$-$ ν_0 for pyridine and ν_0 taken from the hexane data) is least (2.9, 2.7, and 2.4 for **21**, **25**, and **27**, respectively). This observation may be interpreted in terms of a negative contribution to the solvent shift of the epoxide proton of **27** which is temperature independent. It is apparent that if the dotted lines of Figure 1 (curves for the di-*t*-butyl diepoxide) were extrapolated to high temperatures (approximating complex free solutions), they would approach each other at a resonance frequency for the epoxide proton *lower* than that observed for a hexane solution.

The stereochemistry assigned to the stereoisomeric pairs of diepoxides **23**–**24**, **25**–**26**, and **27**–**28** is only tentative[18] and unimportant for the present arguments. The assignments are based on the solvent-shift data and upon the conclusion that the less soluble higher melting isomer has the *trans* configuration.[18] In a *cis* diepoxide, the proton attached to one epoxide ring is further away from the negative end of the local dipole of the other epoxide ring relative to the situation in a *trans* diepoxide. Hence the compounds having the epoxide protons with the larger upfield solvent shifts in benzene are assigned the *cis* stereochemistry.

Experimental Section

Nmr Measurements.—The variable-temperature experiments were carried out using a Varian HA-100 nmr spectrometer with 2% w/v solutions. All other measurements were carried out on a Varian A-56/60 nmr spectrometer with 5% w/v solutions.

Epoxyquinones.—The epoxyquinones reported here were all synthesized by the direct oxidation of the corresponding quinone as reported in an earlier publication.[18]

Registry No.—Benzene, 71-43-2; pyridine, 110-86-1; **2**, 75-21-8; **3**, 15448-47-2; **4** (*cis*), 1758-33-4; **4** (*trans*), 15493-88-6; **5**, 15448-50-7; **6**, 503-30-0; **7**, 109-99-9; **8** (*cis*), 2144-41-4; **8** (*trans*), 15493-89-7; **9**, 13423-15-9; **10**, 142-68-7; **13**, 60-29-7; **14**, 111-43-3; **15**, 108-20-3; **17**, 10476-74-1; **18**, 10476-73-0; **19**, 10476-70-7; **20**, 10476-71-8; **21**, 15448-58-5; **22**, 15448-59-6; **23**, 15448-60-9; **24**, 10476-79-6; **25**, 10476-76-3; **26**, 10476-75-2; **27**, 10476-78-5; **28**, 10476-77-4; **29** (R = H), 15448-65-4; **29** (R = CH_3), 15448-66-5; **29** (R = $(CH_3)_3C$), 15448-67-6.

Acknowledgment.—Two of us (H. W. Moore and H. Raymond Shelden) are indebted to the National Science Foundation for partial support of this project from Grant GP. 5945.

[18] H. W. Moore, *J. Org. Chem.*, **32**, 1996 (1967).

Fluoroalkylamines

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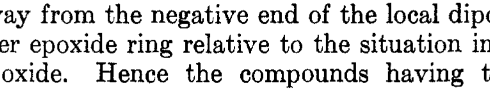
Lewis acids were used to activate fluorimines toward reactions with carbon nucleophiles. A wide variety of fluoroalkylamines was prepared and the chemistry of these very stable compounds was explored. A correlation between F^{19} nmr chemical shifts and the Hammett σ values is discussed.

Primary or secondary amines which contain fluorine atoms attached directly to their α-carbon atoms are known to be relatively unstable.[1] The base-catalyzed loss of the elements of hydrofluoric acid occurs readily (eq 1). The remarkable physical and chemical properties of the fluoro alcohols[2a] derived from fluoro ketones[2b,c] and carbon nucleophiles prompted a study of the fluoroalkylamines which might be derived from fluorimines[3] and carbon nucleophiles (eq 2). Fluoro ketones and fluorimines differ, however, in reactivity toward nucleophiles, the latter being less electrophilic. Only one case of a reaction of a fluorimine with a carbon nucleophile (the very electron-rich isobutylene) has been reported.[4] We have found that Lewis acids activate fluorimines so that they undergo many of the reactions shown by fluoro ketones. This method has proved to be an excellent route to a wide variety of fluoroalkylamines. Several fluoroalkylamines were also prepared by alternate, less general routes.



$$\left[-\overset{\overset{F}{|}}{\underset{|}{C}}-\overset{\overset{H}{|}}{N}-\right] \xrightarrow{-HF} \;{>}C{=}N{<} \qquad (1)$$

$$RH + (R_f)_2C{=}NH \longrightarrow RC(R_f)_2NH_2 \qquad (2)$$

Preparation of Fluoroalkylamines.—α,α-Bis(fluoroalkyl)benzylamines were prepared from fluorimines[3] and aromatic hydrocarbons under vigorous Friedel–Crafts conditions (Table I). The reaction usually was carried out at elevated temperatures in a "Hastelloy"-lined autoclave at autogenous pressure (eq 3). Reactivity closely paralleled normal electrophilic substitution, with electron-donating groups activating and electron-withdrawing groups deactivating the ring. Yields varied from high to low depending on the aromatic hydrocarbon. Disubstitution was observed with phenol and 2 equiv of hexafluoroisopropylidenimine[3] (HFAI), but the hexafluoroisopropylamino group was sufficiently ring deactivating to prevent disubstitution in unactivated aromatic hydrocarbons. *para,para'* disubstitution was observed when compounds containing two benzene rings separated by a heteroatom or carbon chain were employed. 3,5-Dimethyl-4-

$$(R_f)_2C{=}NH + X{-}C_6H_5 \xrightarrow{\text{catalyst}} X{-}C_6H_4{-}C(R_f)_2NH_2 \qquad (3)$$

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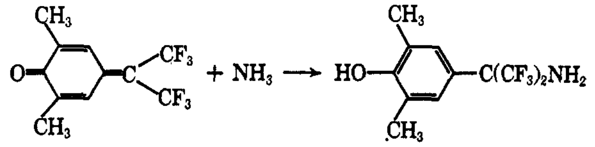
(1) F. S. Fawcett, C. W. Tullock, and D. D. Coffman [*J. Chem. Eng. Data*, **10**, 398 (1965)] describe the properties of N,N-bis(trifluoromethyl)amine; W. J. Middleton and C. G. Krespan [*J. Org. Chem.*, **30**, 1398 (1965)] describe the properties of heptafluoroisopropylamine.

(2) (a) W. J. Middleton and R. V. Lindsey, *J. Amer. Chem. Soc.*, **86**, 4948 (1964); (b) C. G. Krespan and W. J. Middleton, in "Reviews in Fluorine Chemistry," P. Tarrant, Ed., in press; (c) N. P. Gambaryan, E. M. Rokhlin, Yu. A. Zeifman, C. Ching-Yun, and I. L. Knunyants, *Angew. Chem.*, **78**, 1008 (1966).

(3) W. J. Middleton and C. G. Krespan, *J. Org. Chem.*, **30**, 1398 (1965).

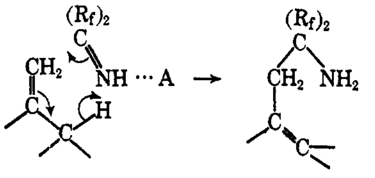
(4) Y. V. Zeifman, N. P. Gambaryan, and I. L. Knunyants, *Izv. Akad. SSSR Ser. Khim.*, **1965** (8), 1472 (1965).

hydroxy-α,α-bis(trifluoromethyl)benzylamine was also prepared by a novel alternate route (eq 4).[5]



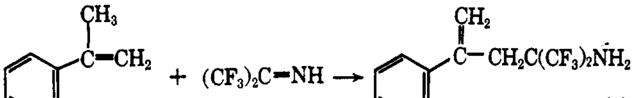
(4)

Terminal olefins which also contain a hydrogen atom in the 3 position react with fluorimines to form adducts in which the double bond migrates (Table III and eq 5). A six-centered mechanism may be involved.

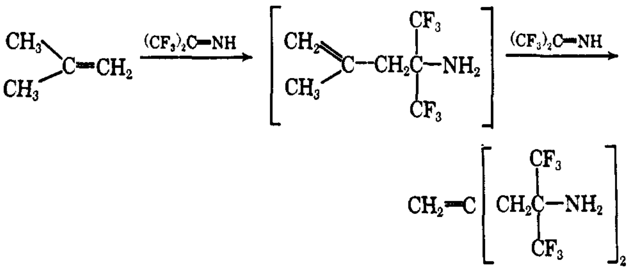


(5)

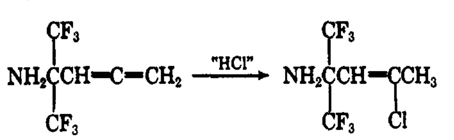
Internal olefins were much less reactive, and under similar conditions no adducts could be isolated; this result is believed to be due to steric rather than electronic factors. The reaction with olefins occurs under milder conditions than with aromatics; thus, for molecules which contain both aromatic ring and a terminal double bond, the latter may react preferentially (eq 6). With the highly reactive olefin, isobutylene, a 2:1 adduct (I) was isolated. Methylacetylene condensed with HFAI (in the presence of BF_3), perhaps in a similar six-centered reaction, but the acid-sensitive product (allene IIa) could be isolated only in trace amounts. When $AlCl_3$ was used as catalyst, IIb was isolated instead of IIa.



(6)



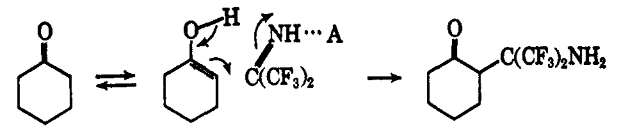
I



$$NH_2C(CF_3)_2CH{=}C{=}CH_2 \xrightarrow{\text{"HCl"}} NH_2C(CF_3)_2CH{=}C(Cl)CH_3$$

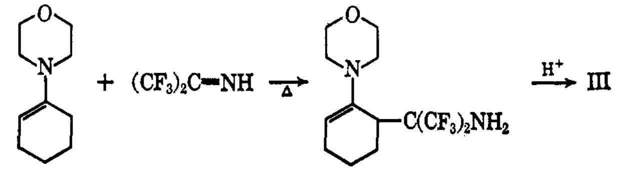
IIa IIb

Lewis acids also catalyze the reaction of fluorimines with active methylene compounds (Table II). These reactions may occur *via* the enol form of the carbonyl group. Ketamine III was prepared alternately by the reaction of HFAI with an enamine;

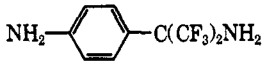


III

this uncatalyzed addition is an example of a reaction of fluorimines with exceptionally strong carbon nucleophiles. A similar sequence was observed with the morpholine enamine of cyclopentanone.



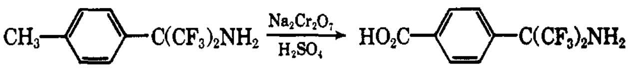
Properties and Chemistry.—One of the most striking properties of fluoroalkylamines in general is their stability. This property is particularly true for the benzylamines, which not only survive the vigorous Friedel-Crafts conditions used to prepare them, but are also stable at elevated temperatures in the presence of metals. Even the adduct (IV) of HFAI and aniline



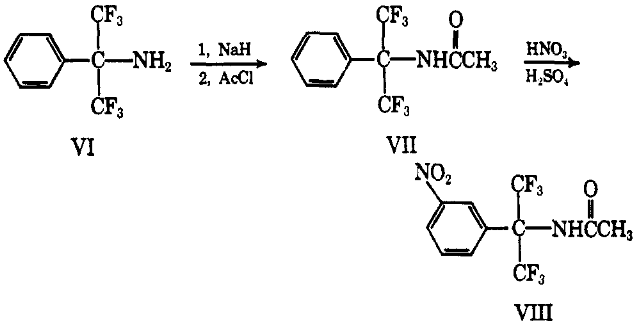
IV

shows no tendency to darken on storage, a property long associated with ordinary aromatic amines. The stability of IV is evidence of the inherent stability of the hexafluoroisopropylamino group and of its strong electron-withdrawing properties, which deactivate the ring.

Chromic acid oxidation of 4-methyl-α,α-bis(trifluoromethyl)benzylamine (V) left the amino group unaffected, while the methyl group was converted to a carboxyl group. Attempted acylation of bis(trifluoromethyl)benzylamine VI with refluxing acetyl chloride was unsuccessful; acetamide VI was prepared, however, *via* the sodium salt. Compound VII underwent ring nitration to give VIII with no hydrolysis products. Hot 50% sulfuric acid was used to hydrolyze VIII to the corresponding free base IX. Ring bromination in the presence of iron gave *m*-bromo-α,α-bis(trifluoromethyl)benzylamine (X). In addi-



V



VI VII VIII

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[5] We are indebted to Dr. W. A. Sheppard for a sample of the starting quinomethan; the preparation and other chemistry of this compound will be published shortly by Dr. Sheppard.

TABLE I.—REACTIONS OF FLUORIMINES WITH AROMATICS TO PREPARE α,α-DI(FLUOROALKYL)BENZYLAMINES

A. $X{-}C_6H_5 + R_fR'_fC{=}NH \longrightarrow p\text{-}X{-}C_6H_4C(R_f)(R'_f)NH_2$

X	R_f	R'_f	Method[a]	Catalyst	Temp, °C	Parent yield	Bp, °C (mm)	Mp, °C	Formula of product[l]
OH	CF_3	CF_3	A, 1, 21	$AlCl_3$		50			
			A, 1, 21	HF	150	73	80 (1.0)	70–73	$C_9H_7F_6NO$
			A, 1, 5	BF_3		40			
OCH_3	CF_3	CF_3	A, 2, 10	$AlCl_3$	150	56	65 (1.2)	53–53.5	$C_{10}H_9F_6NO$
NH_2	CF_3	CF_3	A, 1.7, 11	HF	150	4	81–85 (5–4.5)	69–70 (pentane–ether)	$C_9H_8F_6N_2$
H	CF_3	CF_3	A, 1, 6	$AlCl_3$	200	12[e]	95 (60)		$C_9H_7F_6N$
Cl	CF_3	CF_3	A, 1.6, 11	$AlCl_3$	225[f]	0.6	50 (1.25)		$C_9H_6ClF_6N$
F	CF_3	CF_3	B, 3, 14	$AlCl_3$	250	10	59 (10)		$C_9H_6F_7N$
$N(CH_3)_2$	CF_3	CF_3	A, 1.4, 10	$AlCl_3$	50	36		58.5–59.5 (pentane)	$C_{11}H_{12}F_6N_2$
Ph	CF_3	CF_3	A, 2, 11	$AlCl_3$	150	26	135 (2)	93–95	$C_{15}H_{11}F_6N$
CH_3	CF_3	CF_3	A, 1, 8	$AlCl_3$	150	41	125 (100)		$C_{10}H_9F_6N$
Br	CF_3	CF_3	B, 0.75, 6	$AlCl_3$	275	1	122 (10)	35–36	$C_9H_6BrF_6N$
CH_3	C_2F_5	C_2F_5	B, 0.25, 2	$AlCl_3$	175	8	30 (0.5)		$C_{12}H_9F_{10}N$
CH_3	CF_3	CF_2Cl	B, 0.6, 6	$AlCl_3$	150	28	79 (0.75)		$C_{10}H_9F_5ClN$

B. $RH + (CF_3)_2C{-}NH \longrightarrow R{-}C(CF_3)_2NH_2$

R	Method[a]	Catalyst	Temp, °C	Parent yield	Bp, °C (mm)	Mp, °C	Formula of product[l]
(3,5-Dimethyl-4-hydroxy)-phenyl-	A, 1, 25	HF	150	30	*h*	65–68	$C_{11}H_{11}F_6NO$
9-Anthracenyl	A,[i,j] 1, 6	$AlCl_3$	150	43		210	$C_{17}H_{11}F_6N$
$-C_6H_4-Y-C_6H_4-$[g] Y- -O-	A, 2.4, 12.5	$AlCl_3$	150	37	124 (2)	50–52	$C_{18}H_{12}F_{12}N_2O$
Y- -S-	B, 1.9, 11	$AlCl_3$	150	19	173–176 (3)		$C_{18}H_{12}F_{12}N_2S$
Y- -NH-	B, 1, 15	$AlCl_3$	100	27	175 (7.5) short path	83–85	$C_{18}H_{13}F_{12}N_3$
Y- $-CH_2CH_2-$	B, 2, 11	$AlCl_3$	150	15	145–146 (1–20)	116–117	$C_{20}H_{16}F_{12}N_2$
(1-Hydroxy-4-hexafluoroisopropylamino)phenyl	A, 1.2, 9	$AlCl_3$	200	36	*j*	82–84	$C_{12}H_8F_{12}N_2O$

[a] The following procedures were employed. (A) The reactants were heated in an autoclave for 8 hr. The autoclave was cooled and vented and the residue extracted with ether (filtered, dried, and distilled). (B) Same as A except sodium bicarbonate added before extraction (as solid or in aqueous wash) to neutralize acid. The first number after the method type is the weight ratio of imine to aromatic. The second number is the weight ratio of imine to catalyst. [b] Calibrated at 40, 20, 10, and 5% in $FCCl_3$ and extrapolated to infinite dilution. [c] Not calibrated; $FCCl_3$ as internal standard. [d] There was no visible decomposition of this benzylamine when heated in a sealed tube at 200° for 24 hr without metal or in the presence of Al, Cu, or soft iron; at 300° only minor decomposition was noted.

TABLE II.—REACTIONS OF HEXAFLUOROISOPROPYLIDENIMINE WITH ACTIVE METHYLENE COMPOUNDS

Substrate	Product	Method[a]	Catalyst	Temp, °C	Per cent yield	Bp, °C (mm)	Formula
Cyclohexanone	2-(Hexafluoroisopropylamino)cyclohexanone	A, 1.7, 34	$ZnCl_2$	125	45	84 (6)	$C_9H_{11}F_6NO$
$CH_2(CO_2CH_3)_2$	$(CO_2CH_3)_2CHC(CF_3)_2NH_2$[b]	B, 1.4, 7.3	$ZnCl_2$	100	13	56 (1.2)	$C_8H_9F_6NO_4$
$NCCH_2CO_2CH_3$	$(CO_2CH_3)(CN)CHC(CF_3)_2NH_2$[c]	B, 1.7, 6.5	$ZnCl_2$	100	45	57–59 (0.75)	$C_7H_6F_6N_2O_2$

[a] See Table I, footnote *a*. [b] Not calibrated: $FCCl_3$ as external standard. [b] Registry no.: 1558-89-9. [c] 15580-90-2.

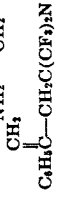
Combustion analyses				
Calcd, %	Found, %	H^1 nmr, τ	F^{19} nmr,[b] ppm	Other data
C, 41.70; H, 2.72	C, 41.70; H, 2.84	A_2B_2 centered at 2.68 (aromatic protons); broad singlets at 1.3 (OH) and 7.1 (NH_2) (acetone-d_6)	+75.15	Uv,[m] $\lambda_{max}^{ethanol}$ 278 (1030), 272 (1285), 225 (10,520); pk_a = 8.6
C, 43.96; H, 3.32 N, 5.13; F, 41.73	C, 43.84; H, 3.53 N, 4.85; F, 41.83	A_2B_2 at 2.8, 6.24 (OCH_3); 7.8 (NH_2) ($CDCl_3$)	+75.09	Gc, collected on silicone grease at 125°
C, 41.88; H, 3.13 N, 10.86; F, 44.00	C, 42.01; H, 2.98 N, 10.17; F, 44.01	A_2B_2 at 2.9; $2NH_2$ at 7.1 (neat)	+75.9[c] (neat)	Uv, $\lambda_{max}^{ethanol}$ 287 (1300), 247 (13,150); pk_a = 3.26, by uv in 55% water–45% dioxane
C, 44.46; H, 2.90 N, 5.76; F, 45.89	C, 44.75; H, 2.72 N, 5.54; F, 46.54	Aromatic protons at 2–3; NH_2 at 7.9 (neat)	+74.83	Uv, $\lambda_{max}^{ethanol}$ 266 (389), 260 (465), 254 (406), 250 (347)
C, 39.94; H, 2.18 N, 5.05; Cl, 12.77	C, 39.40; H, 2.63 N, 4.60; Cl, 12.99	A_2B_2 at 2.45; NH_2 at 7.85 (neat)	+74.5[c] (neat)	Other products found but not investigated
C, 41.39; H, 2.32 N, 5.37; F, 50.93	C, 41.98; H, 2.44 N, 15.48; F, 51.07	A_2B_2 at 2.47 (split further); NH_2 at 7.80 (neat)	+74.96 +111.3	Uv, $\lambda_{max}^{ethanol}$ 266 (271), 259 (269), 257.5 (292), 255 (251), 252.5 (248)
C, 46.15; H, 4.23 N, 9.81; F, 39.83	C, 46.95; H, 4.50 N, 9.45; F, 40.0	A_2B_2 at 2.9; $2CH_3$ at 7.16; NH_2 at 8.05	+75.15	Uv, $\lambda_{max}^{ethanol}$ 262 (21,000); pk_a = 2.26, by uv in 55% water–45% dioxane
C, 56.43; H, 3.48 N, 4.34; F, 35.72	C, 55.64; H, 3.48 H, 4.36; F, 36.49	Aromatic protons at 2.5; NH_2 at 8.0	+74.83	Uv, $\lambda_{max}^{ethanol}$ 252 (19,000)
C, 46.69; H, 3.53 N, 5.45; F, 44.33	C, 46.56; H, 3.61 N, 5.48; F, 44.10	A_2B_2 at 2.6, 7.83 (CH_3); 7.95 (NH_2) (neat)	+74.94	Uv, $\lambda_{max}^{ethanol}$ 268 (114), 265 (196), 259 (243), 252 (199); stability determination[d]
C, 33.56; H, 1.88 N, 4.35; Br, 24.81	C, 34.11; H, 2.08 N, 4.03; Br, 23.79	Broad singlet at 2.4; NH_2 at 7.83 ($CDCl_3$)	+74.96	Mass spectrum, parents at *m/e* 321, 323
C, 40.35; H, 2.54 N, 3.92; F, 53.19	C, 41.14; H, 2.83 N, 3.76; F, 53.44	A_2B_2 at 2.6; CH_3 at 7.63; NH_2 at 7.85	+77.31 ($2CF_3$) +116.7 ($2CF_3$)	
C, 43.88; H, 3.32 N, 5.13; Cl, 12.9	C, 44.60; H, 3.48 N, 4.97; Cl, 12.91	A_2B_2 at 2.6; CH_3 at 7.71; NH_2 at 7.9 (neat)	A_3B_2[k] at +71.07 (CF_3), +59.84 (CF_2Cl)	
			F^{19} nmr[c]	
See Experimental Section		$2CH_3$ at 7.7; aromatic protons at 2.55; NH_2, OH at 7.2 (acetone-d_6)	+74.9 (acetone-d_6)	
C, 59.47; H, 3.23 N, 4.08; F, 33.21	C, 59.97; H, 3.35 N, 4.02; F, 32.60	Aromatic like 9-methylanthracene except more spread out at 2.2–3.8; NH_2 at 7.35 (DMSO-d_6)	+72.2 (DMSO-d_6)	Mass spectrum, parent at *m/e* 343
C, 43.21; H, 2.42 N, 5.60	C, 43.46; H, 2.48 N, 5.60	A_2B_2 at 2.6; NH_2 at 7.95	+74.9 (CCl_4)	Uv, $\lambda_{max}^{ethanol}$ 276 (1050), 268, (1350), 232 (15,050); mass spectrum, parent at *m/e* 500
C, 41.87; H, 2.35 N, 5.43; F, 44.27	C, 42.08; H, 2.58 N, 5.66; F, 44.27	A_2B_2 at 2.4; NH_2 at 7.85 ($CDCl_3$)	+74.5 ($CDCl_3$)	
C, 43.30; H, 2.62 N, 8.42; F, 45.7	C, 43.00; H, 2.60 N, 8.68; F, 44.88	A_2B_2 at 2.7; NH at 4.2; NH_2 at 8.0	+75.1 (CCl_4)	
C, 46.88; H, 3.15 N, 5.47; F, 44.50	C, 47.14; H, 3.26 N, 5.42; F, 44.68	A_2B_2 at 2.55 for aromatic protons; singlet at 7.04 (CH_2CH_2); NH_2 at 7.86 ($CDCl_3$)	+74.8 ($CDCl_3$)	Mass spectrum, parent at *m/e* 512
C, 33.97; H, 1.90 N, 6.61; F, 53.8	C, 34.15; H, 2.21 N, 6.38; F, 53.41	Aromatic protons at 2.0–3.3; $2NH_2$, OH at 8 ($CDCl_3$)	+74.4 +75.1 ($CDCl_3$)	

[e] Higher yields (25–50%) were obtained at 250° when an almost equimolar amount of $AlCl_3$ was employed (method B used). [f] Heated for 16 hr. [g] 2:1 adducts isolated, *para,para'* disubstituted. [h] Product isolated by short-path distillation at 0.3 mm. [i] Carbon disulfide used as solvent. [j] Vacuum sublimation at 0.05 mm employed in isolation of the product. [k] J = 12 cps. [l] Registry no., respectively: 14356-91-3; 14355-84-1; 14356-93-5; 15562-06-8; 14355-88-5; 14639-71-5; 14355-87-4; 14355-86-3; 14356-92-4; 14355-89-6; 14355-96-5; 14355-98-7; 14355-85-2; 14355-91-0; 14355-90-9; 14355-94-3; 14355-92-1; 14355-95-4; 14355-93-2. [m] In mμ (ϵ).

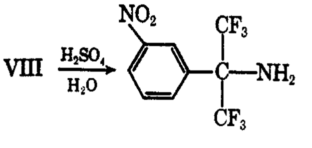
Combustion analyses				
Calcd, %	Found, %	H^1 nmr, τ	F^{19} nmr,[b] ppm	Other data
See Experimental Section			Pair of quartets (J = 9) at +71, 74.5 (CCl_4)	n^{25}D 1.4037; ir, 3400, 1620 cm^{-1} for $-NH_2$ and 1710 cm^{-1} for C=C; strong $-CF_3$ absorption
C, 32.33; H, 3.06 N, 4.72; F, 38.35	C, 33.13; H, 3.30 N, 5.34; F, 38.22	$2CH_3O-$ at 6.25; $-NH_2$ at 7.28; tertiary –H at 6.03 (neat)	Singlet at +74.4 (neat)	
C, 31.82; H, 2.67 N, 10.61	C, 32.83; H, 2.52 N, 10.71	NH_2 at 7.3; CH_3O at 6.11; >CH– at 5.70	A_3B, multiplet (J = 9) at +74 (CCl_4)	Mass spectrum, base peak at parent $-NH_3$; ir, 3425, 3367, 1631 cm^{-1} for NH_2, 2268 for C≡N, and 1765 for C=O

TABLE III

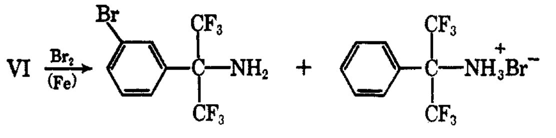
REACTIONS OF HEXAFLUOROISOPROPYLIDENIMINE WITH OLEFINS

Olefin	Product[e]	Method[a]	Catalyst	Temp, °C	Parent yield	Bp, °C (mm)	Formula	Combustion analyses Calcd, %	Found, %	H¹ nmr, τ	F¹⁹ nmr,[b] cps	Other data
$CH_2{=}CHCH_3$	$CH_2{=}CHCH_2C(CF_3)_2NH_2$	A, 3, 3	$AlCl_3$	100	35	97–98	$C_6H_7NF_6$	C, 34.79; H, 3.41 N, 6.77; F, 55.04	C, 34.84; H, 3.11 C, 6.51; F, 55.41	AB_2 at 4.6; doublet (J = 7) at 7.27 (CH_2); singlet at 7.95 (NH_2) (neat)	+75.7 (neat)	Mass spectrum, parent at m/e 207
$CH_3CH_2CH{=}CH_2$	$CH_3CH{=}CHCH_2C(CF_3)_2NH_2$	A, 3, 17	$AlCl_3$	75[c]	19	114–118	$C_7H_9NF_6$	N, 6.34; F, 51.55	N, 5.82; F, 51.59	Multiplet (area 2) at 4.3; singlet (area 2) at 6.5; doublet (J = 6.5; area 2) at 7.36; doublet (J = 5; area 3) at 8.26 (neat)	+75.6 (neat)	Higher boiling product formed
1,7-Octadiene	$[NH_2C(CF_3)_2CH_2CH{=}CHCH_2]_2$	B, 3.4, 11	$AlCl_3$	75[c]	29	98–107 (3–1.5)	$C_{14}H_{16}N_2F_{12}$	C, 38.18; H, 3.67 N, 6.37; F, 51.79	C, 38.76; H, 3.76 N, 6.09; F, 51.97	Vinyl-H at 4.39; isolated $-CH_2$ at 7.43; doublet (J = 7) at 7.80 $-CH_2CH_2-$; NH_2 at 8.25	+76.5 (CCl_4)	Preparative gc employed, mass spectrum, parent at m/e 440
$(CH_3)_2C{=}CH_2$	 $(CF_3)_2C(NH_2){-}CH_2C({=}CH_2)CH_2{-}C(CF_3)_2NH_2$	7, 14[d]	$AlCl_3$	100[d]	18	53 (1.2)	$C_{10}H_{10}F_{12}N_2$	C, 31.11; H, 2.62 N, 7.26; F, 59.07	C, 31.55; H, 2.52 N, 7.03; F, 59.01	Singlets at 4.75 ($=CH_2$), 7.30 ($2CH_2$), and 8.15 ($2NH_2$)	+76.9 (CCl_4)	n^{25}_D 1.3577
Styrene, α-methyl	 $C_6H_5C({=}CH_2){-}CH_2C(CF_3)_2NH_2$	A, 1.3, 4	$ZnCl_2$	125[c]	12	68 (2–3)	$C_{12}H_{11}NF_6$	C, 50.89; H, 3.84 N, 4.95; F, 40.28	C, 51.03; H, 3.96 N, 4.41; F, 40.39	Aromatic –H at 2.72; AB at 4.65 $=CH_2$ at 4.72; CH_2 at 6.92; NH_2 at 8.6	+75.7 (CCl_4)	n^{25}_D 1.4535

[a] See Table I, footnote *a*. [b] Not calibrated; $FCCl_3$ as internal standard. [c] 16 hr. [d] This experiment was carried out by Dr. D. C. England. A glass Carius tube containing the reactants was heated on a steam bath for 23 hr. The nonvolatile components (at room temperature) were mixed with 10% HCl and extracted with CH_2Cl_2 and the resulting extracts dried and distilled. [e] Registry no., respectively: 15580-86-6; 15580-87-7; 15580-88-8; 15717-35-8; 15581-05-2.



IX



X XI

tion to X, an amine hydrobromide (XI) was also isolated from aprotic media but dissociated on storage. The ability of VI to form a hydrobromide suggests that fluoroalkylamines have at least moderate basic character and that their inertness to direct acylation may be due to steric as well as electronic causes.

F¹⁹ Nmr Studies.—Earlier workers[6] have found fluorine contact shifts to be a sensitive probe of charge distribution in the benzene ring. Table IV shows the

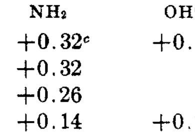
TABLE IV

F^{19} CHEMICAL SHIFTS OF $XC_6H_4C(CF_3)_2Y$ IN PARTS PER MILLION AT INFINITE DILUTION RELATIVE TO THE UNSUBSTITUTED COMPOUNDS

$XC_6H_4C(CF_3)_2Y$ X \ Y	NH_2	OH[a]	F[b]
p-$N(CH_3)_2$	+0.32[c]	+0.35	+0.43
p-OH	+0.32		
p-OCH_3	+0.26		
p-F	+0.14	+0.23	+0.23
p-CH_3	+0.11	+0.09	+0.20
p-Br	+0.11	+0.12	+0.08
p-Ph	0.00		
p-CO_2H	−0.21		−0.17
m-Br	−0.12	+0.11	−0.07
m-NO_2	−0.07	+0.02	−0.07

[a] Reference 6a, in methanol containing 5% $CFCl_3$. [b] Reference 6a, in $CFCl_3$. [c] Values ±0.02 ppm, calibrated at 40, 20, 10, and 5% in $FCCl_3$ and extrapolated to infinite dilution.

change in $-CF_3$ absorption (Δ, ppm, from X = H at +74.83 ppm) with *para* substituent for the bis(trifluoromethyl)benzylamines compared with the corresponding values for bis(trifluoromethyl)benzyl alcohols and fluorides obtained by Sheppard.[6b] A normal correlation curve is found when values for the *para* substituents are plotted against σ_{R°,[7] in agreement with Sheppard's findings. From the chemical shift of the ring fluorine atom in 4-fluorobis(trifluoromethyl)benzylamine (XIIa) (−1.72 ppm from fluorobenzene), it



XIIa, X = NH_2
b, X = OH

appears that the p-hexafluoroisopropylamino group is slightly less electron withdrawing than the p-hexa-

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(6) (a) R. W. Taft, Jr., E. Price, I. R. Fox, I. C. Lewis, K. K. Anderson, and G. T. Davis, *J. Amer. Chem. Soc.*, **85**, 709, 3146 (1963). (b) W. A. Sheppard, *ibid.*, **87**, 2410 (1965), and references cited therein. We thank Dr. Sheppard for his assistance with this study.

(7) R. W. Taft, Jr., S. Ehrenson, I. C. Lewis, and R. E. Glick, *ibid.*, **81**, 5352 (1959).

fluoroisopropanol group (−2.00 ppm from fluorobenzene[6]); this effect probably reflects the difference in electronegativity between oxygen and nitrogen.

Experimental Section[8]

Reactions of Hexafluoroisopropylidenimine (HFAI) with Methylacetylene. A. With Boron Trifluoride Catalysis.—An 8-g sample of methylacetylene (0.2 mol), 0.5 g of hydroquinone, 2 g of boron trifluoride gas, and 34 g of hexafluoroisopropylidenimine[3] (0.2 mol) were heated at 150° for 16 hr. The recovered liquid (7 g) was mixed with 1 g of solid sodium bicarbonate and distilled through a spinning-band column. The material boiling at <58° (1 g) was 68% aminoallene IIa, as estimated by gas chromatographic analysis. A sample was collected by preparative gas chromatography (20% silicone grease column at 69°). The infrared spectrum showed a band at 1955 cm^{-1} for the allene absorption.

Anal. Calcd for $C_6H_5NF_6$: C, 35.13; H, 2.46; F, 55.59. Found: C, 35.50; H, 2.13; F, 56.68.

B. With Aluminum Chloride Catalysis.—When the above reaction was repeated using 3 g of $AlCl_3$ instead of BF_3, the allene was not isolated, but reacted further to give 1.6 g of an "HCl" addition compound, IIb, bp 67° (100 mm). This material showed no allene band in its infrared spectrum, but a >C=C< band at 1660 cm^{-1} instead. F^{19} nmr spectrum showed a singlet at +78.0 ppm from external $FCCl_3$. H^1 nmr spectrum showed vinyl H at τ 4.22 (area 1), $-CH_3$ at 7.48 (area 3), and NH_2 at 7.9 (area 2). The mass spectrum showed peaks at *m/e* 241, 243 (parent), at *m/e* 224, 226 (parent NH_3), and at *m/e* 206 (parent -Cl).

Anal. Calcd for $C_6H_6ClF_6N$: C, 29.83; H, 2.50; N, 5.80. Found: C, 30.29; H, 2.81; N, 5.18.

2-(Hexafluoroisopropylamino)cyclohexanone (III) *via* the Enamine Synthesis. A. Reaction of HFAI with 1-N-Morpholinocyclohexene.—A mixture of 20 g of the enamine[9] and 31 g of HFAI was placed into a 240-ml Hastelloy bomb tube and heated over a period of 6 hr to 150°. The temperature was held at 150° until all the gas was absorbed (4.5 hr). A dark amber liquid, n^{25}_{D} 1.4250, weighing 43 g, was recovered. Distillation of this liquid through a spinning-band column gave a 20-g fraction (50%), bp 110° (3.5 mm) to 104° (0.9 mm) and n^{25}_{D} 1.4479, which solidified on standing (mp 56–58.5°). A sample was recrystallized from pentane and had mp 61.4–63.3°. The infrared spectrum had bands at 3400, 3240, and 1615 cm^{-1} for $-NH_2$ absorption, a band at 1645 cm^{-1} for -C=C- stretch, a band at 3060 cm^{-1} for vinyl -C-H absorption, and a broad band at 1200 cm^{-1} for $-CF_3$ absorption. The F^{19} nmr spectrum clearly showed that the product was a mixture of double-bond isomers; it contained a singlet (19% of the area) at +73.5 ppm from $FCCl_3$ for the isomer with a tetrasubstituted double bond and a pair of quartets (81%) at +71.1 and +72.5 ppm (J = 8 cps) for the isomer with a trisubstituted double bond. The H^1 nmr spectrum supported the structural assignments, as the vinyl proton absorption at τ 4.45 corresponded to slightly less than one proton. Mass spectrometry showed the expected molecular ion peak at 332 and all the expected fragment peaks.

Anal. Calcd for $C_{13}H_{18}F_6N_2O$: C, 47.03; H, 5.47; N, 8.44; F, 34.34. Found: C, 47.32; H, 5.51; N, 8.33; F, 33.83.

B. Hydrolysis of the Enamine Adducts to III.—A suspension of 20 g of the enamine adducts in 150 ml of 3 *N* hydrochloric acid was placed in a stoppered flask and allowed to stand at room temperature for 24 hr. The yellow solution thus obtained was cooled in an ice bath and neutralized to pH 7–8 with solid sodium carbonate. A yellow oil formed. The mixture was extracted with ether, and the combined ether extracts were washed with water and dried over magnesium sulfate. The ether was removed under reduced pressure, and the residue distilled through a spinning-band column. The major product (7.7 g, 72% corrected yield) was the amino ketone III: bp 84° (6 mm), n^{25}_{D} 1.4037. Some (6.3 g) starting material was also recovered. The amino ketone had an infrared spectrum with bands at 3400, 3240, and 1620 cm^{-1}, indicating the $-NH_2$ group, and a strong >C=O absorption at 1710 cm^{-1} as well as strong $-CF_3$ absorption. The F^{19} nmr spectrum showed a pair of quartets at +71.0 and +74.7 ppm from $FCCl_3$ (J = 9 cps).

Anal. Calcd for $C_9H_{11}F_6NO$: C, 41.08; H, 4.22; N, 5.53; F, 43.30. Found: C, 41.17; H, 4.07; N, 5.81; F, 43.01.

2-(Hexafluoroisopropylamino)cyclopentanone *via* Enamine Synthesis. A. Reaction of HFAI with 1-N-Morpholinocyclopentane.—A 19-g sample of the enamine[9] and excess HFAI (40 g) were heated together at 150° for 8 hr in a 240-ml Hastelloy bomb tube. The adduct mixture (31.3 g, 87%), bp 80° (0.5 mm) and n^{25}_{D} 1.4372, was isolated. The infrared spectrum of the product had bands at 3370, 3290, and 1615 cm^{-1} for $-NH_2$ absorption, a -C=C- band at 1640 cm^{-1}, and a strong $-CF_3$ absorption. The F^{19} nmr spectrum showed the product to be a mixture of double-bond isomers. A singlet at +75.5 ppm from $FCCl_3$ (29% of the area) suggested the isomer with a tetrasubstituted double bond, while an eight-peak A_3B_3 pattern centered at +74.6 ppm suggested the isomer with a trisubstituted double bond.

Anal. Calcd for $C_{12}H_{16}N_2F_6O$: C, 45.28; H, 5.07; N, 8.80; F, 35.82. Found: C, 45.42; H, 5.12; N, 8.36; F, 36.13.

B. Hydrolysis.—The adduct mixture was hydrolyzed in 68% yield as described above for the C_6 analog. The amino ketone, 2-(hexafluoroisopropylamino)cyclopentanone, had n^{25}_{D} 1.3880 and bp 60–61° (55 mm). The F^{19} nmr spectrum contained a pair of quartets at 71.6 and +76.7 ppm from $FCCl_3$ (J = 9 cps).

Anal. Calcd for $C_8H_9NOF_6$: C, 38.56; H, 3.50; N, 5.62; F, 45.57. Found: C, 38.83; H, 3.74; N, 5.54; F, 45.57.

4-[1-Amino-2,2,2-trifluoro-1-(trifluoromethyl)ethyl]benzoic Acid.—To a solution of 14 g (excess) of sodium dichromate dihydrate, 20 ml of concentrated sulfuric acid and 30 ml of water was added 8 g (0.031 mol) of 4-methyl-α,α-bis(trifluoromethyl)-benzylamine (III). The mixture was refluxed for 3 hr, stirred 17 hr at room temperature, and poured onto 40 g of ice. The white precipitate was collected on a filter and washed with water (12 g wet). The solid was dissolved in 5% aqueous sodium bicarbonate solution and extracted with ether to remove starting material. Reprecipitation with concentrated hydrochloric acid, washing with water, and drying at 40° under vacuum led to 2.7 g (30%) of the acid, mp 100–101°. The infrared spectrum showed bands at 3413 and 3300 cm^{-1} for NH_2, typical broad OH absorption and a carboxylic acid C=O bond at 1710 cm^{-1}. H^1 nmr spectrum (DMSO-d_6) showed a broad exchange peak at τ 3.4 (3 H) and a multiplet (4 H) at τ 1.8; in $CDCl_3$ the H^1 nmr spectrum was an A_2B_2 pattern (τ 1.9) and a broad peak at τ 4.3 (3 H). F^{19} nmr spectrum was a singlet at +76.42 ppm from internal $FCCl_3$ at infinite dilution. Ultraviolet bands were at λ_{max} 281 mμ (ϵ 1151), 273 (1220), 226 (12,600); the mass spectrum had a parent ion at 287 and required fragments.

Anal. Calcd for $C_{10}H_7F_6NO_2$: C, 41.82; H, 2.46; N, 4.88; F, 39.69; neut equiv, 287. Found: C, 42.45; H, 2.61; N, 5.26; F, 39.30; neut equiv, 280, 277.

N-[α,α-Bis(trifluoromethyl)benzyl]acetamide (VII).—A 12-g (0.05 mol) sample of benzylamine VI in 10 ml of glyme was added to 2.0 g of 54% sodium hydride–mineral oil in 60 ml of glyme and stirred at room temperature for 3 days. Then, 12 g of acetyl chloride was added at <10°. The mixture was refluxed for 3 days and decomposed with ice water. A white precipitate was collected, washed with water and pentane, and dried (12.6 g, 88%). A sample was recrystallized from ether–pentane and had mp 166–168°. F^{19} nmr spectrum showed a singlet at +67.6 ppm (external $FCCl_3$) in DMSO-d_6. The infrared spectrum showed secondary amide bands at 1690 and 1572 cm^{-1}. H^1 nmr spectrum (DMSO-d_6) showed aromatic -H at τ 2.52, $COCH_3$ at 7.80, and NH at 1.5. The ultraviolet spectrum showed λ_{max} 267 mμ (ϵ 279), 261 (345), 255 (280).

Anal. Calcd for $C_{11}H_9F_6NO$: C, 46.32; H, 3.18; N, 4.92. Found: C, 46.11; H, 3.26; N, 5.57.

N-[α,α-Bis(trifluoromethyl)-*m*-nitrobenzyl]acetamide (VIII).—To a 6.0-g sample of N-acetobenzylamine VII dissolved in 20 ml of concentrated sulfuric acid was added dropwise at 20–30° (ice bath) 5 ml of 90% nitric acid. After being stirred at room

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(8) Boiling points and melting points are uncorrected. Nmr spectra were recorded on Varian Associates instruments (A-60, A-56-60, HR-60). Mass spectra were recorded on a CEC 21-103C instrument with a heated inlet at 150°. Ultraviolet spectra were taken in ethanol, and infrared spectra in CCl_4 unless otherwise specified. Fluorine nmr spectra are reported either at infinite dilution from $CFCl_3$ (also used as solvent) taken as 0 ppm (calibrated for quantitative discussion), or in dilute solution containing a trace of $CFCl_3$ or in dilute solution with neat $CFCl_3$ set externally at zero. To distinguish the second and third methods from the first, we shall refer to them as "not calibrated." Proton nmr spectra were measured in CCl_4 unless stated otherwise. Silicone grease columns at 50–250° were employed for gas chromatographic analysis.

(9) G. Stork, A. Brizzolara, H. Sandesman, J. Szuszkovicz, and R. Terrell, *J. Amer. Chem. Soc.*, **85**, 207 (1963).

temperature for 1 hr, the reaction mixture was poured onto ice and extracted with ether. The ether extracts were washed with 5% sodium hydroxide solution and with water and were dried over magnesium sulfate. Evaporation gave 4.9 g (70%) of a white solid (VIII), mp 150–151°. The H^1 nmr spectrum (acetone-d_6) showed a multiplet at τ 1.6–2.5, NH absorption at 1.5, and COCH$_3$ at 7.88. F^{19} nmr spectrum showed a singlet at +69.4 ppm (external FCCl$_3$) in acetone-d_6. The ultraviolet showed λ_{max} 340 mμ (sh, ϵ 114), 257 mμ (ϵ 7970).

Anal. Calcd for $C_{11}H_8N_2O_3F_6$: C, 40.01; H, 2.44; N, 8.49; F, 34.53. Found: C, 40.89; H, 2.69; N, 8.71; F, 34.71.

m-Nitro-α,α-bis(trifluoromethyl)benzylamine.—A 1.0-g sample of N-acetate VIII was refluxed for 4 hr with 20 ml of 50% aqueous sulfuric acid. After being stirred at room temperature for 4 days, the mixture was poured onto ice and extracted with ether. The extract was washed with water and dried over magnesium sulfate; the ether was evaporated; and infrared analysis of the residue indicated that the hydrolysis was incomplete. This residue was combined with 2.0 g of additional N-acetate and 60 ml of 50% sulfuric acid and the mixture was refluxed for 24 hr and worked up as before. The infrared spectrum of the residue (1.93 g) showed little or no starting material present. Short-path distillation gave 0.8 g of amine IX, bp 128–131° (10 mm). H^1 nmr spectrum showed a multiplet (area 4) at τ 1.3–2.5 for aromatic -H and a singlet at 7.66 for NH$_2$. The infrared spectrum showed the characteristic NO$_2$ bands and no amide -CO. The mass spectrum showed the parent and expected fragmentation.

Anal. Calcd for $C_9H_6N_2O_2F_6$: C, 37.56; H, 2.10; N, 9.72; F, 39.56. Found: C, 37.54; H, 2.36; N, 9.72; F, 39.80.

m-Bromo-α,α-bis(trifluoromethyl)benzylamine (X) and Bis-(trifluoromethyl)benzylamine Hydrobromide (XI).—A mixture of 24 g of α,α-bis(trifluoromethyl)benzylamine VI (0.1 mol) and 0.3 g of iron powder was heated at 100° with stirring while 16 g of liquid bromine (0.1 mol) was added in one portion. The reaction mixture was heated at 120° for 1.5 hr and at 100° for 17 hr. Crystals appeared on the thermometer. Filtration and washing with ether gave 4.6 g of a slightly orange solid which was purified by recrystallization from absolute ethanol–ether, mp 170–171°. The ultraviolet spectrum showed aromatic absorption at 266 mμ (ϵ 308), 260 (385), 253 (294), 250 (194). The infrared spectrum showed broad absorption suggestive of an amine hydrobromide. F^{19} nmr spectrum was a singlet at +72.2 ppm from FCCl$_3$. H^1 nmr showed a multiplet at τ 2.3 (5 H aromatic) and a singlet at τ 3.1 (3 H). The solid was, therefore, the hydrobromide XI of the starting amine.

Anal. Calcd for $C_9H_8BrF_6N$: C, 33.35; H, 2.50; F, 35.18; Br, 24.66. Found: C, 33.61; H, 2.82; F, 35.20; Br, 24.17.

The filtrate was taken up in ether, washed with 6 *N* HCl, 10% sodium bisulfite solution, brine, and water, and dried over magnesium sulfate. Infrared and gas chromatographic analyses showed mainly starting material; so the residue was recycled with 1.0 g of iron powder and 13 g of bromine. After the mixture was heated for 1 hr at 120° and 17 hr at 80° (no more crystals appeared), the above work-up was repeated. Distillation (spinning band) afforded 7.4 g (23% yield) of m-bromo-α,α-bis(trifluoromethyl)benzylamine (X), bp 56° (1 mm). The mass spectrum showed the parent ions and expected fragmentation. The ultraviolet spectrum was that of a disubstituted benzene with bands at 275 mμ (ϵ 380), 268 (480) and 262 (362). The F^{19} nmr spectrum showed a singlet at +74.70 ppm (calibrated in FCCl$_3$). The H^1 nmr spectrum showed a complex multiplet at τ 2.3 (total area 4, but o-H at τ 2.05 distinct) and an -NH$_2$ absorption at 7.98.

Anal. Calcd for $C_9H_6BrF_6N$: C, 33.56; H, 1.88; Br, 24.81; F, 35.38; N, 4.35. Found: C, 34.12; H, 2.17; Br, 24.63; F, 35.84; N, 4.12.

3,5-Dimethyl-4-hydroxy-α,α-bis(trifluoromethyl)benzylamine by the Quinomethan Route.—An 8.1-g (0.03 mol) sample of α,α-bis(trifluoromethyl)-2,6-dimethylquinomethan[5] was dissolved in 50 ml of anhydrous ether (orange color) and treated with ammonia gas for 1 hr at 25° and 0.5 hr at 35° (until color faded to light yellow). Excess ammonia and solvent were evaporated and the colorless solid residue was recrystallized from petroleum ether (40–60°) to give white cubes of 3,5-dimethyl-4-hydroxy-α,α-bis(trifluoromethyl)benzylamine (8.0 g, 93%), mp 62–63° (74–75° when the melt was allowed to solidify and then remelted).

Anal. Calcd for $C_{11}H_{11}F_6NO$: C, 46.00; H, 3.86; F, 39.69; N, 4.88. Found: C, 46.15; H, 3.95; F, 39.27; N, 4.72.

See Table I for spectral details.

Registry No.—IIa, 15580-91-3; IIb, 15580-92-4; cyclohexene trisubstituted enamine adduct, 15580-93-5; III, 15580-94-6; cyclopentene tetrasubstituted enamine adduct, 15580-95-7; cyclopentene trisubstituted enamine adduct, 15580-96-8; 2-(hexafluoroisopropylamino)cyclopentanone, 15580-97-9; 4-[1-amino-2,2,2-trifluoro-1-(trifluoromethyl)ethyl]benzoic acid, 15580-98-0; VII, 15580-99-1; VIII, 15581-00-7; IX, 15581-01-8; X, 15581-02-9; XI, 15581-03-0; cyclohexene tetrasubstituted enamine adduct, 15581-06-3.

N,N-Difluoroalkylamines by Direct Fluorination of Alkylamines[1]

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Alkylamines were successfully fluorinated in bicarbonate-buffered aqueous solution to give N,N-difluoroalkylamines. In this way were synthesized N,N-difluorocyclohexylamine, N,N,N′,N′-tetrafluorohexamethylenediamine, N,N-difluoro-n-butylamine, N,N-difluorocyclopentylamine, and N,N-difluoro-t-butylamine. Attempts to convert N,N-dichloroalkylamines into N,N-difluoroalkylamines by metathetical reactions failed. An unusual method of oxidizing primary amines to nitriles was found. Chlorination of alkylamines to N,N-dichloramines followed by cesium fluoride dehydrochlorination gives the corresponding nitrile in high yield.

In 1961 Grakauskas[3] reported the elegant aqueous fluorination of urea to give N,N-difluorourea. Subsequently additional examples of aqueous fluorination were reported[3,4] which gave amide-type N,N-difluoro compounds. In our laboratories in 1959–1961 our goal was to synthesize N,N-difluoroalkylamines by direct fluorination of alkylamines. We succeeded by a procedure similar to that of Grakauskas but included an essential bicarbonate buffer. In this paper we report our successful and unsuccessful attempts to synthesize N,N-difluoroalkylamines.

The first N,N-difluoroalkylamine was synthesized by Frazer[5] who allowed both methyl and ethyl iodides to react with tetrafluorohydrazine in a light-initiated

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(1) Abstracts, the Fourth International Symposium on Fluorine Chemistry, Estes Park, Colo., July 24–28, 1967, p 72.

(2) Department of Chemistry, San Diego State College, San Diego, Calif. 92115.

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