

The Electronic Properties of Fluoroalkyl Groups. Fluorine p - π Interaction¹

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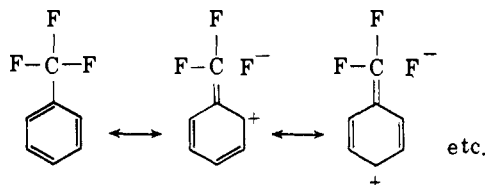
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The inductive and resonance effects of the pentafluoroethyl, nonafluoro-*n*-butyl, and heptafluoroisopropyl groups determined from pK_a measurements on benzoic acids and anilines are similar to those of a trifluoromethyl group. These results are discussed in terms of fluoride ion hyperconjugation and π -inductive effect, and a new explanation is proposed for the +*R* character of the fluoroalkyl groups. The interaction of *p*-electrons of the fluorines with the π -system of the aromatic ring causes significant return of electron density to the ring, partly counteracting the normal strong inductive withdrawal. This effect is more important at the meta than the para position so that the para position appears more strongly deactivated. This hypothesis is strongly supported by a discussion of σ -parameters for other fluorinated groups, such as $C(OH)(CF_3)_2$, $N(CF_3)_2$, and SF_5 , and a new approach to interpretation of F^{19} chemical shift correlations with substituent parameters for benzotrifluorides and arylsulfur pentafluorides.

The strongly deactivating effect of the trifluoromethyl group is well recognized. Quantitative measurements have shown that this effect can be mainly attributed to an inductive withdrawal, but in aromatic systems a significant enhancement by a conjugative contribution (+*R* character) is also found.² Mutual interactions of the nitro or cyano type are not possible, and two other mechanisms have been proposed to explain the +*R* effect of a trifluoromethyl group.^{2a,3,4}

A. Fluoride ion hyperconjugation is as represented by the following resonance pictures.



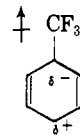
B. π -Inductive effects result where the strong inductive withdrawal of electrons from the neighboring position on the ring is transmitted by normal resonance mechanism to the *ortho* and *para* position.

(1) This work was presented in part at the 19th International Congress of Pure and Applied Chemistry, London, England, July 1963 (see *Angew. Chem.*, **75**, 1033 (1963)), and at the 148th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 1964.

(2) (a) J. D. Roberts, R. L. Webb, and E. A. McElhill, *J. Am. Chem. Soc.*, **72**, 408 (1950); (b) H. van Bekkum, P. E. Verkade, and B. M. Wepster, *Rec. Trav. Chim.*, **78**, 815 (1959).

(3) M. J. S. Dewar, "Hyperconjugation," The Ronald Press Co., New York, N. Y., 1962, p. 159.

(4) A. Streitwieser, Jr., and H. F. Koch, *J. Am. Chem. Soc.*, **86**, 404 (1964).



The fluoride ion hyperconjugation mechanism has also been proposed for stabilization of carbanions⁵ and in a "double bond-no bond resonance" picture⁶ to explain the stability of polyfluorides of methane.

Neither of the above mechanisms is satisfactory in explaining all pertinent data, and pro and con arguments have been presented. In addition to the general arguments against the hyperconjugation mechanism,³ we have noted that the +*R* effect for the SF_5 group is similar in size to that of the trifluoromethyl.⁷ This similarity suggests that the +*R* effect has a common origin, which is considered unlikely to result from hyperconjugation because of the gross differences between CF and SF bonds. On the other hand, the π -inductive effect does not explain why σ_m is the same as σ_p for the $+N(CH_3)_3$ group⁸ without invoking a special field effect from the positive charge.³ The recent report that σ_m and σ_p are both 1.3 for an electrically neutral ICl_2 group⁹ cannot be explained by this theory.

To obtain new experimental results that could resolve this mechanistic question, we undertook to determine the change, if any, in resonance effect that resulted by replacing the fluorines of the CF_3 group with perfluoroalkyl groups. As pointed out previously,¹⁰ the inductive effect of F and CF_3 are almost the same. Consequently we predicted that for the π -inductive mechanism no significant change in resonance effect should occur in going from CF_3 to $C(CF_3)_3$, but for the hyperconjugation mechanism, the +*R* effect should drop significantly.¹¹ In any case, quantitative comparison of the electrical effect of a series of fluoroalkyl groups is of value to gain a better insight into the effects of fluorine substitution.

Recent synthetic developments made possible preparation of a series of fluoroalkyl aromatics that could be employed for the classical measurement of pK_a and dipole moments^{2,3} as well as the recently developed technique of F^{19} n.m.r. chemical shift correlations.^{9,12} In particular, the use of sulfur tetrafluoride¹³ for con-

(5) S. Andreades, *ibid.*, **86**, 2003 (1964).

(6) J. Hine, *ibid.*, **85**, 3239 (1963).

(7) W. A. Sheppard, *ibid.*, **84**, 3072 (1962).

(8) J. D. Roberts, R. A. Clement, and J. J. Drysdale, *ibid.*, **73**, 2181 (1951).

(9) G. A. Maciel, *ibid.*, **86**, 1269 (1964).

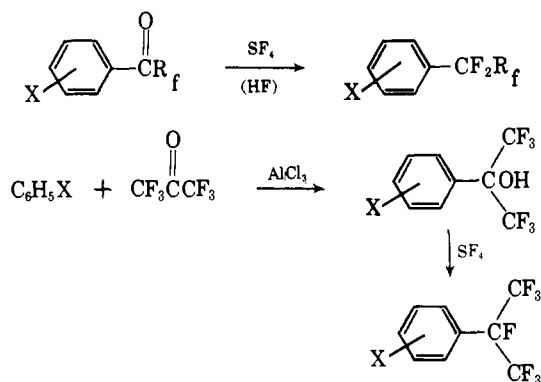
(10) W. A. Sheppard, *ibid.*, **85**, 1314 (1963).

(11) One difficulty in this approach is the argument that the hyperconjugation effect of a $-CF_3$ could be as effective as $-F$.

(12) R. W. Taft, E. Price, I. R. Fox, I. C. Lewis, K. K. Anderson, and G. T. Davis, *J. Am. Chem. Soc.*, **85**, 709, 3146 (1963), and earlier papers referred to in these references.

(13) W. R. Hasek, W. C. Smith, and V. A. Engelhardt, *ibid.*, **82**, 543 (1960).

version of C=O to CF₂ or of COH to CF and condensation of hexafluoroacetone with aromatic compounds¹⁴ were extremely valuable.



Experimental

Materials. All standard chemicals and reagents were obtained from Eastman Kodak or other chemical supply houses. The fluorine-containing starting materials were obtained as follows: Pierce Chemical Co.: *m*- and *p*-(trifluoromethyl)benzoic acids, anilines, and fluorobenzenes, and α,α,α -trifluoroacetophenone and its *meta*- and *para*-fluoro-substituted derivatives; Columbia Organic Chemicals: trifluoroacetic anhydride and trifluoroacetyl and heptafluorobutyryl chloride; Organic Chemicals Department, E. I. du Pont de Nemours and Co.: sulfur tetrafluoride and hexafluoroacetone. Pentafluoroethylbenzene was prepared from trifluoroacetophenone and sulfur tetrafluoride¹³; α,α -bis(trifluoromethyl)benzyl alcohol was prepared by condensation of hexafluoroacetone with benzene.¹⁴

All new compounds and compounds prepared by a new procedure are listed in Table I with physical properties and analytical data. A typical procedure for each type of reaction is given below and referenced in Table I along with the yield; minor modifications are described in footnotes.

The only problem in the synthetic scheme was proof that orientation was as expected in substitution reactions on the aromatic nucleus. In the majority of cases spectral analysis and comparisons provide definitive proof. In one or two cases independent verification by chemical transformations was obtained.

A. Condensation with Perfluorinated Acids, Acid Halides or Anhydrides, and Ketones. 1. *With Acid Anhydrides.* The method for condensation of aryl derivatives with anhydrides or acid halides was patterned after the literature procedures.¹⁵ A mixture of 24.2 g. (0.20 mole) of *N,N*-dimethylaniline and 2 g. of aluminum chloride was put in a four-neck flask fitted with mechanical stirrer, addition funnel, thermometer, and condenser under dry nitrogen atmosphere. Trifluoroacetic anhydride (42.0 g., 0.20 mole) was added dropwise; by adjusting the rate of addition and using intermittent cooling the reaction temperature was maintained at about 25°. Then 20.3 g. (0.20 mole) of

(14) (a) I. L. Knunyants, C.-Y. Chen, N. P. Gambaryan, and E. M. Rokhlin, *Zh. Vses. Khim. Obshchestva im. D. I. Mendeleeva*, **5**, 114 (1960); *Chem. Abstr.*, **54**, 20962 (1960); (b) *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 684 (1962); *Chem. Abstr.*, **57**, 12305 (1962); (c) D. C. England, French Patent 1,325,204 (1963).

(15) (a) J. H. Simons and E. O. Ramler, *J. Am. Chem. Soc.*, **65**, 389 (1943); (b) S. G. Cohen, H. T. Wolosinski, and P. J. Scheuer, *ibid.*, **71**, 3439 (1949).

triethylamine was added dropwise. A mild exothermic reaction was noted. After addition was completed, the reaction mixture was poured over cracked ice and the purplish crystalline solid was filtered off and washed with water. The crude product (25.9 g.) was triturated with pentane and recrystallized from hexane using charcoal. The *p*-(*N,N*-dimethylamino)- α,α,α -trifluoroacetophenone, m.p. 74.5–75.5°, was obtained in a yield of 17.1 g. (39%) as white crystals with a greenish tinge and was used without further purification for the sulfur tetrafluoride reaction. An analytical sample, m.p. 76.5–77.5°, was prepared by sublimation.

2. *With Hexafluoroacetone.*¹⁴ A mixture of 19.2 g. (0.20 mole) of fluorobenzene and 2 g. of aluminum chloride was charged into a 140-ml. Hastelloy-lined pressure vessel. The vessel was cooled in Dry Ice and evacuated, and 34 g. (0.20 mole) of hexafluoroacetone was added. The reactants were heated under autogenous pressure for 8 hr. at 60°. The product was suction filtered to remove aluminum chloride; a small amount of methylene chloride was used as a solvent rinse. The fluoro- α,α -bis(trifluoromethyl)benzyl alcohol was distilled, b.p. 78–80° (40 mm.), yielding 34.7 g. (66%). The orientation was shown to be *para* by proton n.m.r. and infrared analysis.

3. *Grignard with Acid.*¹⁶ *m*-Fluorophenylmagnesium bromide was prepared in the usual way from 50 g. (0.28 mole) of *m*-bromofluorobenzene and 7.2 g. (0.30 mole) of magnesium in 180 ml. of ether. The Grignard solution, kept under nitrogen, was added to 21 g. (0.10 mole) of heptafluorobutyric acid in 50 ml. of ether. A mild exothermic reaction occurred and the reaction temperature was maintained at about 25° by intermittent cooling during addition. After addition was complete, the reaction was refluxed for 4 hr. and allowed to stand overnight; then the mixture was hydrolyzed by pouring into ice and water containing 10 ml. of hydrochloric acid. The ether layer was separated, and the aqueous solution was extracted twice. The combined ether extracts were washed with 5% sodium carbonate solution and dried over magnesium sulfate, filtered, and distilled. *m*-Fluorophenyl heptafluoroisopropyl ketone, b.p. 85° (34 mm.), was collected in a yield of 20.4 g. (67%).

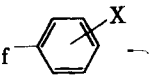
B. Sulfur Tetrafluoride Reactions. The same general procedure was used for reaction of the hydroxyl of ArC(OH)(CF₃)₂ or carbonyl of ArCOR_f with sulfur tetrafluoride.^{13,14c} If an amino group was present, anhydrous hydrogen fluoride was used as combination catalyst and solvent.¹⁷

p-Fluoro- α,α -bis(trifluoromethyl)benzyl alcohol (15.9 g., 0.061 mole) was charged into a 140-ml. Hastelloy-lined pressure vessel. After cooling and evacuating, 16 g. (0.15 mole) of sulfur tetrafluoride was added, and the reactants were heated at 150° for 8 hr. The product was treated with excess sodium fluoride powder or pellets to remove hydrogen fluoride, suction filtered using a small amount of methylene chloride or trichlorofluoromethane as a rinse, and distilled. The *p*-fluoro(heptafluoroisopropyl)benzene, b.p. 126°, was obtained in a yield of 11.2 g. (70%).

(16) (a) K. T. Dishart and R. Levine, *ibid.*, **78**, 2268 (1956); (b) R. Fuchs and G. J. Pack, *J. Org. Chem.*, **22**, 993 (1957); (c) J. H. Simons, W. T. Black, and R. F. Clark, *J. Am. Chem. Soc.*, **75**, 5621 (1953).

(17) M. S. Raasch, *J. Org. Chem.*, **27**, 1406 (1962); see also D. G. Martin and F. Kagan, *ibid.*, **27**, 3164 (1962).

Table I. Fluoroalkyl-Substituted Aromatic Compounds and Precursors. Preparation and Properties

Compd., R _f		B.p., °C. (mm.) ^c	M.p., °C. ^a and/or n _D ²⁰ ^d	Method of preparation, ^b % yield	Formula	Analysis, % ^e							
						Carbon ^d		Hydrogen		Fluorine		Other	
R _f	X					Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
CF ₃	<i>m</i> -N(CH ₃) ₂	82.5 (10)	1.4826	E (65)	C ₉ H ₁₀ F ₃ N ^e								
O=CCF ₃	<i>p</i> -N(CH ₃) ₂	...	74.5-75.5	A1 (39)	C ₁₀ H ₁₀ F ₃ NO	55.3	55.2	4.65	4.63	26.3	26.3	N 6.45	6.67, 6.68
CF ₂ CF ₃	<i>m</i> -NO ₂	68 (4.0)	1.4410	Cl (89)	C ₈ H ₄ F ₃ NO ₂	39.4	39.1	N 5.81	6.40
	<i>m</i> -NH ₂	43 (1.2)	1.4428	D (69)	C ₈ H ₆ F ₃ N	45.5	46.0	2.87	2.84	45.0	44.5	N 6.64	7.18, 7.03
											44.5		
	<i>m</i> -N(CH ₃) ₂	111 (34)	1.4534	E (51)	C ₁₀ H ₁₀ F ₅ N	50.2	50.4	4.22	4.36	39.7	40.0		
	<i>p</i> -N(CH ₃) ₂	93 (6.0)	40.6-41.8	B (32)	C ₁₀ H ₁₀ F ₅ N	50.2	49.9	4.22	4.31	39.7	40.2	N 5.86	5.59
							50.3		4.18				
	<i>m</i> -F	111	1.3807	B (38) ^f	C ₈ H ₄ F ₆	44.9	45.3	1.88	2.11	53.3	53.4		
	<i>p</i> -F	112	1.3809	B (77) ^f	C ₈ H ₄ F ₆	44.9	44.8	1.88	2.18	53.3	52.4		
HOC(CF ₃) ₂	H	104 (124) or 163.0-163.5	1.4120	A2 (84) ^{g,h}	C ₉ H ₆ F ₆ O								
	<i>m</i> -NO ₂	...	117.5-119.0 ⁱ	Cl (55)	C ₉ H ₅ F ₆ NO ₃	37.4	37.9	1.75	2.15	39.4	38.9		
	<i>p</i> -NO ₂	...	70.8-71.8 ^j	H (55)	C ₉ H ₃ F ₆ NO ₃	37.4	37.7	1.74	2.07	39.4	39.3		
	<i>m</i> -NH ₂	...	147.5-148.5 ^j	D (85)	C ₉ H ₇ F ₆ NO	41.8	41.9	2.72	2.50	44.0	44.5	N 5.41	5.31, 5.35
	<i>p</i> -NH ₂	...	150-151.5	A2 (27) ^k	C ₉ H ₇ F ₆ NO	41.8	41.8	2.72	2.95	44.0	43.8		
	<i>m</i> -N(CH ₃) ₂	72 (.8)	68.2-68.9	E (37)	C ₁₁ H ₁₁ F ₆ NO	46.0	46.2	3.87	4.22	39.7	39.8	N 4.88	4.79, 4.90
	<i>p</i> -N(CH ₃) ₂	...	77.4-79.0	A2 (62) ^k	C ₁₁ H ₁₁ F ₆ NO	46.0	46.3	3.87	3.94	39.7	39.7	N 4.88	4.91, 5.22
	<i>m</i> -Br	75 (5.0)	1.4514	C2 (45) ^l	C ₉ H ₅ BrF ₆ O	33.5	33.9	1.56	1.89	35.3	34.7	Br 24.7	24.7
							33.9		1.94		34.7		
	<i>p</i> -Br	...	53.2-54.0 ^m	A2 (37)	C ₉ H ₅ BrF ₆ O	33.5	33.7	1.56	1.56	35.3	35.9		
	<i>m</i> -F	96.5-97.5 (98)	1.4018	G (33)	C ₉ H ₅ F ₇ O	41.3	41.2	1.92	2.09	50.7	50.3		
							41.7		2.24				
	<i>p</i> -F	79-80 (40)	1.4028	A2 (66) ⁿ	C ₉ H ₅ F ₇ O	41.3	41.4	1.92	1.99	50.7	50.5		
	<i>p</i> -CH(CH ₃) ₂	68 (4.0)	1.4282	A2 (81)	C ₁₂ H ₁₂ F ₆ O	50.4	50.7	4.23	4.70	39.8	40.2		
	<i>p</i> -CH ₃	73-76 (10)	1.4204	A2 (69)	C ₁₀ H ₈ F ₆ O	46.5	46.9	3.13	3.35	44.2	44.3		
CF(CH ₃) ₂	H	125	1.3813	B (91) ^{k,o}	C ₉ H ₅ F ₇	43.9	44.5	2.05	2.23	54.0	54.6		
	<i>m</i> -NO ₂	70 (4.0)	1.4262	Cl (89)	C ₉ H ₄ F ₇ NO ₂	45.7	46.3	N 4.82	5.43
	<i>p</i> -NO ₂	50 (0.4)	1.4257	B (49)	C ₉ H ₄ F ₇ NO ₂	37.1	37.7	1.39	1.75	45.7	45.8	N 4.82	4.48, 4.50
	<i>o</i> -NH ₂	50 (2.3)	1.4297	B (8) ^p	C ₉ H ₆ F ₇ N	41.4	41.6	2.32	2.66	50.9	50.6	N 5.37	5.32
	<i>m</i> -NH ₂	77 (6.0)	1.4278	D (74)	C ₉ H ₆ F ₇ N	41.4	41.2	2.32	2.22	50.9	50.3	N 5.37	5.48
	<i>p</i> -NH ₂	61 (2.0)	1.4280	B (19) ^p	C ₉ H ₆ F ₇ N	41.4	41.7	2.32	2.60				
	<i>m</i> -N(CH ₃) ₂	92 (15)	1.4370	E (63)	C ₁₁ H ₁₀ F ₇ N	45.7	45.6	3.47	3.72	46.0	45.8	N 4.85	4.59, 4.49
	<i>p</i> -N(CH ₃) ₂	95 (5.2)	37-38	B (62) ^p	C ₁₁ H ₁₀ F ₇ N	45.7	45.7	3.47	3.91	46.0	45.2	N 4.85	5.37
													5.29
	<i>m</i> -CO ₂ H	...	96.8-97.4	F2 (70) F2 (61)	C ₁₀ H ₆ F ₇ O ₂	41.4	41.3	1.74	1.55	45.8	45.5	Mol wt., 290	Neut. equiv., 288
	<i>p</i> -CO ₂ H	...	100.2-100.6	F1 (71)	C ₁₀ H ₆ F ₇ O ₂	41.4	41.8	1.74	1.84	45.8	45.5	Mol wt., 290	Neut. equiv., 287
							41.5		1.78				
	<i>m</i> -Br	115 (135)	1.4257	C2 (56) B (52)	C ₉ H ₄ BrF ₇	33.3	33.2	1.24	1.52	40.9	40.8	Br 24.6	24.8, 24.0
	<i>p</i> -Br	102 (78)	1.4269	B (55)	C ₉ H ₄ BrF ₇	33.3	33.1	1.24	1.16	40.9	41.4	Br 24.6	24.2
											41.2		
	<i>m</i> -F	53 (60)	1.3744	G (37)	C ₉ H ₄ F ₈	40.9	40.6	1.53	1.55	57.6	57.1		
	<i>p</i> -F	126.5	1.3742	B (70)	C ₉ H ₄ F ₈	40.9	41.4	1.53	1.08	57.6	57.4		
	<i>p</i> -CH ₃	147	1.3923	B (64)	C ₁₀ H ₇ F ₇	46.2	46.4	2.71	2.84	51.1	50.8		
	<i>p</i> -CH(CH ₃) ₂	95-96 (49)	1.4050	B (54)	C ₁₂ H ₁₁ F ₇	50.0	51.0	3.85	3.91	46.2	45.4		

O=C(CF ₃) ₂	H	71 (22)	1.4105	A3 (58) ^g	C ₁₀ H ₅ F ₇ O	45.4	45.0	3.18	3.35	41.0	41.6	N 4.42	4.41, 4.57
	<i>p</i> -N(CH ₃) ₂	101 (35)	36.0-37.5	A1 (11) ^g	C ₁₂ H ₁₀ F ₇ NO	41.1	41.6	1.38	1.68	52.0	52.1		
CF ₃ CF ₃	<i>m</i> -F	85 (34)	1.4021	A3 (67)	C ₁₀ H ₄ F ₈ O	41.1	41.5	1.38	1.37	52.0	51.9		
	<i>p</i> -F	109 (90)	1.4047	A3 (50)	C ₁₀ H ₄ F ₈ O	40.6	41.1	1.70	2.18	57.8	56.5		
<i>n</i> -(CF ₃) ₂ CF ₃	H	150	1.3697	B (84)	C ₁₀ H ₅ F ₉	41.0	41.0	1.80	1.80	50.1	50.4	N 4.11	4.58
	<i>m</i> -NO ₂	66 (6.0)	1.4107	Cl (80)	C ₁₀ H ₄ F ₉ NO ₂	35.2	35.6	1.19	1.25	50.1	50.4		
<i>m</i> -NH ₂	<i>m</i> -NH ₂	91 (9.5)	1.4095	D (98)	C ₁₀ H ₆ F ₉ N	38.6	39.0	1.95	2.06	54.9	54.6		
	<i>m</i> -N(CH ₃) ₂	95 (7.2)	1.4220	E (47)	C ₁₂ H ₁₀ F ₉ N	42.5	43.1	2.97	2.19	50.4	50.7	N 4.13	3.97
<i>p</i> -N(CH ₃) ₂	<i>p</i> -N(CH ₃) ₂	68 (0.70)	37.5-38	B (73)	C ₁₃ H ₁₀ F ₉ N	42.5	42.4	2.97	3.16	50.4	50.5, 50.6		
	<i>m</i> -F	147	1.3632	B (78)	C ₁₀ H ₄ F ₁₀	38.2	38.4	1.28	1.66	60.5	60.5		
<i>p</i> -F	<i>p</i> -F	95 (104)	1.3648	B (63)	C ₁₀ H ₄ F ₁₀	38.2	38.7	1.28	1.53	60.5	60.0		
	<i>m</i> -N(CH ₃) ₂	94 (4.3)	1.4861	E (51) ^g	C ₈ H ₁₀ F ₃ NS	38.9	39.6	4.08	4.45	38.4	39.4	S 13.0	12.3
SF ₅	<i>m</i> -N(CH ₃) ₂	77 (4.7)	1.4704	E (51) ^g	C ₉ H ₁₀ F ₃ NO	52.7	53.1	4.91	5.07	27.8	27.9	N 6.83	7.07
	OCF ₃	86 (9.5)	1.4671	E (56) ^g	C ₉ H ₁₀ F ₃ NO	52.7	53.3	4.91	5.04	27.8	28.1		
OCF ₃	<i>p</i> -N(CH ₃) ₂	74 (0.9)	1.5165	E (59) ^g	C ₉ H ₁₀ F ₃ NS					25.8	24.5	N 6.34; S 14.5	6.61; 14.9
	SCF ₃												

^a Boiling and melting points are uncorrected. ^b Letter and numeral designation refers to procedure listed in Experimental. Any unusual conditions or results are recorded in footnotes. ^c All compounds were also characterized by infrared, ultraviolet, and F¹⁹ and H¹ n.m.r. spectral analysis. ^d Carbon analysis on compounds containing fluorine are often 0.4 to 0.7% high, although not reproducibly so. ^e Lit.^{2a} b.p. 89.5-90.4 (15 mm.), ⁿ_D²⁰ 1.4824, prepared by methylation with methyl iodide. ^f Trichlorofluoromethane used as solvent in SF₆ reaction. ^g Lit.^{14c} b.p. 50° (10 mm.) and 163.0-163.5, ⁿ_D²⁰ 1.4128, prepared by phenylmagnesium bromide with hexafluoroacetone and as above; see also ref. 14a and b. ^h We are indebted to Dr. W. J. Middleton of this laboratory for this experiment. ⁱ Recrystallized from benzene-hexane solvent mixture. ^j Recrystallized from carbon tetrachloride. ^k Lit.¹⁴ m.p. 154-155°, approximately 10% *ortho* isomer recovered from carbon tetrachloride solvent of recrystallization. ^l Excess bromine used, obtained some higher b.p. 105° (5.5 mm.) liquid that was characterized as dibromination product but isomer position not determined. ^m Recrystallized from hexane. ⁿ Orientation only *para* as determined by infrared and n.m.r. spectral analysis. ^o Lit.^{14c} b.p. 125°. ^p Anhydrous hydrogen fluoride added as catalyst and solvent. ^q Lit.¹⁶ b.p. 173.5°, ⁿ_D²⁰ 1.4130. ^r Acylation carried out with heptafluorobutyl chloride. ^s *m*-Aminophenylsulfur pentafluoride prepared as described by W. A. Sheppard, *J. Am. Chem. Soc.*, **84**, 3064 (1962). ^t Trifluoromethoxyanilines prepared as by W. A. Sheppard, *J. Org. Chem.*, **29**, 1 (1964). ^u *m*-Trifluoromethylthioaniline was as by L. M. Yagupolsky and M. S. Marenets, *J. Gen. Chem. USSR*, **24**, 885 (1954).

C. *Electrophilic Substitutions.* The trifluoromethyl group is known to be a strong *meta*-orienting group^{2a} in electrophilic aromatic substitution, and the other fluoroalkyl groups are also expected to be *meta* orienting. *meta* Orientation by all groups studied in bromination and nitration was confirmed by spectral analysis and in some cases by chemical conversions.

1. *Nitration.* A mixture of 19.6 g. (0.10 mole) of (pentafluoroethyl)benzene and 60 ml. of concentrated sulfuric acid was placed in a 100-ml. flask fitted with a thermometer, magnetic stirrer, and addition funnel with a Drierite guard tube. Approximately 20 ml. of fuming nitric acid (90%) was added dropwise to the mixture with stirring while the temperature was maintained between 20 and 30° by an ice bath. The reaction was extremely exothermic during addition and, after the addition was completed and the ice bath was removed, a slight exothermic reaction continued. After approximately 30 min., the mixture was poured over approximately 100 g. of cracked ice, and the product was extracted in ether. The ether extracts were washed with 5% sodium hydroxide solution, then with water, and dried over anhydrous magnesium sulfate. The product was distilled through a 45-cm. spinning-band column to obtain 21.5 g. (89%) of *m*-nitro(pentafluoroethyl)benzene, b.p. 68° (4.0 mm.). The expected *meta* orientation was verified by infrared and proton n.m.r. spectral analysis.

The *m*-nitro- α,α -bis(trifluoromethyl)benzyl alcohol prepared by this method had a melting point approximately 50° higher than the *para* isomer (prepared by method H). Orientation of the nitro group to the *meta* position by the hexafluoroisopropyl alcohol substituent was indicated by the spectral analysis and was verified by reduction of the nitro compound to the corresponding aniline. This aniline was compared to authentic samples of the *ortho* and *para* isomers prepared by method A2 and could only have *meta* orientation. The melting point reversal for the *meta* and *para* isomers is believed to result from some combination of unusual crystal packing of the large hexafluoro-2-propanol substituent with the strong hydrogen bonding character of the OH.

2. *Bromination.* A mixture of 24.6 g. (0.10 mole) of (heptafluoroisopropyl)benzene and 0.3 g. of iron powder was heated to 80-100° with stirring, and 16.0 g. (0.10 mole) of bromine was added rapidly. After heating at 120° for 1 hr., the reaction mixture was cooled, filtered, and taken up in pentane. The pentane solution was washed successively with 50-ml. portions of 6 *N* hydrochloric acid, 10% sodium bisulfite, and saturated sodium chloride solution, dried, and distilled. The *m*-bromo(heptafluoroisopropyl)benzene, b.p. 114-115° (135 mm.), was obtained in a yield of 18.0 g. (56%) and was characterized as a *meta* isomer by proton n.m.r. and infrared spectral analysis with comparisons to the spectra of the *para* isomer.

In addition the bromination product from α,α -bis(trifluoromethyl)benzyl alcohol was treated with sulfur tetrafluoride to give a product identical with the *m*-bromo(heptafluoroisopropyl)benzene described above.

D. *Reduction.* *m*-Nitro(heptafluoroisopropyl)benzene, 14.5 g. (0.050 mole) in 150 ml. of absolute ethanol containing 6.0 ml. of 9.1 *N* anhydrous hydrogen chloride in ethanol and 0.3 g. of platinum

oxide, was hydrogenated in a Parr apparatus at 40 p.s.i. of hydrogen. The theoretical amount of hydrogen was taken up. The catalyst was removed by filtration, and the solvent was evaporated under nitrogen. The dry aniline hydrochloride was stirred with an excess of 10% aqueous sodium bicarbonate solution layered with ether. The ether layer was separated, washed with water, dried over magnesium sulfate, filtered, and distilled. *m*-(Heptafluoroisopropyl)aniline, b.p. 77° (6.0 mm.), was obtained in a yield of 9.6 g. (74%).

E. Dimethylation of Anilines. A literature method for dimethylating anilines with methyl iodide^{2a} was not satisfactory because of low yields and somewhat tedious experimental procedure. A much simpler method employing trimethyl phosphate¹⁸ was employed.

A solution of 13.0 g. (0.050 mole) of *m*-(heptafluoroisopropyl)aniline and 7.0 g. (0.050 mole) of trimethyl phosphate was placed in a 300-ml., side-arm flask with thermometer, magnetic stirrer, and air condenser topped with a water condenser. The reaction was gradually heated in an oil bath with stirring. At 160°, a mild exothermic reaction occurred, and the reaction temperature became equivalent to that of the oil bath for a short period. Reflux started, and the reaction gradually separated into two phases. After 2–3 hr. at reflux (oil bath at 180–200°), the reaction was cooled to room temperature and a solution of 7.5 g. of sodium hydroxide in 50 ml. of water was added. The mixture was stirred vigorously for 90 min. to hydrolyze the phosphate ester. An additional 50–100 ml. of water was added, and the oil was extracted with two 75-ml. portions of ether. (The phosphate salts had to be removed by suction filtration if they precipitated before or during extraction.) The combined ether extracts were dried over magnesium sulfate and sodium hydroxide pellets, filtered, and distilled. The *m*-(heptafluoroisopropyl)-*N,N*-dimethylaniline, b.p. 92° (15 mm.), was obtained in a yield of 9.1 g. (63%). From infrared analysis, it was shown that the product contained a trace of secondary aniline. This was removed by refluxing the product with 0.5 ml. of acetic anhydride followed by redistillation on a spinning-band column. In other experiments, it was shown that no secondary aniline by-product was formed if a few per cent molar excess of phosphate was used.

F. Preparation of Benzoic Acids. 1. Bromination, Hydrolysis, and Oxidation. A solution of 5.20 g. (0.020 mole) of *p*-(heptafluoroisopropyl)toluene and 6.40 g. (0.040 mole) of bromine in 50 ml. of carbon tetrachloride was irradiated under reflux overnight with a G.E. sun lamp. At the end of this time, the bromine color had disappeared and considerable hydrogen bromide had evolved. The solvent was distilled through a Vigreux column, and the residue was stirred with 50 ml. of concentrated nitric acid for 3 days at room temperature, then 3 days at 70°. An additional 25 ml. of nitric acid was added, and stirring was continued for 2 days with intermittent heating. The reaction mixture was poured into ice and water, and the crystalline product was suction filtered, washed several times with water, and air dried (yield 5.8 g., m.p. 90–93°). The *p*-(heptafluoroisopropyl)benzoic acid was recrystallized twice from hexane and sublimed,

white crystals, m.p. 99.8–100.4°, yielding 4.1 g. (71%).

2. Carbonation of Grignard. The Grignard was prepared in the normal manner by the addition of 6.4 g. (0.020 mole) of *m*-bromo(heptafluoroisopropyl)benzene in 15 ml. of ether to 0.7 g. (0.031 g.-atom) of magnesium turnings in 8 ml. of ether. Dry carbon dioxide gas was passed over the Grignard solution cooled to –5°. Hydrolysis was accomplished with 25 ml. of 30% sulfuric acid and the product was separated by ether extraction. The crude product was obtained as white crystals, m.p. 87–90°, yield 4.0 g. (70%). An analytical sample of *m*-(heptafluoroisopropyl)benzoic acid, m.p. 96.8–97.4°, was prepared by three successive recrystallizations from hexane followed by sublimation.

G. Aryl Fluorides by Diazotizations. The literature procedure¹⁹ was used starting with 9.15 g. (0.035 mole) of *m*-amino- α,α -bis(trifluoromethyl)benzyl alcohol and using all other reagents on one-tenth the scale. The diazonium hexafluorophosphate intermediate was obtained in a yield of 9.5 g., m.p. 149–150° dec. The *m*-fluoro- α,α -bis(trifluoromethyl)benzyl alcohol, b.p. 96.5–97.5° (98 mm.), was obtained in a yield of 3.02 g. (33%).

H. Oxidation of Anilines. The procedures described by Emmons²⁰ using peracetic or pertrifluoroacetic acids were employed. Either procedure was satisfactory, but the use of pertrifluoroacetic acid was preferred because of better solubility of the reactant.

A solution of 34 ml. (0.24 mole) of trifluoroacetic acid, 5.6 ml. (0.20 mole) of 90% hydrogen peroxide, and 50 ml. of chloroform was prepared as described.^{20a} *p*-Amino- α,α -bis(trifluoromethyl)benzyl alcohol was added portionwise. No reaction was noted after the initial addition at 20°, and the solution was warmed

Table II. Ionization Constant Data on Reference *N,N*-Dimethylanilines in 45% Dioxane–55% Water, 25.0°^a

$\text{XC}_6\text{H}_4\text{N}(\text{CH}_3)_2 \rightleftharpoons \text{XC}_6\text{H}_4\text{N}(\text{CH}_3)_2 + \text{H}^+$				
X of $\text{XC}_6\text{H}_4\text{N}-$ $(\text{CH}_3)_2$	H	λ_{max} , m μ	$-\log k$	σ^b
H		252	4.14	0
CH ₃	<i>meta</i>	253	4.31	–0.069
	<i>para</i>	250	4.60	–0.170
Cl	<i>meta</i>	259	2.45	+0.373
	<i>para</i>	262	3.09	0.227
Br	<i>para</i>	262	2.95	0.232
	<i>meta</i>	251	1.17	0.710
NO ₂	<i>para</i>	413	(–.75) ^c	1.27
	<i>meta</i>	259	(1.51) ^d	(0.65) ^d
OCF ₃	<i>meta</i>	302	(2.02) ^d	(0.52) ^d
	<i>para</i>	307	(2.81) ^d	(0.33) ^d
SCF ₃	<i>meta</i>	323	(2.02) ^d	(0.52) ^d
	<i>para</i>	280	(1.40) ^d	(0.68) ^d

^a Calculated least-squares best fit (values in parenthesis not used) slope (ρ) = +4.053 ± 0.020, intercept ($\log k_0$) –4.000. ^b Values from H. H. Jaffé, *Chem. Rev.*, **53** (1953). ^c Anilinium salt too acidic for buffer system; $-\log k$ determined by extrapolation of (H^+) to zero concentration and not used in least-squares calculation of slopes. ^d Not used because prepared after calculation of slope. Calculated σ -values are slightly larger than values reported from anilinium ion $\text{p}K_a$ data (ref. 7 and 10); if intercept value is used for $\log k_0$, values are lowered about 0.03 units and agreement is excellent.

(19) K. G. Rutherford and W. Redmond, *Org. Syn.*, **43**, 12 (1960).

(20) (a) W. D. Emmons, *J. Am. Chem. Soc.*, **76**, 3470 (1954); (b) *ibid.*, **79**, 5528 (1957).

(18) D. G. Thomas, J. H. Billman, and C. E. Davis, *J. Am. Chem. Soc.*, **68**, 895 (1946).

Table III. pK_a Measurements

Substituent X	Benzoic acids $\text{XC}_6\text{H}_4\text{CO}_2\text{H} \rightleftharpoons \text{XC}_6\text{H}_4\text{CO}_2^- + \text{H}^+$ ^a		Anilines $\text{XC}_6\text{H}_4\text{NH}_3^+ \rightleftharpoons \text{XC}_6\text{H}_4\text{NH}_2 + \text{H}^+$ ^b		N,N-Dimethylanilines $\text{XC}_6\text{H}_4\text{N}^+\text{H}(\text{CH}_3)_2 \rightleftharpoons \text{XC}_6\text{H}_4\text{N}(\text{CH}_3)_2 + \text{H}^+$ ^c	
		pK_a	$\lambda_{\text{max}}, \text{m}\mu$	pK_a	$\lambda_{\text{max}}, \text{m}\mu$	pK_a
H		5.66 (5.71) ^d	231	4.557	252	4.14 (4.00) ^h
CF ₃	<i>ortho</i>	...	288	1.74
	<i>meta</i>	5.05 (5.11) ^d	236	3.20 (3.41) ^{d,e}	260	2.06, 2.07 ^f
	<i>para</i>	4.89 (4.94) ^d	274	2.75 (2.57) ^{d,e}	268	1.56
CF ₂ CF ₃	<i>meta</i>	...	290	3.17	260	1.90
	<i>para</i>	270	1.19, 1.23 ^f
(CF ₂) ₂ CF ₃	<i>meta</i>	...	292-297	3.12	261	1.77
	<i>para</i>	273	1.05, 1.04 ^f
CF(CF ₃) ₂	<i>ortho</i>	...	292	1.94 ^g
	<i>meta</i>	5.12	289	3.11	260	1.79
	<i>para</i>	4.89	243	2.69	268	1.33, 1.30 ^f
C(OH)(CF ₃) ₂	<i>ortho</i>	...	290	3.18
	<i>meta</i>	...	287	3.60	258	2.66
	<i>para</i>	...	274	3.24	264	2.24

^a $\rho = +1.467$ (ref. 2a); 50% water-ethanol, 25.0°. ^b $\rho = +2.767$, A. Bryson, *J. Am. Chem. Soc.*, **82**, 4859 (1960); water, 25°. ^c $\rho = +4.053$; 45% dioxane-55% water, 25°. ^d See ref. 2a. ^e For a discussion of reason for discrepancy see ref. 7, footnote 12 and experimental description for determination of ionization constants measurement of anilines. ^f Second determination. ^g Solvent 10% ethanol-water since sample insoluble in water. ^h Intercept value, used for calculation of σ -values.

until at 35° an exothermic reaction started the solution to reflux.

Refluxing continued until addition was completed and was then continued for an additional 15 min. by external heating. The solvent was removed at reduced pressure, and the dark, oily residue was treated with 75 ml. of ice water. The oily layer was separated (a small amount of methylene chloride was used in transfer), dried over magnesium sulfate, filtered, and evaporated. The residue was sublimed to give 7.9 g. of discolored white crystals, m.p. 55-65°. After several recrystallizations from carbon tetrachloride followed by sublimation, the *p*-nitro- α,α -bis(trifluoromethyl)benzyl alcohol was obtained as white crystals of constant melting point (70.8-71.8°).

The unusual fact that the *meta* isomer has a higher melting point than the *para* was discussed under section C1.

I. Ionization Constant Measurements. The procedures described previously¹⁰ were used to determine the ionization constants of anilines and benzoic acids with the refinement that a Beckman research pH meter was used in titration of the benzoic acids. Because of poor solubility, the N,N-dimethylanilines could not be run in water. A solvent of 45% dioxane-55% water was chosen according to the method of Willi.²¹ Unfortunately his data in this system were meager and were obtained at 20 instead of 25° preferred in our laboratories. Therefore, a series of reference anilines were employed (ionization constant data in Table II) and a new ρ -value determined by the method of best fit by least squares using a standard computer program. The fit was excellent with the exception, as is often found, of the unsubstituted aniline. The values were $\rho = +4.053$; $\log k_0$, intercept -4.00, measured -4.14. All ionization constant data are summarized in Table III.

J. N.m.r. Calibrations. The F¹⁹ n.m.r. calibrations were carried out as described previously²² or as by Taft and co-workers.¹² For calibration, trichlorofluoro-

(21) A. V. Willi, *Helv. Chim. Acta*, **40**, 2019 (1957).

(22) D. R. Eaton and W. A. Sheppard, *J. Am. Chem. Soc.*, **85**, 1310 (1963).

Table IV. F¹⁹ Chemical Shifts for Fluorobenzene (XC₆H₄F) in CCl₃F at Infinite Dilution and at 5% Solutions in CCl₄

XC ₆ H ₄ F Substituent X	Chemical shift (δ) in p.p.m. relative to C ₆ H ₅ F	
	In CCl ₃ F ^a	In CCl ₄ ^b
NH ₂ <i>meta</i>	+0.50	+0.50 ^c
<i>para</i>	+13.97	+14.20 ^c
NO ₂ <i>meta</i>	-3.47	-3.45 ^c
<i>para</i>	-9.48	-9.55 ^c
CH ₃ <i>meta</i>	+1.10	+1.18 ^c
<i>para</i>	+5.44	+5.40 ^c
Cl <i>meta</i>	-2.04	-2.0 ^c (approx.)
<i>para</i>	+3.10	+3.10 ^c
Br <i>meta</i>	-2.39	-2.43 ^c
<i>para</i>	+2.46	+2.50 ^c
OH <i>meta</i>	-1.58	-1.43 ^c
<i>para</i>	+10.39	+10.85 ^c
O=CCF ₂ <i>meta</i>	-2.72	-2.63 ^c
<i>para</i>	-12.20	-12.35 ^c
O=CCF ₂ CF ₂ CF ₃ <i>meta</i>	-2.69	...
<i>para</i>	-12.35	...
CF ₃ <i>meta</i>	-2.20	-2.21 (-2.13 ^c)
<i>para</i>	-5.09	-5.24 (-5.15 ^c)
CF ₂ CF ₃ <i>meta</i>	-2.29	...
<i>para</i>	-5.44	...
CF ₂ CF ₂ CF ₂ CF ₃ <i>meta</i>	-2.30 ^d	...
<i>para</i>	-5.58	...
CF(CF ₃) ₂ <i>meta</i>	-2.80	-2.93
<i>para</i>	-4.03	-4.14
C(OH)(CF ₃) ₂ <i>meta</i>	-1.35	-1.88
<i>para</i>	-2.00	-2.37

^a CCl₃F as solvent and internal calibrating agent; C₆H₅F at 6382 c.p.s. relative to CCl₃F. ^b C₆H₄F₂ or C₄Cl₄F₄ (1,1,2,2-tetrachloro-3,3,4,4-tetrafluorocyclobutane) as internal calibrating agents; C₆H₅F at -81 c.p.s. relative to C₄Cl₄F₄. ^c Values from ref. 12. ^d Chemical shift patterns for aryl fluorine and one of CF₂ groups overlap. An approximate value (within at least ± 5 c.p.s.) was estimated from complex pattern.

methane was generally chosen as solvent because of its advantage as an internal calibrant.²³ As well as the standard method of calibrating by superimposing an audio frequency on the sweep field to produce side band peaks of the reference, a new method of employing dual frequency side-band modulations from twin

(23) G. Filipovich and G. V. D. Tiers, *J. Phys. Chem.*, **63**, 761 (1959).

Table V. F^{19} Chemical Shifts (p.p.m.) of the Fluorines in Substituted Fluoroalkyl Aromatic Compounds ($XC_6H_4R_f$) at Infinite Dilution in CCl_3F (or CH_3OH) Relative to Unsubstituted Compound^{a, b}

X	R_f									
	CF_3	$CF(CF_3)_2$	CF_2CF_3	CF_2CF_3	$CF(CF_3)_2$	$C(OH)(CF_3)_2^b$	$CF_2CF_2-CF_2CF_3$	$CF_2CF_2-CF_2CF_3$	$CF_2CF_2-CF_2CF_3$	$CF_2CF_2-CF_2CF_3$
H	0 (3598) ^c	0 (10349) ^c	0 (6536) ^c	0 (4831) ^c	0 (4305) ^c	0 (4222) ^c	0(6307) ^{c, d}	0 (6957) ^{c, d}	0 (7116) ^{c, d}	0 (4616) ^c
NO_2 meta	+0.16	-1.04	-0.31	-0.23	-0.07	+0.02	-0.18	-0.37	-0.12	-0.07
NO_2 para	0.34	-1.14			-0.29	-0.25				
NH_2 meta	0.14	-0.51	+0.07	-0.09	-0.04	-0.07	-0.19	0	+0.02	-0.04
NH_2 para	-1.46	-1.04			+0.39	+0.37				
$N(CH_3)_2$ meta	-0.06	-0.45	-0.16	-0.16	-0.09		-0.15	0	+0.12	0
$N(CH_3)_2$ para	-1.77	-1.11	-1.62	+0.14	+0.43	+0.35	-1.51	+0.11	+0.05	+0.05
F meta	+0.12	-0.97	-0.28	-0.14	+0.05	+0.07	-0.28	-0.09	-0.02	-0.02
F para	-0.73	-1.32	-0.78	+0.05	+0.23	+0.23	-0.89	0	-0.02	-0.05
Br meta	+0.07	-0.52			-0.07	+0.11				
Br para	-0.04	-0.33			+0.08	+0.12				
CH_3 para		-0.20			+0.20					
$CH(CH_3)_2$ para		-0.33			+0.12	+0.09				
CO_2H meta		-0.47			-0.04					
CO_2H para		-0.33			-0.17					

^a Spin-spin coupling between fluorines and/or protons was found as expected for these compounds but is omitted for simplicity. ^b The solutions of $XC_6H_4C(OH)(CF_3)_2$ were generally of too low solubility in CCl_3F . Methanol containing 5% CCl_3F was used as solvent for this series. ^c Absolute calibration of $C_6H_5R_f$ relative to CCl_3F (in p.p.m.) at infinite dilution in CCl_3F (or CH_3OH). ^d Tentative assignment based on size of chemical shift change with substituents.

Table VI. F^{19} Chemical Shifts of $FC_6H_4R_f$ to Determine Solvent Effects δ_F (p.p.m.) Relative to Parent^a

$FC_6H_4R_f$	CCl_4			CH_3OH			CH_3CN		
	ring F	$\alpha-F$	$\beta-F$	ring F	$\alpha-F$	$\beta-F$	ring F	$\alpha-F$	$\beta-F$
<i>m</i> - $FC_6H_4CF_3$	-2.21	+0.07	...	-2.59	+0.11	...	-2.29	+0.09	...
	(-2.13) ^b			(-2.50) ^b			(-2.30) ^b		
<i>p</i> - $FC_6H_4CF_3$	-5.24	-0.76	...	-5.87	-0.73	...	-5.80	-0.76	...
	(-5.15) ^b			(-5.90) ^b			(-5.90) ^b		
<i>m</i> - $FC_6H_4CF(CF_3)$	-2.93	-0.85	-0.03	-3.14	-0.82	-0.02	-2.89	-0.84	-0.40
<i>p</i> - $FC_6H_4CF(CF_3)_2$	-4.14	-1.21	+0.17	-4.70	-1.21	+0.12	-4.54	-1.21	-0.24
<i>m</i> - $FC_6H_4C(OH)(CF_3)_2$	-1.88	...	+0.02	-1.23	...	+0.07	-1.68	...	+0.02
<i>p</i> - $FC_6H_4C(OH)(CF_3)_2$	-2.37	...	+0.20	-1.51	...	+0.19	-2.16	...	+0.16

^a Calibration at 5% by volume solution, reference to internal calibrant of 1,1,2,2-tetrachloro-3,3,4,4-tetrafluorocyclobutane (2% concentration in solvent). ^b Value from ref. 12.

oscillators was found superior for more precise measurement of the chemical shift of multiple fluoroaromatic resonance. In most cases measurements were made at four different concentrations (40, 20, 10, and 5%), and chemical shifts were obtained by extrapolation to infinite dilution. The calibrations were reproducible to within ± 2 , and generally to within less than ± 1 c.p.s. The data obtained in the solvent trichlorofluoromethane were identical, within experimental error, with data obtained in this laboratory and by Taft^{12, 24} at 5 to 10% solution in carbon tetrachloride with the exception of compounds containing NH_2 or OH groups that could hydrogen bond. A series of measurements in carbon tetrachloride, methanol, and acetonitrile at 5%

(24) R. W. Taft, private communication.

concentration using 1,1,2,2-tetrachloro-3,3,4,4-tetrafluorocyclobutane as internal calibrant were also made to study solvent effects. All n.m.r. data are reported in Tables IV, V, and VI.

K. Substituent Parameters. The Hammett σ -constants were calculated by standard methods²⁵ from the ionization constant data and are summarized in Table VII. The σ_1 , σ_R , and σ_R^0 parameters were calculated by the method of Taft.²⁶ Substituent constants are calculated from the F^{19} n.m.r. chemical shift data according to the literature procedure,¹² using the equations

(25) See Table II, footnote b.

(26) R. W. Taft and I. G. Lewis, *J. Am. Chem. Soc.*, **81**, 5343 (1959); R. W. Taft, *J. Phys. Chem.*, **64**, 1805 (1960).

Table VII. Substituent Parameters

Substituent	Method ^a	Hammett ^b		Taft ^c		
		σ_m	σ_p	σ_1	σ_R	σ_R^0
CF ₃	B	0.42 (0.43) ^d	0.53 (0.54) ^d	0.33	0.18	
	A	0.49 (0.41) ^{d,e}	0.62 (0.74) ^{d,e}	0.44	0.18	
	DMA	0.48 (0.42) ^{d,f}	0.60 (0.64) ^{d,f}	
	F	0.44	0.49	0.39 (0.39) ^g	...	0.10 (0.10) ^g
CF ₂ CF ₃	A	0.50	
	DMA	0.52	0.69	
	F	0.47	0.52	0.41	...	0.11
<i>n</i> -(CF ₂) ₃ CF ₃	A	0.52	
	DMA	0.55	0.73	
	F	0.47 ^h	0.52	0.39	...	0.11
CF(CF ₃) ₂	B	0.37	0.53	0.25	0.26	
	A	0.52	0.68	0.48	0.17	
	DMA	0.54	0.66	
	F	0.50	0.52	0.48	...	0.04
C(OH)(CF ₃) ₂	A	0.35	0.48	0.31	0.15	
	DMA	0.33	0.44	
	F	0.29	0.30	0.28	...	0.02

^a Data calculated from ionization constants of: B, benzoic acids; A, anilinium ions; DMA, dimethylanilinium ions; and F, F¹⁹ n.m.r. chemical shift data. ^b Calculated using Hammett equation from ionization constant data and log k_o and ρ as given in Table III. For values from F¹⁹ measurements see footnote c. ^c Calculated as described in ref. 26 using values of $\rho_1 + 1.50$, $\alpha = 0.42$ for ionization constants of benzoic acids; $\rho_1 + 2.90$, $\alpha = 0.15$ for ionization of anilinium ions; no values available for N,N-dimethylanilines. The σ_1 and σ_R^0 values were determined directly from F¹⁹ chemical shifts using correlation curves and equations given in ref. 12. σ_m and σ_p for chemical shifts are σ_m^0 and σ_p^0 calculated by $\sigma_m^0 = \sigma_1 + 0.50\sigma_R^0$ and $\sigma_p^0 = \sigma_1 + \sigma_R^0$ (see ref. 12). ^d Literature value in parenthesis, ref. 2a. ^e See Table III, footnote e. ^f Literature value (ref. 2a) determined in water at 25°. ^g Literature value, ref. 12. ^h Approximate value, see Table IV, footnote d.

$$\delta_H^{m-X} = (-7.10)\sigma_1 + 0.60$$

$$\sigma_R^0 = (-0.0339)(\delta_H^{p-X} - \delta_H^{m-X})$$

L. *Dipole Moments.* The dipole moments were determined by literature methods⁷ employing a Wissenschaftlich Technische Werkstätten dipolmeter Type DM 01, Cell DFL1 (20-ml. volume). The data are given in Tables VIII and IX. A precision of ± 0.02 D. is ascribed to the dipole moment results given in Table IX.

Table VIII. Dielectric Constants, Densities, and Polarizations in Benzene at 25°

Compd.	F_2	ϵ	D	P_2
Benzene (solvent)	0.0000	2.2740	0.87220	26.694
C ₆ H ₅ CF ₃	0.00577	0.87571	2.3288	169.45
	0.01016	0.87765	2.3676	166.38
	0.02487	0.88325	2.4963	162.30
	0.03368	0.88613	2.5727	160.67
C ₆ H ₅ CF ₂ CF ₃	0.00534	0.87691	2.3276	186.36
	0.01071	0.88044	2.3780	183.65
	0.02191	0.88760	2.4805	179.47
	0.03316	0.89532	2.5822	175.64
C ₆ H ₅ CF ₂ CF ₂ CF ₃	0.00521	0.87970	2.3289	210.94
	0.01075	0.88618	2.3826	207.84
	0.02171	0.89936	2.4857	202.41
	0.03241	0.91710	2.5834	198.91
C ₆ H ₅ CF(CF ₃) ₂	0.00532	0.87836	2.3245	187.18
	0.01068	0.88344	2.3695	181.63
	0.02065	0.89252	2.4523	177.87
	0.03244	0.90358	2.5488	174.42
<i>p</i> -(CH ₃) ₂ NC ₆ H ₄ CF(CF ₃) ₂	0.00539	0.87938	2.4390	493.86
	0.01042	0.88539	2.5872	479.77
	0.02023	0.89497	2.8699	454.31

Results and Discussion

The substituent constant data in Table VII and dipole moment data in Table IX show that the inductive (I) and resonance (R) effects of fluoroalkyl groups are influenced to some extent by the type of measurements,

but the general trend is increase in +I with increase in bulk of fluorinated group, with slight increases or decreases in +R. However, the data do not clearly support either of the two mechanisms proposed to explain the origin of the +R effect of a fluoroalkyl group.

The pK_a data on anilinium and N,N-dimethylanilinium ions suggest that the +R effect for CF₃ and CF(CF₃)₂ groups are equivalent within experimental error, but that the +I effect increases slightly for the perfluoroisopropyl group. From the N,N-dimethylanilinium ionization constant data, the perfluoroethyl and *n*-butyl groups show a progressive increase in both inductive and resonance effects with fluorine content. However, the heptafluoroisopropyl group relative to the ethyl and *n*-butyl groups appears to have a slightly decreased resonance effect. The α -hydroxyhexafluoroisopropyl group, which contains no α -fluorine and no possibility for contributions from fluoride ion hyperconjugative structures, also has a very significant resonance effect. The pK_a data for the benzoic acids show an increased +R effect but a decreased +I for the heptafluoroisopropyl groups relative to the trifluoromethyl group.

All the ionization constant data show that the fluoroalkyl groups have similar size resonance effects and support the π -inductive rather than fluoride ion hyperconjugation mechanism. The small variations in +I and +R effects for the fluoroalkyl groups may reside chiefly in changes in solvation of the protonated and unprotonated states rather than in electronic influence,^{27,28} particularly since solvation effects may be enhanced considerably by the unusual interactions of fluoroalkyl groups with solvents.

(27) R. A. Clement, J. N. Naghizadeh, and M. R. Rice, *J. Am. Chem. Soc.*, **82**, 2449 (1960), have demonstrated that differences in solvation effects during solvolysis of benzyl chlorides are large enough to in part explain apparent electronic differences of alkyl groups.

(28) C. D. Ritchie and W. F. Sager in "Physical Organic Chemistry," Vol. 2, S. G. Cohen, A. Streitwieser, and R. W. Taft, Ed., Interscience Publishers, Inc., Division of John Wiley and Sons, Inc., New York, N. Y., p. 381.

Table IX. Molar Refractions, Polarizations, and Dipole Moments

Compd.	MR	P_{∞}^a	μ , D.	
			Measured	Calcd. ^b
$C_6H_5CF_3$	31.29	170.29	2.61 (2.60) ^c	
$C_6H_5CF_2CF_3$	36.16	188.04	2.73	
$C_6H_5CF_2CF_2CF_2CF_3$	45.90	212.80	2.86	
$C_6H_5CF(CF_3)_2$	41.03	187.88	2.68	
$C_6H_5N(CH_3)_2$	1.58 ^c	
<i>p</i> -(CH_3) ₂ NC ₆ H ₄ CF ₃	4.62 ^c	4.18 ^c ($\Delta = 0.44$)
<i>p</i> -(CH_3) ₂ NC ₆ H ₄ CF(CF ₃) ₂	54.19	507.90	4.71	4.26 ($\Delta = 0.45$)

^a At 25°. ^b By vector sum. ^c For literature value, see ref. 2a.

The F^{19} chemical shift data show that the inductive effect of the fluoroalkyl groups increases with increasing fluorine content and branching. However, the resonance effect is not clear and appears to increase for the perfluoroethyl but to decrease significantly for the heptafluoroisopropyl and α -hydroxyhexafluoroisopropyl groups. This technique offers a very sensitive probe for changes in electron density in an aromatic ring and is free of interference from solvent effects.¹² However, changes from anisotropic effects of substituents are not completely understood. In the present system, the very bulky heptafluoroisopropyl and α -hydroxyhexafluoroisopropyl groups of high electron density probably have a disrupting influence on the ring current. Solvent effect studies on the chemical shifts of *para*-substituted fluoroaromatics have been proposed by Taft and co-workers¹² as a method of estimating contributions by highly polarized forms such as hyperconjugation structures. Studies on the heptafluoroisopropyl and α -hydroxyhexafluoroisopropyl groups relative to the trifluoromethyl showed no gross differences over a wide range of solvent types (Table VI), arguing against hyperconjugative contributions. One surprising and unexplained effect is the relatively large downfield chemical shift for the β -fluorines of *p*-fluoro(heptafluoroisopropyl)benzene in acetonitrile.

The chemical shifts of all the fluorines on the fluoroalkyl groups were determined relative to the ring substituents (Table V). The normal correlation plots^{12,22} of δ_m vs. σ_I and δ_p vs. σ_R could be made for the α - or β -fluorines in all cases. The changes in chemical shift for all of the β -fluorines with substituents were significant and very similar, and almost one-third that noted for the α -fluorines. However, for α -fluorines, the tertiary F of the heptafluoroisopropyl group gave an entirely different type of correlation plot than the primary F of the trifluoromethyl, particularly for the δ_m vs. σ_I correlation plot where a reversal in the slope was observed. Also, the reversal in slope of δ_p vs. σ_R correlation plots with increase in number of intervening bonds between the fluorine and the substituent was again found.²² The trifluoromethyl group of the *n*-butyl chain did not show chemical shift changes that were outside experimental error although from models it was predicted that the chain could be arranged so that the CF_3 group would interact with the π -system. This chemical shift data is not readily interpreted at present but a new approach to analysis of F^{19} chemical shift correlations is discussed below.

The dipole moment data (Table IX) again show no difference in resonance effects between CF_3 and $CF(CF_3)_2$ groups.

Several interpretations have been considered for the data.

1. The techniques are not sufficiently sensitive and free of variables (solvation effects in pK_a measurements, anisotropic effects in F^{19} chemical shifts) to unequivocally provide support for any one mechanism. However, a significant +R effect is observed for all fluoroalkyl groups and suggests that π -inductive effects are most important but may be enhanced by fluoride ion hyperconjugation, particularly in the anilines where delocalization of the *p*-electrons on nitrogen can help stabilize the no bond structures.

2. Trifluoromethide ($-CF_3$) no bond hyperconjugation structures are almost as effective as fluoride ion type.

3. The lone pairs of electrons on the fluorine of the fluorinated group interact with the π -system of the aromatic ring and alter the electron density in the ring in a manner that gives the observed effects.

We cannot reconcile the present data, the evidence discussed in the introduction, and data on other fluorinated groups which will be discussed below with either of the first two interpretations. We will now endeavor to explain and develop supporting arguments for the last proposal.

The p - π interaction of fluorine in fluorobenzenes is sufficiently great that the donation of electrons into the ring by resonance almost counteracts the strong inductive withdrawal.²⁹ Similarly in benzotrifluorides, interaction of the *p*-electrons of the fluorines of the CF_3 with the π -system of the ring should occur, although to a much lesser extent because of a poorer angle and a greater distance for overlap. The net result would be a small return of electron density to the ring partly counteracting the strong inductive withdrawal. On the basis of the collected evidence, a greater portion of electron density is believed to return to the *meta* than to the *para* position.

In Figure 1, the calculated distances of the fluorines from the nearest carbons of the ring in benzotrifluorides is shown with a sketch drawn approximately to scale indicating the proposed overlap. The sum of the van der Waals radii for fluorine (1.35 Å) and aromatic carbon (1.70 Å) is 3.05 Å. The fluorines and carbon one of the aromatic ring are at a distance of 2.36 Å, and the fluorines can be 2.66 Å from the *ortho* carbons.³⁰ These atoms are well within the distances for

(29) From fluorobenzoic acid ionization constants, $\sigma_m = +0.34$, $\sigma_p = +0.06$ (ref. 25). In measurements where the reaction site has a high electron demand, σ_p for fluorine becomes negative (see ref. 4).

(30) Professor D. J. Cram suggested in a private discussion that the C-C-F angles may be greater than the normal tetrahedral value of 109°. This would increase the F to C distances, but even at an angle of

significant interaction. Through-space interaction between two fluorines that are separated by 2.76 Å. or less has been proposed to explain through space spin-spin coupling of fluorine.³¹ Also in 1,2-fluorohaloethylenes, the *cis* form is more stable than the *trans*.³² An explanation for the reversal of the stability usually observed for 1,2-disubstituted ethylenes is a decrease in energy of the *cis* form through p-p interaction between fluorine and the other halogen.

The σ -parameters for a series of other fluorinated substituents are given in Table X, and the internuclear distances of the fluorines in these groups and the ring carbons are given in Table XI. Because the +R effect

Table X. Substituted Parameters of Fluorinated Groups.

		σ_m	σ_p	σ_1	σ_R
CF ₃	A ^a	0.49	0.65	0.44	0.18
	B	0.42	0.53	0.33	0.18
SF ₅	A	0.63	0.86	0.56	0.27
	B	0.61	0.68	0.54	0.14
N(CF ₃) ₂	A	0.47	0.53	0.44	0.06
	B	0.40	0.53	0.29	0.23
SCF ₃	A	0.46	0.64	0.40	0.22
	B	0.40	0.50	0.31	0.17
OCF ₃	A	0.47	0.27	0.50	-0.23
	B	0.38 ^b	0.35 ^b	0.39 ^b	-0.04 ^b

^a Measured from: A, pK_a of anilinium ions, water; B, pK_a of benzoic acids, 50% water-ethanol. ^b These σ -parameters are revised over values given in ref. 10; pK_a measurements reported are correct but calculated σ -parameters were slightly in error. Differences are only of a quantitative nature and do not effect qualitative interpretation. The σ_1 and σ_R values for the CF₃ and SF₅ groups calculated for benzoic acid data are also slightly revised.

Table XI. Internuclear Distances between Centers of Fluorine and Ring Carbons^a

Ring substituent	Distance, Å.		No. of available F
	F to C-1 ^b	F to C-2 ^b	
-CF ₃	2.4	2.7	3
-C-CF ₃	2.5	2.0	3 to 9
-N-CF ₃	2.4	1.7	6
-SF ₅	2.5	2.2	4
-SCF ₃	2.5	2.2	3
-OCF ₃	2.4	2.0	3

^a Measured from Dreiding models; configurations chosen to give shortest distances. ^b C-1, carbon to which substituent is attached. C-2, carbon *ortho* to position where substituent is attached.

for the SF₅ group was about the same as that for CF₃, we have argued against the fluorine no bond resonance mechanism (see introduction and ref. 7). However, since the F to C aromatic distances can be about the same for CF₃ and SF₅, the p- π interaction mechanism predicts similar size +R effects. The N(CF₃)₂ group is only *para* directing to electrophilic aromatic substitution but unexpectedly is found by pK_a measurements to be a +R group.³³ The unshared pairs of

120°, the distances are 2.50 and 2.88 Å. No measurements of bond distances and angles have been reported for benzotrifluoride.

(31) S. Ng and C. H. Sederholm, *J. Chem. Phys.*, **40**, 2090 (1964). The 2.76-Å. limit required for coupling is approximately twice the accepted van der Waals distance for fluorine.

(32) (a) A. Demiel, *J. Org. Chem.*, **27**, 3500 (1962); (b) H. G. Viehe, J. Dale, and E. Franchimont, *Ber.*, **97**, 244 (1964).

(33) W. A. Sheppard and F. S. Fawcett, Abstract of Paper, 148th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 1964, p. 12K.

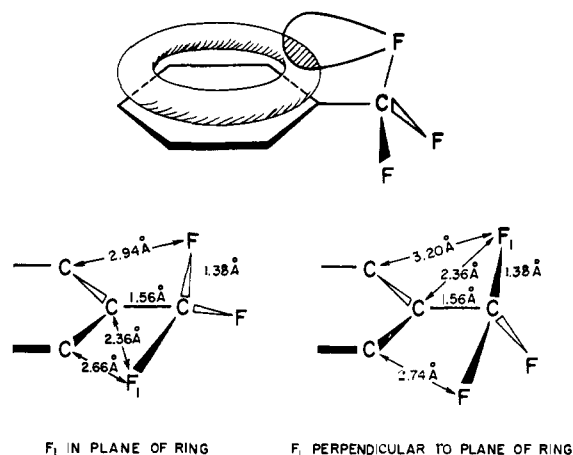


Figure 1. Diagrams showing atomic distances (calculated for tetrahedral angles) and orbital overlap in benzotrifluoride.

electrons on nitrogen are available to stabilize a transition state for attack of an electrophilic reagent in the *para* position. Although the availability of the unshared pair of electrons is greatly reduced by the two CF₃ groups, it is expected that σ_p would always be a little smaller than σ_m (compare, for example, the trimethylammonium group⁸). These results cannot be readily explained by the previously accepted mechanisms, but since the F to C aromatic distances in the N(CF₃)₂ group can be closer than for CF₃, the p- π interaction mechanism provides a rational explanation. The perfluoroalkyl groups are also expected to behave like CF₃ since again the F to C aromatic distances are similar although changes in overlap angles may cause small differences. The number of fluorines available for interaction must also be considered and three β -fluorines in a rotating trifluoromethyl group may be equivalent to one α -fluorine.³⁴

For an OCF₃ group, apparently the p- π overlap is not sufficient to overcome the -R effect of the group. However, the -R effect is greatly reduced relative to an OCH₃. The dipole moment data for aryltrifluoromethyl ethers¹⁰ indicated that the angle C-O-CF₃ may be greater than the assumed 90°, which would considerably increase the F to C aromatic distances and decrease p- π overlap. The +R effect for the SCF₃ group was attributed to d-orbital participation but may be due in part to p- π interaction.¹⁰

The most convincing argument for fluorine p- π interaction is from analysis of F¹⁹ chemical shift data for arylsulfur pentafluorides²² and benzotrifluorides. For the apex fluorine in arylsulfur pentafluorides, the chemical shifts were found to correlate directly with Hammett σ -parameters. The apex fluorine cannot interact directly with the π -system of the ring, and the chemical shift is influenced only by normal inductive and resonance effects transmitted through the molecule.³⁵ In all other cases of fluorine or fluorinated groups attached to the aromatic system,³⁶ an artificial

(34) The chemical shift effects on the β -fluorines from substituents through p- π interaction should consequently be decreased by about one-third, as found (see Table V).

(35) For a discussion mechanism of transmission of inductive and resonance effects see ref. 3, and 28, p. 384.

(36) The one exception to this statement is for the SO₂CF₃ group. Apparently the SO₂ group shields the fluorine from direct interaction with the π -system (ref. 22).

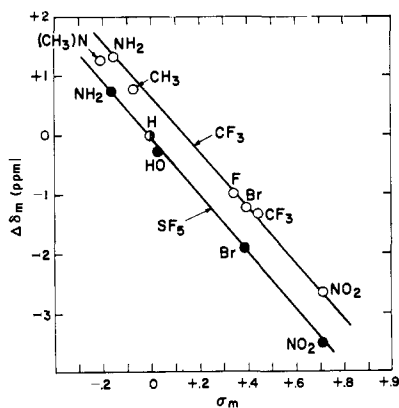


Figure 2. Correlation plot of F^{19} chemical shift differences vs. σ_m : ●, $\delta_m^{SF_3 \text{ basal}} - \delta_m^{SF_3 \text{ apex}}$; ○, $\delta_m^{CF_3} - \delta_m^{SF_3 \text{ apex}}$.

method of correlation involving δ_m vs. σ_1 and δ_p vs. σ_R must be employed.^{12,22} The difference between the chemical shift of the apex fluorine and that of the basal fluorines in the SF_3 group is assumed to arise chiefly from the effect of p- π interaction. The extent of p- π interaction should correlate directly with the π -system charge density which is roughly proportional to the σ -values. For the *meta* substituents a straight-line correlation between $\Delta\delta$ and σ_m is found as shown in Figure 2. A similar correlation is found for the *para* series (Figure 3), but the slope of the line is less, indicating that *para* substituents influence the field of the fluorine significantly less than those in the *meta* position. (Conversely, the fluorine will influence the *meta* position of the ring to a greater extent than the *para*.) A similar analysis of the benzo-trifluoride chemical shift data again using the chemical shift of the apex fluorine of SF_3 as a standard for the contribution from induction and resonance effects gives correlation lines of the same slope although with slightly displaced intercepts (see Figures 2 and 3). General application of this method of analyzing fluorine chemical shift data in aromatic systems is being examined.

The effect of the p- π interaction on the *ortho* position cannot be determined from the present data. (pK_a data for some *o*-fluoroalkylanilines are given in Table III.) Possibly the return of electron density is most strongly felt at the *ortho* position and drops off gradually in progressing to the *meta* and *para* positions, in a fashion analogous to a field effect.³⁷ But a p- π effect at the *ortho* position may be completely masked by other factors resulting from the steric proximity. Another point in considering p- π interaction is that the most effective overlap could occur in the π -system between C-1 and C-2 of the ring or possibly even over the *ortho* position.³⁸ Contributing resonance forms

(37) The fluoride ion hyperconjugation mechanism is generally accepted to explain the stabilizing influence of β -fluorines on negative charges (ref. 5 and 6). However, we suggest, on the basis of the above discussion, that α -fluorines may partially counteract their normal stabilizing effect by a tendency to donate electron density from p-orbitals and that β -fluorines show only the normal inductive effect.

(38) E.s.r. studies on the radicals formed from reduction of (fluoro-

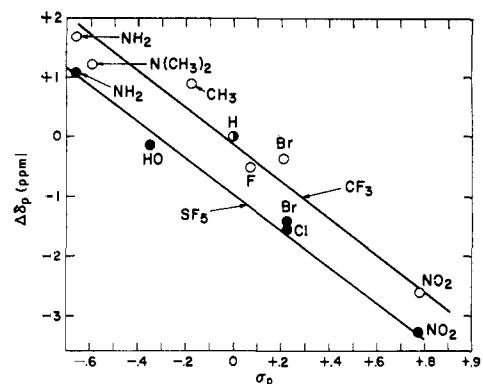
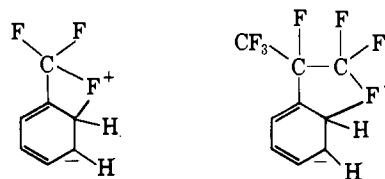


Figure 3. Correlation plot of F^{19} chemical shift differences vs. σ_p : ●, $\delta_p^{SF_3 \text{ basal}} - \delta_p^{SF_3 \text{ apex}}$; ○, $\delta_p^{CF_3} - \delta_p^{SF_3 \text{ apex}}$.

describing a 1,4- or 1,5-interaction could be drawn as



In conclusion, the p- π approach should be considered in dealing with any substituent that contains atoms with unshared electron pairs. Fluorine may be particularly effective because its p-orbitals are of a size and compactness that would give optimum overlap with carbon p-orbitals. Large atoms such as Br in CBr_3 may be much less effective than F in CF_3 for p- π interaction. Ritchie and Sager³⁹ have pointed out that groups with unshared pairs of electrons are anomalous in structure-reactivity correlations. We are undertaking a theoretical study of the problem of the effect of unshared pairs on a π -system⁴⁰ and are collecting additional experimental data for groups such as halo-methyls and other fluorinated substituents.⁴¹

alkyl)nitrobenzenes are being carried out by Dr. M. T. Jones of this laboratory and may provide some definitive evidence on this problem.

(39) Ref. 28, p. 395.

(40) In collaboration with Dr. H. E. Simmons and C. D. Ritchie. Preliminary molecular orbital calculations on benzo-trifluoride using the extended Hückel theory of Hoffman, *J. Chem. Phys.*, **39**, 1397 (1963), show return of electron density to the ring from a p-orbital of fluorine; a slightly greater return to the *meta* position is possible but is dependent on the choice of the C-F bond length. These calculations supported the idea that p- π interaction in benzo-trifluoride may be important.

(41) Two other explanations for the results have been brought to our attention. Dr. Van Gulick suggested that fluorine-hydrogen bonding to the *ortho* hydrogen induces carbanion character at the *ortho* carbon which could be transmitted by resonance to C-3 and C-5. However, the $C(OCH_3)_3$ group shows a -R effect (unpublished data) which is contrary to the result expected by this argument. Also J. N. Murrell in "The Theory of Electronic Spectra of Organic Molecules," John Wiley and Sons, Inc., New York, N. Y., 1963, Chapters 9 and 10, argues that fluorine shows a much stronger inductive effect than chlorine but a much weaker mesomeric effect, in contrast to the normally accepted view that fluorine has the greatest resonance interaction (donation) of the halogen series. He proposes instead that fluorine has a very strong inductive π -electron repulsion. The present data could be accommodated in the framework of this argument if the fluoroalkyl group interacted with the π -system by strong inductive repulsion of the π -electrons.