	$PhCH_2$	82.4
H	*n*-Pr	101.8	Ph	Et	77.5
H	*i*-Pr	93.6	Ph	$PhCH_2$	78.2
H	*i*-Bu	103.1	$PhCH_2$	Me	81.7
H	*t*-Bu	94.2	cyclohexyl (a)		82
H	Ph	95.1	cyclohexyl (e)		77.5
H	$PhCH_2$	97.4	*exo*-norbornyl		72.9
Me	Me	80.7	H	F	64.8
Me	Et	79.9	Me	F	47.5
Me	*n*-Pr	81.8	Ph	F	47
			F	F	15.3

[a] In parts per million. Difluoride shifts are at lower field than those of monofluorides.

Table XI. β-Fluorine Substituent Effects by Replacing Methyl With Fluorine, R_1R_2CFMe vs. $R_1R_2CF_2$

R_1	R_2	shift diff[a]	R_1	R_2	shift diff[a]
H	H	67.9			
H	Me	55.2	Me	Ph	49.6
H	Et	53.2	Ph	Ph	46.5
H	*n*-Pr	56.0	H	F	31.4
H	Ph	55.6	Me	F	22.0
Me	Me	46.3	Ph	F	24
Me	Et	45.9	F	F	0.8

[a] In parts per million. Difluoride resonances are at lower field than those of monofluorides.

The precision of the methyl–fluorine correlation is higher, but these pairs are less readily available than the hydrogen–fluorine pairs. The β effect of fluorine on fluorine is approximately twice that of carbon on fluorine. Compounds where R_1 and R_2 are fluorine are also different from their hydrocarbon analogues.

γ-Fluorine Effect. Table IX lists the chemical shifts of some 1,2-difluoro compounds and the effect of introducing each γ-fluorine on the other where the monofluoro compound's shifts are available. It is a pity that such an important compound as 1,2-difluorocyclohexane has been repeatedly prepared[29] without stating whether the procedure produced the cis or trans isomer or a mixture of isomers and with no fluorine NMR data. Nevertheless, from the observed pairs of shifts and known conformations of such flexible molecules as 1,2-difluoroethane, we conclude that the gauche γ effect of fluorine on fluorine is about −15 ppm and the trans γ effect is essentially zero. In cases such as 1,2-difluoro-1-phenylpropane where the γ effects are anomalous, conformational changes are most likely to occur as fluorine is substituted for hydrogen. The γ-fluorine parameter is not independent of the rest of the molecule, however. Adding fluorines to the β-carbon of 1,1,1-trifluoroethane results in a $^1/_3\ (2g + t)$ effect for each added fluorine, yet the resonance of the trifluoromethyl group moves upfield by 17, 9, and 3 ppm as each additional γ-fluorine is added.[9,30] The final $(2g + t)$ value is −30 ppm for mono-, di-, and trifluoroethanes. The rules for lightly fluorinated systems will most likely require "correction

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(33) R. O. Duthaler and J. D. Roberts, *J. Am. Chem. Soc.*, **100**, 3889 (1978).

Table XII. Comparison of Fluorine and Carbon Parameters

observed nucleus	perturbing nucleus	β effect,[a] ppm	gauche γ effect,[a] ppm
Me	C	9	−5
Me	F	8	−10
F	C	40	−9
F	F	90	−15

[a] Positive effects are shifts to lower field.

terms" before they can be applied to heavily fluorinated systems.

Comparison of Fluorine and Carbon Effects. The original explanation of the gauche effect of carbon on carbon[3] was in terms of hydrogen repulsions being transmitted to their directly bonded carbon. This explanation cannot reconcile that fluorine and carbon in similar geometries mutually shift each other to higher field. Table XII compares the β and γ effects of fluorine and carbon on each other in all possible combinations. The β effect is most sensitive to the nucleus being observed, the γ effect is equally sensitive to both. The direction of the effect does not depend on the identity of either nucleus.

Effect of a Difluoromethyl Group. To understand perfluoro carbon chains, we next study the effect of difluoromethyl groups on each other. A very good system in which to study these effects is poly(vinylidene fluoride).[34] Head-to-head dyads provide γ effects while head-to-tail dyads provide δ effects. Tetrads provide ϵ effects. A statistical analysis of the data gives a −18.1-ppm γ effect, a +3.0-ppm δ effect, and a nonsignificant 0.1-ppm ϵ effect. The standard error of the calculation is 0.7 ppm, and the RSQ is 0.997. If the polymer chain were perfectly extended, the introduction of a vicinal CF_2 group would shift each original fluorine by one gauche and one trans effect. Any bending of the chain would introduce a contribution of two gauche interactions and one trans interaction per two fluorines. If the γ parameters are transferable, a small amount of chain bending at the head-to-head dyads seems indicated.

Molecular Mechanics Calculations. Molecular mechanics has provided a useful framework for discussing the conformations of saturated hydrocarbons.[35] Calculations using the Allinger program MMI reproduce satisfactorily the difference in energy between such monofluorides as axial and equatorial fluorocyclohexane (0.2 kcal/mol calcd, 0.4 obsd) and gauche and *trans*-1-fluoropropane (gauche preferred by 0.2 kcal/mol, for the calculated and observed values).

We applied this computational method to vicinal di- and tetrafluorides as models for poly(vinyl fluoride) and poly(vinylidene fluoride). The dielectric constant was set at 4.0 in the calculations. The calculated steric energies for some conformations of 2,3- and 2,4-difluoropentane are given in Table XIII. The numbering pattern for the branched-chain conformation is shown in Figure 3.

Table XIII. Steric Energies of Difluoropentanes[a]

extended chain		branched chain	
fluorine locations	steric energy	fluorine locations	steric energy
9, 11	6.39	9, 11	7.53
meso		10, 12	6.88
		11, 13	6.40
		12, 14	6.65
9, 12	5.70	9, 12	6.60
d, *l*		10, 11	6.47
		11, 14	6.77
		12, 13	6.88
9, 13	5.40	9, 13	5.69
isotactic		10, 14	5.20
9, 14	4.57	9, 14	5.55
syndiotactic		10, 13	6.20

[a] Steric energies in kilcalories per mole.

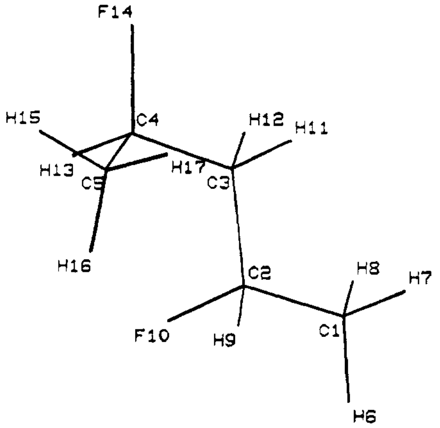

Figure 3. Numbering of the branched conformation of substituted pentanes. Atoms 9, 11, and 13 are on the same side of the extended chain.

Of the HH dyads, the extended-chain *d,l* conformation is calculated to be the most stable, but not by much. In the head-to-tail dyad, the syndiotactic conformer is more stable than the isotactic form. The 1,3 fluorine–fluorine interactions in the extended-chain, isotactic conformer are apparently destabilizing, and a branched conformer is actually preferred. The fluorine NMR signal of the meso head-to-head dyad of poly(vinyl flouride) is 11 ppm upfield from an isolated fluorine while the *d,l* dyad is 16 ppm upfield.[31] The −16-ppm shift suggests that the second fluorine enters nearly 100% gauche to the first. Molecular mechanics calculations predict that the meso isomer would be shifted 9.3 ppm upfield while the *d,l* would be shifted only 3.6 ppm. Although the absolute values of the predicted shifts are too low, the difference of 5 ppm is well explained. The program calculates that 1,2-difluoroethane should be 84% gauche while the NMR shift would suggest a higher value. Apparently the program understates the gauche fluorine–fluorine interaction, at least as applied to these lightly fluorinated molecules in solution. The program predicts that 2,2,3,3-tetrafluorobutane should be 67% trans, which would lead to the prediction of a −17.3-ppm γ effect in poly(vinylidine fluoride) which is very close to the −18.1 ppm observed. Molecular mechanics and fluorine NMR shifts appear to be basically consistent in their explanation of the conformations of lightly fluorinated polymers.

Because the relative substituent effects for carbon and fluorine are not proportional for all parameters, the linear correlation of the shifts of these two nuclei previously found[31] was valid only with the limited set of compounds considered. Straight lines correlating the NMR properties of different nuclei are probably valid in the grossest sense, but when fine details like long-range substituent effects or conformational analysis are considered, present knowledge is inadequate to reliably predict shifts from structure or structure from shifts.

Experimental Section

Fluorine NMR spectra were obtained with a Varian XL-100 spectrometer operating at 94.1 MHz both with and without proton

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(34) R. C. Ferguson and E. G. Brame, Jr., *J. Phys. Chem.*, **83**, 1397 (1979).

(35) N. L. Allinger, M. T. Tribble, M. A. Miller, and D. H. Wertz, *J. Am. Chem. Soc.*, **93**, 1637 (1971).

decoupling. Some preliminary spectra were obtained with a Varian A-56/60 spectrometer operating at 56.4 MHz. The fluorides were examined as prepared in methylene chloride solutions with $CFCl_3$ as an internal standard and lock. The fluorine chemical shifts of all the compounds in this paper are upfield from the reference. All alcohols and carbonyl compounds were available from commercial sources and were used as received. Multiplets are indicated in the tables as follows: d, doublet; t, triplet; q, quartet; p, pentet; s, septet.

Method A. Alcohol Plus (Diethylamino)sulfur Trifluoride (DAST).[18] A 5-mL vial with 1 mL of CH_2Cl_2 and 50-100 μL of alcohol was cooled to -78 °C. To this solution was added 50 μL of DAST. The solution was warmed to room temperature. For some alcohols, elimination to olefin occurred as the temperature was raised; these were examined in a precooled spectrometer at -80 °C.

Method B. Carbonyl Compound Plus DAST. A 5-mL vial with 1 mL of CH_2Cl_2 and 50-100 μL of ketone or aldehyde was treated with 50 μL of DAST at room temperature.

Method C. Alcohol Plus 2-Chloro-1,1,2-trifluoroethylamine (FAR).[19] A 5-mL vial with 1 mL of CH_2Cl_2 and 100 μL of alcohol was treated with FAR at -78 °C. The solution was warmed slowly to room temperature.

Registry No. 1a, 562-49-2; 1**b**, 19031-61-9; **2a**, 464-06-2; **2b**, 354-09-6; **3a**, 353-36-6; **3b**, 420-26-8; **3c**, 353-61-7; **3d**, 420-45-1; **3e**, 75-37-6; **4a**, 59006-05-2; **4b**, 2924-20-1; **4c**, 335-04-6; **4d**, 74185-61-8; **4e**, 53731-23-0; methyl fluoride, 593-53-3; propyl fluoride, 460-13-9; butyl fluoride, 2366-52-1; 3-methylbutyl fluoride, 407-06-7; 2-methylpropyl fluoride, 359-00-2; 2-methylpentyl fluoride, 62127-27-9; 2-ethylbutyl fluoride, 62127-36-0; 3,3-dimethylbutyl fluoride, 371-64-2; allyl fluoride, 818-92-8; propargyl fluoride, 2805-22-3; 2-methoxyethyl fluoride, 627-43-0; *tert*-2-butenyl fluoride, 920-35-4; 2-butyl fluoride, 359-01-3; 2-pentyl fluoride, 590-87-4; 3-pentyl fluoride, 41909-29-9; 3-octyl fluoride, 20469-83-4; 4-methyl-2-pentyl fluoride, 62127-32-6; 2-methyl-3-pentyl fluoride, 62127-33-7; cyclohexyl fluoride, 372-46-3; *cis*-3-methylcyclohexyl fluoride, 74185-62-9; *trans*-3-methylcyclohexyl fluoride, 74185-63-0; *cis*-4-methylcyclohexyl fluoride, 74185-64-1; *trans*-4-methylcyclohexyl fluoride, 74185-65-2; *trans*-2-phenylcyclohexyl fluoride, 74185-66-3; 1-buten-3-yl fluoride, 53731-19-4; 1-penten-4-yl fluoride, 66702-91-8; cyclohex-1-en-4-yl fluoride, 2266-53-7; 1-indanyl fluoride, 62393-01-5; *exo*-norbornyl fluoride, 765-92-4; cyclooctyl fluoride, 53731-16-1; 2-methyl-2-butyl fluoride, 661-53-0; 3-ethyl-3-pentyl fluoride, 649-80-9; 2-methyl-2-pentyl fluoride, 62127-30-4; 1-methyl-1-cyclohexyl fluoride, 66922-12-1; 1-adamantyl fluoride, 768-92-3; 3,3-dimethylpropargyl fluoride, 74185-67-4; methylene difluoride, 75-10-5; propylidene difluoride, 430-61-5; butylidene difluoride, 2358-38-5; pentylidene difluoride, 62127-40-6; hexylidene difluoride, 62127-41-7; 3-methylbutylidene difluoride, 53731-22-9; 3-methylpentylidene difluoride, 74185-68-5; 2-ethylbutylidene difluoride, 74185-69-6; 2-methylpropylidene difluoride, 62126-91-4; 2-methylbutylidene difluoride, 66688-67-3; 2-ethylhexylidene difluoride, 74185-70-9; cyclohexylmethylene difluoride, 329-29-3; 2-propylidene difluoride, 420-45-1; 2-butylidene difluoride, 353-81-1; 2-pentylidene difluoride, 371-65-3; 4-methyl-2-pentylidene difluoride, 371-70-0; 4-heptylidene difluoride, 53731-27-4; 3-methyl-2-pentylidene difluoride, 74185-71-0; 2-phenylcyclohexylidene difluoride, 57514-11-1; cyclohexylidene difluoride, 371-90-4; norbornylidene difluoride, 22847-05-8; 2-methylcyclohexylidene difluoride, 74185-72-1; 3-methylcyclohexylidene difluoride, 74185-73-2; 4-methylcyclohexylidene difluoride, 74185-74-3; 5,6,6-trifluorocholestane, 74185-75-4; 6,6-difluorocholestane, 74185-76-5; 1,1′-(1,1,2-trifluoro-1,2-ethanediyl)bisbenzene, 68936-77-6; 1,1′-(1,1-difluoro-1,2-ethanediyl)bisbenzene, 350-62-9; 1,1′-(1-fluoro-1,2-ethanediyl)bisbenzene, 74185-77-6; (R*,R*)-(±)-2,3-difluoropentane, 74185-78-7; (R*,S*)-(±)-2,3-difluoropentane, 74185-79-8; (*meso*)-2,4-difluoropentane, 22464-30-8; (±)-2,4-difluoropentane, 22464-29-5; $PhCH_2CH_2F$, 458-87-7; $PhCH_2F$, 350-50-5; $PhCH_2CHFCH_2Ph$, 74185-80-1; PhCHFEt, 19031-70-0; $PhCH_2CHFMe$, 40888-89-9; Ph_2CHF, 579-55-5; PhCHFMe, 7100-97-2; $PhCFMe_2$, 74185-81-2; Ph_2CFMe, 74185-82-3; Ph_3CF, 427-36-1; Ph_2CHCHF_2, 387-04-2; $PhCH_2CHF_2$, 10541-59-0; 2-Ph-c-HxF_2, 57514-11-1; $PhCHF_2$, 455-31-2; $PhCF_2Et$, 74185-83-4; $PhCH_2CF_2CH_2Ph$, 74185-84-5; $PhCH_2CF_2Ph$, 350-62-9; $PhCH_2CF_2Me$, 58325-18-1; Ph_2CF_2, 360-11-2; $PhCF_2Me$, 657-35-2; $PhCF_3$, 98-08-8.

Gaseous Anion Chemistry. Hydrogen-Deuterium Exchange in Mono- and Dialcohol Alkoxide Ions: Ionization Reactions in Dialcohols

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The subject of this work is H-D exchange in certain gaseous anions using D_2 as the exchanging agent. The anions involved are produced from ethylene glycol, 1,3-propanediol, 1,4-butanediol, ethanol, 1-propanol, and 1-butanol. Spectra and postulated ionization reactions for these mono- and dialcohols are given. Hydrogen-deuterium exchange occurs in the $(M - 1)^-$ and $(2M - 1)^-$ ions of ethylene glycol, 1,3-propanediol, and 1,4-butanediol. The amount of exchange occurring is 3-8 times greater in $(2M - 1)^-$ than in $(M - 1)^-$. The amount of H-D exchange occurring in ethanol, 1-propanol, and 1-butanol is small or zero in the $(2M - 1)^-$ ions and in the $(M - 1)^-$ ion for 1-butanol [the only $(M - 1)^-$ ion which could be examined experimentally]. The amount of exchange occurring in the $(2M - 1)^-$ and $(M - 1)^-$ ions from ethylene glycol is not affected by the total pressure or composition of the reaction mixture in the ionization chamber of the mass spectrometer. A novel hydrogen-bridging mechanism is suggested to account for the observed exchange occurring in the dialcohols.

A number of investigations of the OH^- negative chemical ionization mass spectrometry of various compounds have recently been made.[1-5] In these studies, unusual and interesting reactions of gaseous anions have been observed, and we plan to make studies using deuterium labeling to elucidate their mechanisms. However, since with our high-pressure chemical ionization apparatus the gaseous anions to be investigated would suffer many collisions with gas molecules during the period of their residence in the ionization chamber, the stability of the labels with respect to exchange with the gas molecules must first be investigated before the mechanistic studies utilizing labels can properly be undertaken. We have made a number of studies of the exchange between the hydrogen atoms in various protium anions and D_2. We find that exchange does occur for certain compounds, and we report here our findings with mono- and dialcohols. The investigation

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