butoxide (1.1 g.) in anhydrous *t*-butyl alcohol (5 ml.) was stirred at room temperature, under nitrogen, for 2 hr. Acetic anhydride (2 ml.) was added, the solution stirred for an additional 5 min., and poured into water. The precipitate was crystallized several times from aqueous methanol contained a drop of pyridine to yield an analytical specimen of enol acetate, m.p. 138–140°, $\lambda_{max}^{KBr}$ 5.75 $\mu$ (17-keto and $\Delta^{3,5}$-enol acetate), $\lambda_{max}^{EtOH}$ 245 m$\mu$, $\epsilon$ 19,200.

*Anal.* Calcd. for $C_{22}H_{30}O_3 \cdot 0.5H_2O$: C, 75.21; H, 8.83. Found: C, 74.95; H, 8.93.

**Relative Rates of Formation of the $\Delta^{3,5}$-Anion from the Isomeric 6-Methylandrost-4-ene-3,17-diones with Potassium *t*-Butoxide.**—A solution of 6$\beta$-methylandrost-4-ene-3,17-dione[28] (25 mg.) in anhydrous *t*-butyl alcohol (1 ml.) was treated with potassium *t*-butoxide (50 mg., 5 equiv.) and stirred for 1 hr. at 25°. Acetic anhydride (0.2 ml.) was added and stirring continued for an additional 5 min. Water was added and the crystalline precipitate (24 mg.) filtered. Separation by silica gel thin layer chromatography (benzene–ethyl acetate, 7:3) established the presence of unreacted starting material and the enol acetate, 3-acetoxy-6-methyl-androst-3,5-diene-17-one, in a weight ratio of 5:4 (41% conversion). No 6$\beta$-methyl-$\Delta^4$-3-ketone was detected. Identical treatment of 6$\alpha$-methylandrost-4-ene-3,17-dione led to recovery of ketone and enol acetate in a weight ratio of 1:8 (87% conversion). Assuming quantitative formation of enol acetate from the $\Delta^{3,5}$-anion[4] and second-order kinetics, the 6$\alpha$-methyl isomer underwent conjugate anion formation at about four times the rate of the 6$\beta$-methyl compound.

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[CONTRIBUTION FROM THE CENTRAL RESEARCH DEPARTMENT, E. I. DU PONT DE NEMOURS AND CO., INC., WILMINGTON 98, DEL.]

# Fluorocarbanions. Rates of Base-Catalyzed Hydrogen–Deuterium Exchange, Isotope Effects, and Acidity of Monohydrofluorocarbons[1]

BY S. ANDREADES

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The formation of perfluorocarbanions from monohydrofluorocarbons bearing hydrogen in primary, secondary, and tertiary positions has been demonstrated by isotopic exchange in sodium methoxide–methanol solution. The kinetics of exchange measured by $F^{19}$ n.m.r., infrared, and mass spectral techniques give relative reactivities of 1.0, 6, 2 × $10^5$, and $10^9$ for fluoroform, 1-H-pentadecafluoroheptane, 2-H-heptafluoropropane, and tris(trifluoromethyl)methane, respectively. Heptafluoro-*n*-propyl and heptafluoroisopropyl carbanions, in the form of lithio derivatives generated from the corresponding monohydrofluorocarbons, have been trapped by reaction with propionaldehyde. The solvent isotope effect for labeled methanol, $(k_{CH_3OD}/k_{CH_3OH}) = 1.5$, was determined using rates of tritium exchange for the primary system. Activation parameters and solvent-corrected deuterium isotope effects are reported and used in a discussion of the mechanism of exchange and the acidity of monohydrofluorocarbons.

## Introduction

Although fluorocarbanions are presumed intermediates in a variety of reactions, such as alkaline decarboxylation,[2] the attack of anions on fluorocarbonyl compounds,[3] and the attack of carbanions[4] or fluoride ion[5] on fluoroolefins, detailed mechanistic studies concerning the nature of perfluorocarbanions have not appeared.

Monohydrofluorocarbons, in general, have been considered relatively inert[6] to common reagents, for example, concentrated potassium hydroxide at 100°.[6] In a series of extensive and definitive investigations of the mechanism of hydrolysis of mixed halomethanes,[2b,7] Hine and co-workers found the basic hydrolysis of fluoroform too slow to measure[7] ($<10^{-6}$ l. mole$^{-1}$ sec.$^{-1}$ at 50°). Recently, reports have appeared that pentafluoroethane, 1-H-heptafluoropropane, and fluoroform undergo no deuterium or tritium exchange after 21–47 days in labeled, alkaline aqueous dioxane.[8] In the present paper, a detailed investigation of primary, secondary, and tertiary fluorocarbanions generated from monohydrofluorocarbons is described.

## Method and Results

Monohydrofluorocarbons have been found to undergo readily base-catalyzed exchange in sodium methoxide–methanol solution according to eq. 1 in which $R_f$ designates a perfluoroalkyl moiety. Four simple mono-

$$R_fH + CH_3OD \underset{k_D}{\overset{k_H}{\rightleftarrows}} R_fD + CH_3OH \qquad (1)$$
$$(NaOCH_3)$$

hydrofluorocarbon systems (fluoroform, $I_H$; 1-H-perfluoroheptane, $II_H$; 2-H-heptafluoropropane, $III_H$; and tris(trifluoromethyl)methane, $IV_H$) were chosen as precursors to the primary, secondary, and tertiary fluorocarbanions I–IV. Compound $II_H$ was included not only because of inherent interest in the $-CF_2H$ function but also because it is the only liquid (b.p. 95–96°) in the series and the homogeneity of its solutions[9] could conveniently be checked without vapor pressure measurements.

$CF_3^{\ominus}$

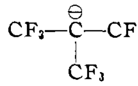
I

$CF_3(CF_2)_5CF_2^{\ominus}$

II


$CF_3\overset{\ominus}{\underset{F}{C}}CF_3$

III


$CF_3-\overset{\ominus}{\underset{CF_3}{C}}-CF_3$

IV

The rates of exchange (Table I) were measured in both the forward ($k_H$) and reverse ($k_D$) directions starting with the appropriate isotopically labeled substrate

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[1] This work was presented in part at the 144th National Meeting of the American Chemical Society, April, 1963, Los Angeles, Calif.; Abstracts, p. 56M.

[2] (a) I. Auerbach, F. H. Verhoek, and A. L. Henne, *J. Am. Chem. Soc.*, **72**, 299 (1950); (b) J. Hine, N. W. Burske, M. Hine, and P. B. Langford, *ibid.*, **79**, 1406 (1957).

[3] See, *e.g.*, E. T. McBee, O. R. Pierce, H. W. Kilbourne, and E. R. Wilson, *ibid.*, **75**, 3152 (1953).

[4] S. Dixon, *J. Org. Chem.*, **21**, 400 (1956); P. Tarrant and D. A. Warner, *J. Am. Chem. Soc.*, **76**, 1624 (1954); D. C. England, L. R. Melby, M. A. Dietrich, and R. V. Lindsey, Jr., *ibid.*, **82**, 5116 (1960).

[5] W. T. Miller, Jr., W. Frass, and P. R. Resnick, *ibid.*, **83**, 1767 (1961), W. T. Miller, Jr., J. H. Fried, and H. Goldwhite, *ibid.*, **82**, 3091 (1960); J. H. Fried and W. T. Miller, Jr., *ibid.*, **81**, 2078 (1959).

[6] J. H. Simons, "Fluorine Chemistry," Academic Press, Inc., New York, N. Y., 1950, Vol. I, pp. 466, 468; Vol. II, p. 337. R. N. Haszeldine and A. G. Sharpe, "Fluorine and Its Compounds," Methuen and Co., Ltd., London, 1951, p. 73.

[7] J. Hine, A. M. Dowell, Jr., and J. E. Singley, Jr., *J. Am. Chem. Soc.*, **78**, 479 (1956); J. Hine and P. B. Langford, *ibid.*, **79**, 5497 (1957); and other related papers by Hine and co-workers.

[8] L. H. Slaugh and E. Bergman, *J. Org. Chem.*, **26**, 3158 (1961).

[9] The lack of detectable exchange reported by Slaugh and Bergman[8] was most likely due to extremely low solubilities of the substrates in aqueous dioxane.

TABLE I

PSEUDO-FIRST-ORDER RATE CONSTANTS FOR EXCHANGE

| No. | Substrate | Temp. $\pm 0.05°$ | $[R_fH]$,[a] moles/l. | $[NaOCH_3]$,[a] mole/l. | $10^6k_H$,[b] sec.$^{-1}$ | $10^6k_D$,[b] sec.$^{-1}$ | $k_H/k_D$ $\pm 0.1$ | $(k_H/k_D)^c$ | $\Delta H \ne$,[d] kcal./mole | $\Delta S \ne$,[e] e.u. |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | $CF_3H(D)$ | 70.0 | 0.81 | 0.21 | 3.43 | 1.11 | 3.1 | 2.1 | .. | ... |
| 2 | $CF_3(CF_2)_6H(D)$ | 50.2 | 1.55 | .31 | 2.16 | 0.625 | 3.5 | 2.3 | 28.1 | 2.3 |
| 3 | $CF_3(CF_2)_6H(D)$ | 60.0 | 1.55 | .31 | 7.85 | 2.45 | 3.2 | 2.1 | | |
| 4 | $CF_3(CF_2)_6H(D)$ | 70.0 | 1.55 | .31 | 28.8 | 9.39 | 3.1 | 2.1 | | |
| 5 | $CF_3(CF_2)_6H$ | 70.0 | 1.55 | .15 | 13.9 | ... | ... | ... | .. | ... |
| 6 | $CF_3(CF_2)_6H$ | 70.0 | 0.76 | .17 | 18.4 | ... | ... | ... | .. | ... |
| 7 | $CF_3(CF_2)_6H$ | 70.0 | 0.93 | .185 | 19.9 | ... | ... | ... | | |
| 8 | $CF_3(CF_2)_6D(T)$ | 70.0 | 1.55 | .145 | ... | 3.98 | ... | ... | | |
| 9 | $(CF_3)_2CFH(D)$ | 0.1 | 0.81 | .21 | 67.6 | 18.3 | 3.7 | 2.5 | 20.3 | −2.8 |
| 10 | $(CF_3)_2CFH(D)$ | 10.0 | .81 | .21 | 270 | 73.7 | 3.7 | 2.5 | | |
| 11 | $(CF_3)_2CFH(D)$ | 20.0 | .81 | .21 | 936 | 260 | 3.6 | 2.4 | | |
| 12 | $(CF_3)_2CFH$ | 0.1 | .81 | .10 | 31.1 | | | | | |
| 13 | $(CF_3)_2CFH$ | 0.1 | .97 | .21 | 62 | | | | | |
| 14 | $(CF_3)_2CFH$ | 0.1 | .40 | .21 | 85 | | | | | |
| 15 | $(CF_3)_2CFH$ | 20.0 | .81 | .05 | 182 | | | | | |
| 16[h] | $(CF_3)_3CH$ | −29 | .81 | .001 | $1 \times 10^3$ | | | | | |
| 17 | Fluorene-*t* | 69.3 | .083[i] | .038 | 151[j] | | | | | |

[a] Solutions were prepared on a weight basis. Molarities listed were determined by back titration of the acidified solutions. [b] Mean deviation was generally ±2%. Reproducibility was generally no worse than 5%. Average of duplicate runs (10–20 points) using the expression $k = \frac{2.303 \log}{t} \frac{C_\infty - C_0}{C_\infty - C}$ (see Experimental). [c] Corrected for solvent isotope effect (see text). [d] ±0.3 kcal./mole. [e] ±1 e.u. calculated from second-order rate constants. [f] This run included 0.18 *M* sodium perchlorate. [g] $10^6k_T$ (determined simultaneously) = 2.87 ± 0.08. [h] ±1°, approximate *k* to within a factor of 10. [i] Concentration of 9-tritiofluorene. [j] $10^6k_T \pm 2$.

and using $F^{19}$ n.m.r. infrared and mass spectral techniques which are described below. The resulting isotope effects ($k_H/k_D$), which include a solvent isotope effect, were corrected [$(k_H/k_D)$,[c] Table I] by measuring rates of tritium exchange in the system $II_T$ (*vide infra*).

The disappearance of sodium methoxide (from β-elimination of HF[10]), determined titrimetrically, is *ca.* $^1/_{200}$th that of the exchange of $II_H$ and one equivalent of fluoride ion is liberated per equivalent of methoxide ion consumed after necessarily long reaction times. An elimination–addition mechanism for exchange is ruled out since no $CF_3(CF_2)_4CFHCF_3$ is produced from $I_H$ as judged by n.m.r. and mass spectra of recovered substrate.[10] Furthermore, <1% of $II_H$ is formed from a mixture of hexafluoropropene, methanol, sodium methoxide, and sodium fluoride under the exchange conditions.[11] No exchange occurs in the absence of base under the reaction conditions; *$IV_H$, however, exchanges slowly in pure boiling ethanol-O-d.* The exchange is first order in $R_fH$ both within a given run and in different runs in which the fluorocarbon concentration was changed (see runs 5–8, 9, 13, 14, Table I). The exchange is also first order in sodium methoxide (runs 4, 5, 9, 11, 12, 15), but since the concentration of base remains essentially constant throughout the reaction, pseudo-first-order rate constants were obtained. To avoid forward and backward reaction corrections,[12] the rate constants were generally calculated on the basis of the first 30% reaction, although the actual value of *k* was generally changed by less than 5–10% if calculated for 80% reaction or if a correction[12] is applied to the latter experimental rate constant.

Experimental infinity points after 10–30 half-lives were in excellent agreement (*ca.* 5%) with calculated infinity values assuming statistical distribution indicating no significant isotope effect on the equilibrium distribution of deuterium.

The extreme reactivity of $IV_H$ even in dilute sodium methoxide solutions at −30° and the facile loss of hydrogen fluoride in this system caused considerable difficulty. Compound $IV_H$ exchanged readily in boiling ethanol-O-*d* (*vide infra*). Consequently, only an approximate base-catalyzed rate of exchange was determined at −30°.

**Preparation of Labeled Monohydrofluorocarbons.**—Direct synthetic routes were found more convenient than exchanges for the preparation of labeled substrates. Compounds $I_D$, $II_D$, and $II_T$ were prepared by decarboxylation[13] of the appropriate potassium salt in labeled ethylene glycol (eq. 2).

$$CF_3(CF_2)_6COOK + (CH_2OD)_2 \xrightarrow[\Delta]{} CF_3(CF_2)_6D + CO_2 + KO(CH_2)_2OD \quad (2)$$

Compound $III_D$ was prepared by hydrolysis and a similar decarboxylation of perfluoroisobutyryl fluoride,[14a] and $III_D$ and $IV_D$ were prepared by the potassium fluoride-catalyzed addition[14b] of deuterium fluoride to hexafluoropropene and octafluoroisobutene, respectively,

$$2(CF_3)_2C{=}CF_2 + COF_2 + D_2O \xrightarrow{KF} CO_2 + 2(CF_3)_3CD \quad (3)$$

under pressure. The necessity of preparing anhydrous deuterium fluoride in advance was obviated by combining the calculated amounts of carbonyl fluoride and deuterium oxide in the reaction vessel containing the potassium fluoride. The product hydrofluorocarbons were purified by preparative scale vapor phase chromatography and used both for the exchanges and for the preparation of known mixtures to check the various analytical techniques.

**Mass Spectral Analyses.**—Mass spectral measurements provided the most convenient and accurate

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[10] *Cf.* J. Hine and N. W. Burske, *J. Am. Chem. Soc.*, **78**, 3337 (1956).

[11] The addition of fluoride ion to perfluoro-1-alkenes would invariably occur at the 1-position; see, *e.g.*, ref. 4. Furthermore, in alcoholic solvents, fluoride ion is so heavily solvated that no nucleophilic attack would be expected.

[12] A. Streitwieser, Jr., D. E. Van Sickle, and W. C. Langworthy, *J. Am. Chem. Soc.*, **84**, 244 (1962).

[13] J. D. LaZerte, L. J. Hals, T. S. Reid, and G. H. Smith, *ibid.*, **75**, 4525 (1953).

[14] (a) F. S. Fawcett, C. W. Tullock, and D. D. Coffman, *ibid.*, **84**, 4275 (1962); (b) *cf.* I. L. Knunyants, V. V. Shokina, and N. D. Kuleshova, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, **9**, 1693 (1960).

method for the determination of isotopic mixtures of monohydrofluorocarbons. For example, methanolic solutions in which reaction was stopped by chilling or by the addition of acetic acid were analyzed directly, thus avoiding the necessity for isolation. Sensitivity and reproducibility are illustrated in the following sample data for II$_H$ and II$_D$ in which a 1% change in

| | Known | Found |
|---|---|---|
| Mole % II$_D$ | 9.0 | 9.0, 9.2, 8.9 |
| Mole % II$_D$ | 8.1 | 8.0, 8.0, 8.1 |

isotopic composition was easily detected. This was true for mixtures rich in either heavy or light component, although reproducibility sometimes varied by ±0.2–0.3% (absolute) in the more dilute solutions. The agreement with known mixtures confirmed the fact that the sensitivity and cracking patterns for the isomeric pair are essentially identical.

The most abundant hydrogen-containing ions were used and, where possible, were checked with less abundant ions. The analysis of II$_H$–II$_D$ was based on the *m/e* 52 ($CF_2D^+$) and *m/e* 51 ($CF_2H^+$) which are the 100% peaks. Since the low abundance *m/e* 50 ($CF_2^+$, 1.35% in each isomer) could be neglected, the only necessary correction to the *m/e* 52 intensity[15] was the $C^{13}F_2H$ due to the natural abundance of $C^{13}$. Similarly, useful peaks and relative abundances for the other systems included *m/e* 51–52 (100%), I$_H$–I$_D$; *m/e* 151–152 (39%), *m/e* 82–83 (19%), III$_H$–III$_D$; *m/e* 113–114 (45%), *m/e* 201–202 (23%), IV$_H$–IV$_D$. Less abundant hydrogen-containing ions in II$_H$–II$_D$ were 101–102 (24%) and 151–152 (13%). As indicated above, the method was generally accurate to within ±0.1% absolute.

**Fluorine N.m.r. Analyses.**—Fluorine n.m.r. analyses proved extremely useful in that, again, samples quenched by chilling or acidification could be analyzed directly and no separate internal standard was necessary. Following the disappearance of a proton resonance due to a single hydrogen would have necessitated a separate (possibly complicating) internal standard.

As an example, the $F^{19}$ n.m.r. spectra of II$_H$, II$_D$, a mixture, and the proton resonance of II$_H$ are given in Fig. 1. As can be seen, not only does the doublet $CF_2H$ resonance (due to spin coupling with hydrogen) collapse to a broadened $CF_2D$ resonance (spin coupling to deuterium not resolved), but a pronounced isotopic chemical shift[16] (*ca.* 0.6 p.p.m.) occurs toward higher field.

This isotopic chemical shift proved advantageous throughout the series.[16] For example, when the $CF_2H$ region of a solution containing a II$_H$–II$_D$ mixture is electronically integrated, the excess area under the high field component of the "unsymmetrical" doublet represents the relative amount of II$_D$; *i.e.*, mole % II$_D$ = $(x - y)/(x + y) \times 100$ where $x$ and $y$ equal the areas of the high and low field peaks of the doublet, respectively. In this instance, the n.m.r. analyses were accurate to about ±1% over a wide range of concentrations checked using known mixtures. In IV$_H$–IV$_D$, the $CF_3$ resonance was used while in III$_H$–III$_D$, both the $CF_3$ and the C–F resonances were useful, although the multiply split CF peak gave much less accurate analyses in this system.

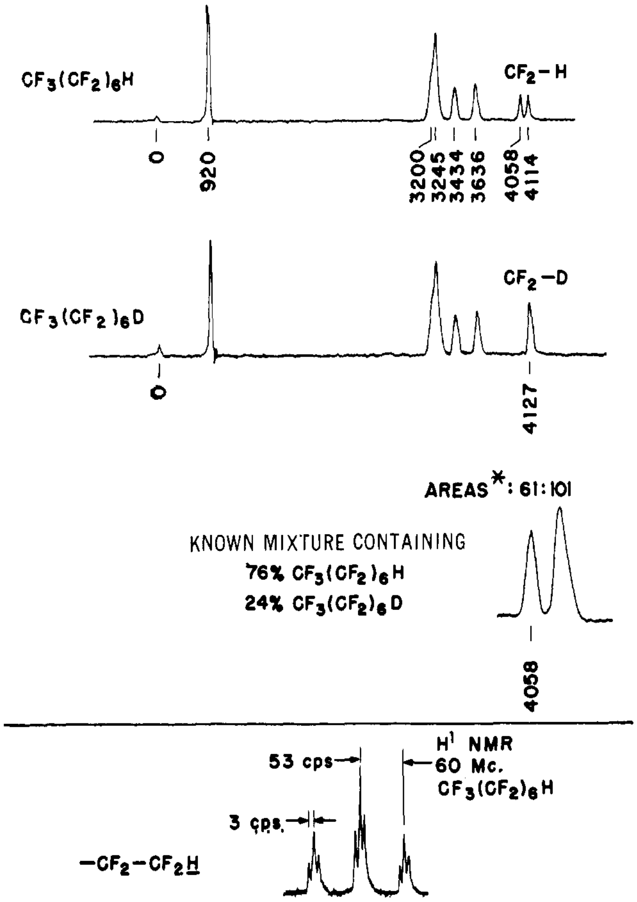

Fig. 1.—$F^{19}$ n.m.r. spectra of 1-H-perfluoroheptane (II$_H$) 1-D-perfluoroheptane (II$_D$), a known mixture of II$_H$ + II$_D$, and the $H^1$ n.m.r. spectrum of II$_H$. $F^{19}$ n.m.r. spectra were obtained at 56.4 Mc. and externally referenced from 1,2-difluoro-1,1,2,2-tetrachloroethane. Calibrations are given in c.p.s. and may be referenced to fluorotrichloromethane by adding 3800 c.p.s. The $H^1$ n.m.r. spectrum was centered at 4.1 τ. * Areas by electronic intergration. Calculated isotopic composition: 75.3% $CF_3(CF_2)_6H$; 24.7% $CF_3(CF_2)_6D$.

**Infrared Spectral Analyses.**—In the usual manner for quantitative infrared analysis, bands were selected which were characteristic of one isomer and absent in the isotopic isomer. However, of the three analytical methods this last procedure was least convenient since isolation of the isotopic mixture was necessary. Useful bands in cm.$^{-1}$ were 925, II$_H$; 1010, II$_D$; 3030, 1380, I$_H$; 2160, 980, 971, I$_D$; 2985, 909, 859, III$_H$; 1031, 823, III$_D$; 2985, 1111, 922, IV$_H$; 1020, IV$_D$. Using known mixtures, the method was accurate to about ±2% and, consequently, was used only as an independent spot check on the other methods.

**Solvent Isotope Effect Correction for Methanol Solutions.**—Since the forward ($k_H$) and reverse ($k_D$) rates of exchange were necessarily measured in $CH_3OD$ and $CH_3OH$, respectively, a correction for the difference in rates in the two isotopic solvents must be applied. In effect, the required unknown (which is not directly measurable) is the rate of the unlabeled substrate ($R_fH$) in unlabeled methanol. This value was determined by simultaneously measuring $k_D$ and $k_T$

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(15) *Cf.* G. H. Miller and E. W. R. Steacie, *J. Am. Chem. Soc.*, **80**, 6486 (1958).

(16) This phenomenon in which deuterium exerts a greater shielding effect than hydrogen on fluorine nuclei two bonds removed was found to be quite general in the systems in which R$_f$ = I–IV (*cf.* G. V. D. Tiers, *J. Am. Chem. Soc.*, **79**, 5585 (1957)). Furthermore, a shift in the same direction, although smaller in magnitude, was noted for fluorines three bonds removed. These effects are being examined in more detail.

(rate of exchange of the tritium-labeled substrate) in unlabeled methanol using the primary system $II_D$–$II_T$ (eq. 4). Recovered substrate from each kinetic point was purified by preparative vapor phase chromatography and analyzed both by mass spectra for deute-

$$\left.\begin{matrix}CF_3(CF_2)_6D\\ CF_3(CF_2)_6T\end{matrix}\right\} + CH_3OH \xrightarrow[70.0°]{NaOCH_3} CF_3(CF_2)_6H + \begin{matrix}CH_3OD\\ CH_3OT\end{matrix} \quad (4)$$

rium and by scintillation counting for tritium. In this manner, the ratio $k_D/k_T = (3.98 \times 10^{-6})/(2.87 \times 10^{-6}) = 1.39 \pm 0.08$ was determined. Using the relationship derived by Swain and co-workers[17] in a transposed form, the corrected deuterium isotope effect in light methanol is calculated to be $k_H/k_D = (k_D/k_T)^{2.26} = 2.1 \pm 0.1$. Comparing this value to the higher one obtained from $k_H$ in methanol-O-*d*, it can be seen that exchanges are 50% faster in heavy methanol than in light methanol[18,19]; *i.e.*, $k_{H(CH_3OD)}/k_{H(CH_3OH)} = 1.5 \pm 0.1$.

## Discussion

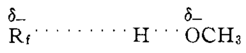
Although base-catalyzed exchange strongly indicates but does not uniquely demand a carbanion mechanism, there seems little doubt that in the present work distinct carbanions are involved. Aside from the demonstration of base-catalyzed exchange in an ionizing solvent, it should also be noted that a necessarily ionic sodium salt is generated, and organolithium intermediates formed from monohydrofluorocarbons were successfully trapped (*vide infra*). Furthermore, no single-step, base-catalyzed exchange reaction of a carbon-bound hydrogen has ever been demonstrated.[20]

A discussion of these data must first account for the dramatic differences in reactivity. Comparing second-order rate constants, the relative reactivities for exchange are: $I_H$, 1.0 < $II_H$, 6 < $III_H$, 2 × $10^5$ < $IV_H$, $10^9$. Table I reveals an activation energy decrease of 7.8 kcal./mole in changing from the primary ($II_H$) to the secondary system ($III_H$). If comparable ground state energies for the hydrocarbons are assumed and the carbanion is chosen as a close approximation to the transition state for this highly endothermic activation process,[21] the observed differences reflect decreasing stability in the fluorocarbanion series: 3° > 2° > 1°. These results indicate β-fluorine is far more stabilizing than α-fluorine and may be rationalized in terms of hyperconjugative "no-bond" resonance involving β-fluorine atoms.[19b,22] Thus, charge delocalization involves an additional nine, six, and two degenerate resonance extremes in IV, III, and II, respectively, leading to diminishing stability of the carbanions in that order.[23] Such stabilization is impossible in I. This concept is consistent with a large mass of chemical data concerning fluoroalkyl compounds of which pertinent examples are the relative reactivities of and direction of ionic additions to various fluoroolefins.[4,15a,25,26]

Inductive effects, although undoubtedly operating, seem insufficient to account for the large reactivity differences observed. An α-fluorine, while less stabilizing than a β-fluorine, certainly stabilizes a carbanion more than hydrogen. For example, trifluoroacetic acid undergoes alkaline decarboxylation[2a] far more readily than acetic acid but less readily than trichloroacetic acid.[27] Furthermore, the well known inductive effect of fluorine drops rapidly with each intervening bond—trifluoroacetic acid is a stronger acid than β,β,β-trifluoropropionic acid by 3.5 powers of 10[28a]; σ-constant determinations of $CF_3$ and $(CF_3)_2CF$ groups (which deal with ground state equilibria) also show only small inductive differences.[22,28b]

A reliable assessment of the role of steric strain in these systems must await stereochemical studies of fluorocarbanions.[29]

**Transition State for Exchange.**—All of the data obtained are consistent with a transition state on the product side of symmetrical as in structure V: (a) in view of the high activation energies, the fluorocarbanion



$$\overset{\delta-}{R_f}\cdots\cdots\cdots H\cdots\overset{\delta-}{OCH_3}$$

V

intermediate must be a good model for the transition state and must certainly have progressed well along the reaction coordinate[21]; (b) the fact that the sodium salt is generated (as opposed to a largely covalent Grignard reagent, for example) indicates an essentially completely ionic carbon–metal bond; (c) no significant salt effect with added sodium perchlorate (run 7, Table I) indicates solvated methoxide ions rather than ion pairs are involved in the exchange even at 0.1–0.2 *M* concentrations.[30] If an equilibrium between dissoci-

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(17) C. G. Swain, E. C. Stivers, J. F. Reuwer, Jr., and L. J. Schaad, *J. Am. Chem. Soc.*, **80**, 5885 (1958).

(18) This statement is at least true for the primary system $II_H$, but, within the framework of the Swain equation,[17] should apply generally to base-catalyzed exchange phenomena in methanol solutions. The quoted error is an ideal one assuming the expression relating the various isotopic effects is exact.

(19) It is interesting to compare this value with the value reported for aqueous media in which base-catalyzed exchanges are 39% faster in heavy water than in light water (a) S. H. Maron and V. K. LaMer, *J. Am. Chem. Soc.*, **60**, 2588 (1938); (b) J. Hine, R. Wiesboeck, and R. G. Ghirardelli, *ibid.*, **83**, 1219 (1961).

(20) J. Hine, R. Wiesboeck, and O. B. Ramsey, *ibid.*, **83**, 1222 (1961).

(21) G. S. Hammond, *ibid.*, **77**, 334 (1955).

(22) (a) J. D. Roberts, R. L. Webb, and E. A. McElhill, *ibid.*, **72**, 408 (1950); (b) R. S. Mulliken, *Tetrahedron*, **17**, 203 (1962).

(23) "No-bond" resonance is a controversial concept which may aptly be compared to the hyperconjugation controversy in the carbonium ion field. It seems rather widely accepted[22b,24] that hyperconjugation plays an important role in carbonium ion transition states, but a negligible role in stabilizing ground states of olefins.[24] Similarly, in the opinion of the author, "no-bond" resonance may reasonably stabilize fully charged fluorocarbanions where electron supply is great while playing a negligible or minor role in affecting equilibria between ground states or the stability of fluoroolefins. However, Hine[24b] has summarized evidence for stabilization of even ground states by double-bond-no-bond resonance.

(24) (a) See, for example, L. S. Bartell, *Tetrahedron*, **17**, 184 (1962); *cf.* also V. J. Shiner, Jr., "Conference on Hyperconjugation," Pergamon Press, New York, N. Y., 1959, p. 168; (b) J. Hine, Abstracts, 18th National Organic Chemistry Symposium of the American Chemical Society, Columbus, Ohio, June 16–20, 1963, p. 85; *J. Am. Chem. Soc.*, **85**, 3239 (1963).

(25) S. Andreades, *J. Org. Chem.*, **27**, 4163 (1962).

(26) See, *e.g.*, I. L. Knunyants, L. S. German, and B. L. Dyatkin, *Izv. Akad. Nauk SSSR*, 1353 (1956); I. L. Knunyants, A. I. Schekotikhin, and A. V. Fokin, *ibid.*, 843 (1956).

(27) F. H. Verhoek, *J. Am. Chem. Soc.*, **56**, 571 (1934); R. A. Fairclough, *J. Chem. Soc.*, 1186 (1938).

(28) (a) A. L. Henne and C. J. Fox, *J. Am. Chem. Soc.*, **73**, 2323 (1951); (b) W. A. Sheppard, private communication.

(29) Comparisons of acidity or rates of exchange of a bridgehead hydrogen on a fluorinated bicyclic system (*cf.* P. D. Bartlett and G. F. Woods, *J. Am. Chem. Soc.*, **62**, 2933 (1940)) with similar measurements on an open-chain analog (such as $IV_H$) should prove extremely revealing concerning resonance or inductive effect arguments. Some experiments in this direction are in progress.

(30) (a) Conductivity measurements of sodium methoxide in methanol show no deviation from the Onsager equation indicating no ion association at least up to the concentrations (0.002 *M*) examined.[30b] (b) G. E. M. Jones and O. L. Hughes, *J. Chem. Soc.*, 1197 (1934); W. F. K. Wynne-Jones, *J. Phys. Chem.*, **31**, 1647 (1927); S. D. Hamann and W. Strauss, *Discussions Faraday Soc.*, **22**, 70 (1956). (c) D. J. Cram, B. Rickborn, C. A. Kingsbury, and P. Haberfield, *J. Am. Chem. Soc.*, **83**, 3678 (1961); J. Reinheimer, W. F. Kieffer, S. W. Frey, J. C. Cochran, and E. W. Barr, *ibid.*, **80**, 164 (1958). (d) Unless ion paired $NaOCH_3$ species were also effective catalysts; *cf.* ref. 30c.

ated ions and ion pairs were involved, addition of common sodium ions would be expected to suppress the dissociation and depress the rate[30d]; (d) the magnitude of the isotope effects. Point (d) requires elaboration and is discussed below.

**Isotope Effects.**—If the usual factors such as anharmonicity and the changes in other vibration frequencies are neglected, the loss of a C–H stretching mode yields a theoretical maximum isotope effect of $k_H/k_D \cong 7$ at 50°.[31] However, in a simple three-center system (approximated by V), the maximum isotope effect would be expected only in a completely symmetrical situation in which the symmetric vibration does not involve motion of the hydrogen atom.[32] The low measured $k_H/k_D$ values (*ca.* 3.1 at 70°) in the present work decreased even further ($k_H/k_D = 2.1$ at 70°)[33] when corrected by rates of tritium exchange (*vide supra*). These low values are indicative of a highly unsymmetrical transition state placed on the product side for reasons mentioned above. A kinetic complication which could also result in decreased isotope effects is discussed later.

In view of the different activation energies, the degree of deviation from a truly symmetric stretching mode in the transition states should increase as $R_f$ is changed from IV to I. Thus, the isotope effects might be expected to increase in the order I < II < III < IV. Although the solvent-corrected value for I at 70° was indeed low ($k_H/k_D = 2.09$), all values at a given temperature (including $III_H$ extrapolated to 70°) are probably within experimental error ($k_H/k_D = 2.1$). It is possible that isotope effects will be most sensitive to changes in near symmetrical transition states. Unfortunately, data for $IV_H$, which should give the largest $k_H/k_D$ ratio, were of insufficient accuracy in sodium methoxide–methanol solution to warrant a $k_H/k_D$ determination.

There is an added kinetic complication which may lower an observed exchange kinetic isotope effect. Thus, if in the process of exchange, the initially-formed carbanion (eq. 5) returns to substrate much more

$$R_fH + {}^{\ominus}OCH_3 \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} [R_f{}^{\ominus} + HOCH_3] \xrightarrow{\overset{*}{H}OCH_3} R_fH^* \quad (5)$$

rapidly than it becomes protonated by a bulk solvent molecule, the observed isotope effect will be lower than the true isotope effect ($k_1{}^H/k_1{}^D$) by a factor equal to the reciprocal reverse isotope effect ($k_{-1}{}^D/k_1{}^H$).[34]

The above complication does not seem to be important in the present work. In eq. 5, as the base strength of $R_f^-$ increased, much more internal return ($k_{-1}$) relative to $k_2$ would be expected, resulting in a decrease in the observed isotope effect. This is not the case. The isotope effects are essentially invariant with a change in substrate. Furthermore, one cannot invoke a cancellation of effects (internal return *vs.* position of the transition state) since, according to the arguments presented above regarding an unsymmetrical transition state, the two effects must be in the same direction, *i.e.*, the strongest base ($CF_3{}^{\ominus}$) should give the smallest isotope effect.

**Acidity Correlation.**—The assignment of relative $pK_a$ values to extremely weak acids, first from metalation exchange equilibria[35,36] and later through the recognition of a useful (but not universally valid) correlation between relative rates of proton exchange reactions and equilibrium acidities,[37] has gained considerable interest. Recently, the latter method has received extensive study, particularly with potassium amide–liquid ammonia[38] and with lithium cyclohexylamide–cyclohexylamine[12,39] systems.

Systems $I_H$–$IV_H$ should display an acidity correlation with exchange rates for several reasons. In addition to points (a) through (d) above, in which it is emphasized that a highly ionic sodium salt of a carbanion is involved, it is also significant that the entropies of activation ($II_H$ and $III_H$, Table I) are both near zero and do not differ significantly between the primary and secondary systems. The small entropy differences actually oppose the enthalpy changes. Thus, essentially all the activation energy is in the enthalpy term. Since our results were obtained in sodium methoxide–methanol solutions, it was necessary to obtain some rates of exchange in this same medium of some previously determined systems. Consequently, 9-tritiofluorene was prepared and its rate of exchange was determined in sodium methoxide–methanol solution. It was found that 9-tritiofluorene has a second-order exchange rate constant 200 times greater than $k_2$ (exchange) for $II_T$, indicating fluorene[40] to be a stronger acid than $II_H$. Since $IV_H$ exchanges in boiling ethanol-O-*d*, it may be assigned an approximate $pK_a$ value of 11.[41] Fluorene has been assigned a $pK_a \cong 25$,[37] and for comparison, cyclopentadiene a $pK_a \cong 15$.[42] Placing second-order rate constants (calculated from Table I) on a plot of log $k_{ex}$ *vs.* $pK_a$ determined by fluorene and fluoradene indicates approximate $pK_a$'s of 31, 30, 20, and 11 for $I_H$–$IV_H$, respectively.

The simple sodium methoxide–methanol medium seems suitable for estimating relative acidities of weakly acidic hydrocarbons in the $pK_a$ range 16–35. Traces of water seem to have little or no effect on the observed rate constants.[30c,43]

**Trapping Experiments.**—In order to demonstrate synthetically that a fluorocarbanion (or a carbanion-type intermediate) can indeed by formed from a monohydrofluorocarbon (as opposed to a single step exchange or a concerted HF elimination), trapping experiments were designed. It was anticipated that in alcoholic

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(31) L. Melander, "Isotope Effects on Reaction Rates," The Ronald Press Co., New York, N. Y., 1960, p. 22.

(32) F. H. Westheimer, *Chem. Rev.*, **61**, 265 (1961).

(33) *Cf.* the smaller isotope effects ($k_H/k_D \approx 1.3$) observed in aqueous media for exchanges of 2,2-dihalo-1,1,1-trifluoroethanes.[10,19b]

(34) D. J. Cram, D. A. Scott, and W. D. Nielsen, *J. Am. Chem. Soc.*, **83**, 3696 (1961); see also D. J. Cram and L. Gosser, *ibid.*, **85**, 3890 (1963).

(35) J. B. Conant and G. W. Wheland, *ibid.*, **54**, 1212 (1932).

(36) W. K. McEwen, *ibid.*, **58**, 1124 (1936).

(37) R. G. Pearson and R. L. Dillon, *ibid.*, **75**, 2439 (1953).

(38) A. I. Shatenshtein, *Dokl. Akad. Nauk SSSR*, **70**, 1029 (1950); *Zh. Fiz. Khim.*, **25**, 1206 (1951); "Isotopic Exchange and the Replacement of Hydrogen in Organic Compounds," Academy of Sciences of the USSR, Moscow, 1960.

(39) A. Streitwieser, Jr., and D. E. Van Sickle, *J. Am. Chem. Soc.*, **84**, 249 (1962), *et seq.*

(40) (a) *Cf.* M. S. Kharasch, W. G. Brown, and J. McNab, *J. Org. Chem.*, **2**, 36 (1937); (b) G. W. H. Scherf and R. K. Brown, *Can. J. Chem.*, **39**, 856 (1961); A. I. Shatenshtein and E. N. Zvyagintseva, *Dokl. Akad. Nauk SSSR*, **117**, 852 (1957).

(41) *Cf.* H. Rapoport and G. Smolinsky, *J. Am. Chem. Soc.*, **82**, 934 (1960).

(42) R. E. Dessy, *ibid.*, **84**, 2899 (1962).

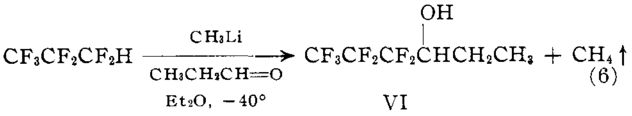
(43) "Dry" methanol in Pyrex vessels will always contain traces of water and $B(OCH_3)_3$; S. W. Benson, "The Foundations of Chemical Kinetics," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, p. 558; R. B. Porter, *J. Phys. Chem.*, **61**, 1260 (1957).

solutions, reprotonation of the extremely basic fluorocarbanion would effectively compete over many other conceivable reactions even though the carbanion is regenerated many times. Consequently, trapping experiments were carried out in a relatively inert medium (diethyl ether) and the formation of a fluoroorganometallic with known synthetic capabilities (*e.g.*, perfluoroalkyllithio derivatives) was selected.

Since most effective bases chosen to remove the proton from $R_fH$ would also rapidly attack a trapping reagent such as a carbonyl compound, a variety of bases was tested in order to find one reactive enough to remove the hydrogen rapidly at low temperatures in ether. Although lithium aluminum hydride, sodium hydride, methylmagnesium iodide, and isopropylmagnesium bromide were ineffective up to room temperature, methyllithium reacted rapidly with a secondary monohydrofluorocarbon at −70° and with a primary monohydrofluorocarbon at −30° to evolve methane.

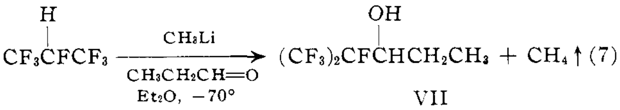
However, the resulting perfluoroalkyllithio derivative was unstable and eliminated lithium fluoride even at −70°.[44] For example, if $\mathrm{III_H}$ was allowed to react with one equivalent of methyllithium at −70° until methane evolution had stopped, followed by the subsequent addition of acetone or carbon dioxide, only hexafluoropropene (65–75% yield) was formed. No alcohol or carboxylic acid was obtained. With excess methyllithium, further attack on the fluoroolefin occurred and 2,3,4,4,4-pentafluoro-2-butene was obtained in yields up to 80%.

The following competition experiments in which propionaldehyde and methyllithium were added simultaneously to rapidly stirred, cooled ether solutions of 1-hydroheptafluoropropane or $\mathrm{III_H}$ proved successful.



$$\mathrm{CF_3CF_2CF_2H} \xrightarrow[\mathrm{CH_3CH_2CH{=}O}\atop \mathrm{Et_2O},\ -40^\circ]{\mathrm{CH_3Li}} \mathrm{CF_3CF_2CF_2}\overset{\mathrm{OH}}{\overset{|}{\mathrm{C}}}\mathrm{HCH_2CH_3} + \mathrm{CH_4}\uparrow \quad (6)$$

VI



$$\mathrm{CF_3}\overset{\mathrm{H}}{\overset{|}{\mathrm{C}}}\mathrm{FCF_3} \xrightarrow[\mathrm{CH_3CH_2CH{=}O}\atop \mathrm{Et_2O},\ -70^\circ]{\mathrm{CH_3Li}} \mathrm{(CF_3)_2CF}\overset{\mathrm{OH}}{\overset{|}{\mathrm{C}}}\mathrm{HCH_2CH_3} + \mathrm{CH_4}\uparrow \quad (7)$$

VII

The major product in each case was 2-butanol but the heptafluorohexanols VI and VII were isolated in 5% yields by preparative vapor phase chromatography. The structures were confirmed by independent syntheses from the corresponding perfluoroalkyl iodides in a similar competition involving halogen metal interchange with methyllithium at low temperatures.[45]

### Experimental[46]

**1-Hydro- and 1-Deuterioperfluoroheptane ($\mathrm{II_H}$ and $\mathrm{II_D}$).**—Compound $\mathrm{II_H}$ was prepared by alkaline decarboxylation[13] of perfluorooctanoic acid[48]; $\mathrm{II_D}$ was prepared by a modification of this method. In a solution of 2.8 g. (0.05 mole) of potassium hydroxide in 16.0 g. (0.25 mole) of ethylene glycol and 52.0 g. (2.6 moles) of deuterium oxide (>99.5%, General Dynamics Corp.) was dissolved 21.0 g. (0.05 mole) of perfluorooctanoic acid. The mixture was distilled to remove the water and as the temperature rose to about 140–150° smooth evolution of carbon dioxide occurred and 16 g. of product was obtained as a lower layer in the distillate. The material was dried over anhydrous sodium sulfate and distilled to collect 13.0 g. (91%) of $\mathrm{II_D}$, b.p. 93–95°, which was found to be 90.0% $\mathrm{II_D}$, 10.0% $\mathrm{II_H}$, by infrared and mass spectral analyses.

**1-Tritio- and 1-Deuterioperfluoroheptane Mixture ($\mathrm{II_T}$–$\mathrm{II_D}$).**—Using a similar procedure to the above, a mixture of 5.6 g. (0.1 mole) of potassium hydroxide, 32.0 g. (0.5 mole) of ethylene glycol, 100.0 g. (5.0 moles) of deuterium oxide, 39.4 g. (0.1 mole) of perfluorooctanoic acid, and 1.0 g. (100 mc.) of tritiated water (New England Nuclear Corp., Boston, Mass.) gave 24.3 g., b.p. 93–95°, of $\mathrm{II_D}$–$\mathrm{II_H}$. Scintillation counting[46] showed the material had a radioactive level of 14.126 μc./g. and mass spectral analyses revealed 88.6% deuteration.

**Fluoroform-*d* ($\mathrm{I_D}$).**—Fluoroform was obtained from the Organic Chemicals Department, E. I. du Pont de Nemours and Co. To 100 g. (5.0 moles) of deuterium oxide was added 27.1 g. (0.125 mole) of trifluoroacetic anhydride, 16 g. (0.25 mole) of ethylene glycol, and 14 g. (0.25 mole) of potassium hydroxide. The procedure described for $\mathrm{II_D}$ was followed except that the reflux condenser was connected to a liquid nitrogen-cooled trap while a slow stream of helium was passed through the entire apparatus. The carbon dioxide–fluoroform-*d* mixture in the trap was then vaporized through an Ascarite column and recondensed in a cylinder to collect 15.3 g. (86%) of fluoroform-*d*. After preparative vapor phase chromatography, mass spectral analysis showed the material was better than 99% pure and contained 90.0% fluoroform-*d*, 10.0% fluoroform.

**2-Hydro- and 2-Deuterioheptafluoropropane ($\mathrm{III_H}$, $\mathrm{III_D}$).**—To 100 g. (5.0 moles) of partially frozen, stirred deuterium oxide was added in small portions under dry nitrogen, 10.2 g. (0.444 mole) of sodium. To the cold mixture of sodium deuteroxide was added 50.0 g. (0.222 mole) of perfluoroisobutyryl fluoride,[14a] and the procedure described for $\mathrm{II_D}$ was followed except that the product was collected in a Dry Ice-cooled trap. Distillation of the product in the trap gave 18.1 g., b.p. −13 to −11° (containing 84% product, 11% $CO_2$, and 3% acid fluoride by v.p.c. and mass spectral analysis) and 9.5 g., b.p. −11 to −2° (11% $CO_2$, 14% acid fluoride). The combined fractions when purified by preparative vapor phase chromatography gave material >99% pure which was 95.2% $\mathrm{III_D}$, 4.8% $\mathrm{III_H}$ by mass spectral, infrared, and n.m.r. analyses. Pure $\mathrm{III_H}$ was prepared as above using sodium hydroxide; $\mathrm{III_H}$ and (with corresponding modifications) $\mathrm{III_D}$ were also prepared by the addition of hydrogen fluoride to hexafluoropropene[14b] and by the hydrolysis of bis(perfluoroisopropyl)mercury[49] with aqueous potassium iodide. The $F^{19}$ n.m.r. spectrum of $\mathrm{III_H}$, referenced internally with $CFCl_3$, showed a $CF_3$ quartet ($J_{\mathrm{CF_3-F}}$ 11, $J_{\mathrm{CF_3-H}}$ 5.5 c.p.s.) at 76.6 p.p.m. and a C–F doublet split into septets ($J_{\mathrm{F-H}}$ 45, $J_{\mathrm{F-CF_3}}$ 11 c.p.s.) centered at 214.7 p.p.m. The $F^{19}$ n.m.r. spectrum of

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[44] In connection with other studies and in accord with the above result, the intermediate organolithium compounds from addition of phenyllithium to fluoroolefins could not be trapped under similar conditions at low temperatures: S. Andreades, to be published.

[45] (a) R. D. Chambers, W. K. R. Musgrave, and J. Savory, *J. Chem. Soc.*, 1993 (1962); (b) J. A. Beel, H. C. Clark, and D. Whyman, *ibid.*, 4423 (1962); (c) O. R. Pierce, E. T. McBee, and G. F. Judd, *J. Am. Chem. Soc.*, **76**, 474 (1954). The above experiments do not rule out a concerted addition mechanism, as pointed out by a referee.

[46] (a) $F^{19}$ n.m.r. spectra were obtained on a Varian Associates 60-Mc. high resolution n.m.r. spectrometer, and electronic integrations were obtained using an associated Varian Associates n.m.r. integrator (Model V-3521) and a Moseley Autograf recorder (Model 2S). Infrared spectra were taken on a Perkin–Elmer Model 21 spectrophotometer and mass spectra[47] on a Consolidated Electrodynamics Corp. Model 21-103C mass spectrometer using a room temperature inlet, an ionizing potential of 70 e.v. and an ionizing current of 10.5 μamp. Scintillation counting[47] was carried out in *m*-xylene solutions at −8° using a Packard Tri-Carb liquid scintillation spectrometer, Model 314. 2,5-Diphenyloxazole (PPO) and 1,4-bis-2-(5-phenyloxazolyl)benzene (POPOP) were used as scintillators. All compounds used in the kinetic studies ($\mathrm{I_H}$–$\mathrm{IV_H}$, $\mathrm{I_D}$–$\mathrm{IV_D}$) and recovered radioactive samples ($\mathrm{II_D}$-$\mathrm{II_T}$) were purified by preparative vapor phase chromatography.[47] The ethyl ester of Kel–F Acid No. 8114 (Minnesota Mining and Mfg. Co.) supported on Chromosorb P (Johns Manville Co.) was used as a column packing for all systems except $\mathrm{II_{H(D,T)}}$ which was chromatographed on 20% w./w. of the diglyceride of ω-trifluorohexanoic acid on 40–60 mesh Columpak (Fisher Scientific Co.). The latter packing was also used for purification of the fluorohexanols obtained in the trapping experiments.

[47] Mass spectral measurements were carried out by Mr. W. M. Kipp and Mr. W. B. Askew; vapor phase chromatographic separations by Mrs. A. B. Richmond and Mr. J. W. Robson; and radioactive assays by Mr. R. S. Blake.

[48] This acid was obtained from the Columbia Organic Chemicals Company and contained about 13% of branched-chain isomer. However, the branching was further removed than the β-position on the chain as shown by $F^{19}$ and $H^1$ n.m.r. spectra. Furthermore, this branching could not interfere in the analyses of the derived $\mathrm{II_H}$–$\mathrm{II_D}$ since only the $CF_2H$ or $CF_2D$ would be used in the n.m.r. and mass spectral methods.

[49] P. E. Aldrich, E. G. Howard, W. J. Linn, W. J. Middleton, and W. H. Sharkey, *J. Org. Chem.*, **28**, 184 (1963).

III$_D$ gave a CF$_3$ doublet ($J_{CF_3-F}$ 11, $J_{DF} \cong 1$ c.p.s.) and a C–F septet of triplets ($J_{F-CF_3}$ 11 c.p.s.). A mixture of III$_H$–III$_D$ showed an upfield shift of 0.44 and 0.04 p.p.m. for the CF and CF$_3$ in III$_D$, respectively, relative to III$_H$. The H$^1$ n.m.r. spectrum showed a doublet of septets ($J_{HF}$ 44.5, $J_{H-CF_3}$ 5.1 c.p.s.) centered at 6.0 $\tau$ (ext. ref.).

**Tris(trifluoromethyl)methane-*d* (IV$_H$ and IV$_D$).**—Tris(trifluoromethyl)methane was prepared by the addition of hydrogen fluoride to perfluoroisobutylene in the presence of potassium fluoride under pressure.[14b] *Note: perfluoroisobutylene is extremely toxic even at levels of <1 p.p.m. Suitable precautions should be observed during its use.* After purification to >99% by vapor phase chromatography, the F$^{19}$ n.m.r. spectrum showed a doublet ($J$ 7 c.p.s.) at +64.5 p.p.m. from fluorotrichloromethane while the proton n.m.r. spectrum showed a symmetrical decet ($J$ 7 c.p.s.) centered at 6.74 $\tau$. To prepare IV$_D$, deuterium fluoride was prepared *in situ* in the following manner. Under dry nitrogen, 1.0 g. of potassium fluoride and 3.0 g. (0.15 mole) of deuterium oxide were added to a 240-ml. Hastelloy pressure vessel which was then sealed, cooled in Dry Ice, and evacuated. Then, 11.0 g. (0.17 mole) of carbonyl fluoride[14a] was added and the vessel was heated to 50° for 0.5 hr. and cooled to −70°. Most of the resulting carbon dioxide was removed by evacuating the vessel to 200 mm. Twenty grams (0.1 mole) of perfluoroisobutylene was added, and the mixture was heated at 200° for 20 hr. The volatile product (24 g.) contained unreacted starting materials and was purified by preparative vapor phase chromatography to obtain 10 g. of >99% pure IV$_D$ which was 95% deuterated by mass spectral and infrared analyses. The F$^{19}$ n.m.r. pattern showed an equal intensity triplet ($J_{DF}$ 1 c.p.s.) at +64.5 p.p.m. from fluorotrichloromethane. Mixtures of IV$_H$ and IV$_D$ showed an upfield shift of 0.085 p.p.m. of the CF$_3$ resonance in IV$_D$.

**9-Tritiofluorene.**—In a modification of a procedure for 9-deuteriofluorene,[40b] 16.6 g. (0.1 mole) of fluorene, 5.61 g. (0.1 mole) of potassium hydroxide, and 1.0 g. (0.056 mole, 250 μc.) of tritiated water in 50 ml. of ethylene glycol dimethyl ether were refluxed under dry nitrogen for 10 hr. A pale red color appeared after 5 min. but changed to pale green after 1 hr. The mixture was not homogeneous even after 1 hr. of reflux. After the work-up described,[40b] 14.0 g. of 9-tritiofluorene was obtained. Radioactive assay by scintillation counting[46] gave a level of 73.4 μc./g.

**Kinetics. Method A. Gases.**—Since systems I$_H$, I$_D$, III$_H$, III$_D$, IV$_H$, and IV$_D$ are all gases, each sample for a series of points in a kinetic run had to be prepared separately in a sealed n.m.r. tube. Thus, each kinetic point was a separate run and was subject to individual volumetric or weighing and sampling errors as well as the normal analytical errors. A typical kinetic run is described for III$_H$. In a dry nitrogen atmosphere, a solution of 0.04082 g. of sodium methoxide in 10.0 g. of methanol-O-*d* (Merck Sharp and Dohme of Canada, Ltd.) was prepared. A reproducible volume (0.3 ml.) of this solution was placed in each of 20 flamed-out n.m.r. tubes using a microliter gas tight syringe with a Chaney adaptor (No. 1750 NCH, Hamilton Co., Inc., Whittier, Calif.). Periodic tares served to check reproducibility; *e.g.*, 0.2493 g. of solution in one tube, 0.2497 g. in another. Each tube was placed on a vacuum manifold, cooled in liquid nitrogen, and evacuated. Each tube was then charged with a gas sample of III$_H$ from a 23.0-ml. bulb filled to 250 mm. with III$_H$ and, finally, the tube was sealed under vacuum. Periodic tares again checked reproducibility: tube 1, 0.0483 g. of III$_H$; tube 2, 0.0494 g. of III$_H$. The tubes, in this case, were warmed to about −30°, agitated briefly to effect mixing, and immersed in a bath at 20.0 ± 0.05°, reserving one tube cooled in liquid nitrogen as an actual zero. Another zero point taken after 2-min. equilibration in the bath was the same as the actual zero. Samples in this case were withdrawn every 5 min. and plunged into liquid nitrogen. Each frozen sample was then opened in a dry nitrogen atmosphere, *ca.* 0.03 ml. of acetic acid was added, and the sample was resealed and allowed to warm to room temperature with shaking. (For the most reactive system IV, the lower melting propionic acid was used in place of acetic acid.) The n.m.r. analyses were then carried out (in most cases) and finally each sample was analyzed in duplicate by mass spectra on both the vapor and the liquid. No significant differences between vapor and liquid analyses were noted. Analyses were checked using known isotopic mixtures throughout the concentration ranges involved. The base concentrations were checked titrimetrically by preparing large volumes of the solutions (with fluorocarbon) at 0–20°. It was unnecessary to acidify the least reactive systems (I and II).

A semilog plot against time of the hydrogen content (*vs.* deuterium) minus the infinity value gave, generally, an excellent straight line, particularly in view of the separate sampling errors involved in each individual point. Generally, pseudo-first-order rate constants were calculated at each point for long time intervals using the expression $k = 2.303/t \log \frac{C_\infty - C_0}{C_\infty - C}$, and the average value taken. A sample is given in Table II. Slight decreasing trends (<10% over 75% reaction) generally were noted only at high concentrations of base (>0.25 $M$) and substrate (>1 $M$).

**Method B (II$_H$ and II$_D$).**—A typical procedure is given for II$_H$. A solution of 0.0818 g. (0.00151 mole) of sodium methoxide in 5.00 g. of methanol and 5.60 g. (0.0151 mole) of II$_H$ was prepared in a dry box containing a dry nitrogen atmosphere; *ca.* 0.3–0.5 ml. of this solution was placed in each of 20 dry n.m.r. tubes which were then sealed and immersed in a constant temperature bath maintained at 70.0 ± 0.05°. Samples in this case were withdrawn and cooled in Dry Ice every 45 min. leaving one in for an infinity point. Base concentrations were checked titrimetrically on larger volumes of solution. The tubes were warmed to 0–20° briefly for n.m.r. analyses and then recooled in Dry Ice until opened for mass spectral analyses.

TABLE II

KINETIC DATA FOR THE EXCHANGE OF 2-HYDROHEPTAFLUOROPROPANE IN SODIUM METHOXIDE–METHANOL-O-*d* SOLUTION AT 20.0 ± 0.05° (RUN 15, TABLE I)

| $t$, sec. | Mole % R$_f$H | $10^4k$,[a] sec.$^{-1}$ |
|---|---|---|
| 0 | 100.0 | |
| 900 | 85.9, 86.2 | 1.77 |
| 1200 | 81.9, 81.7 | 1.79 |
| 1500 | 77.1, 77.2 | 1.85 |
| 2100 | 69.8, 69.9 | 1.83 |
| 2400 | 67.2, 67.0 | 1.79 |
| 2700 | 63.9, 63.7 | 1.79 |
| 3000 | 59.4, 59.4 | 1.88 |
| 3300 | 58.8, 58.1 | 1.76 |
| 3600 | 53.3, 53.7 | 1.89 |
| 4200 | 49.6, 49.6 | 1.82 |
| 4500 | 46.8, 47.0 | 1.84 |
| 4800 | 44.2, 43.8 | 1.88 |
| 5100 | 42.4, 42.3 | 1.85 |
| 5400 | 41.2, 41.2 | 1.81 |
| 5700 | 39.4, 39.4 | 1.81 |
| 6300 | 36.2, 36.5 | 1.78 |
| 28,800 | 5.7, 5.7 | . . |
| | | 1.82 ± 0.03 |

[a] Calculated for long time intervals using the first-order expression $k = \frac{2.303}{t} \log \frac{C_\infty - C_0}{C_\infty - C}$. The same average $k$ is obtained with the short interval method.

**Method C. Radioactive Runs (II$_D$–II$_T$).**—Since isolation of pure substrate was required in the radioactive exchanges, a sample procedure is outlined. A solution of 0.1636 g. (0.00303 mole) of sodium methoxide and 11.20 g. (0.0302 mole) of II$_D$–II$_T$ (as synthesized above, 14.13 μc./g.) in 10.31 g. of methanol was prepared, divided among eleven sealed tubes, and treated as described in method B. Tubes were withdrawn and cooled in Dry Ice every 6 hr. except for an infinity point. After neutralization with acetic acid, a pure sample of II$_D$–II$_T$ was isolated from each tube by preparative vapor phase chromatography (*vide supra*). Each sample was then analyzed by scintillation counting and mass spectra for tritium and deuterium, respectively. Sample data are given in Table III. $k_T$ shows no drift while a slight drift (<4% over 50% reaction) in $k_D$ may be noted. The slight drift in $k_D$, therefore, is probably due to a combination of factors: (a) the accumulation of large amounts of deuterium label in the solvent at increasing extents of reaction, and (b) a constant error in ($C_\infty - C$) becomes an increasing error in the log ($C_\infty - C_0/C_\infty - C$).

**Rate of Exchange of 9-Tritiofluorene.**—In an atmosphere of dry nitrogen, 0.4090 g. (0.00757 mole) of sodium methoxide and

TABLE III

KINETIC DATA FOR THE SIMULTANEOUS EXCHANGE OF TRITIUM AND DEUTERIUM IN $II_T$ AND $II_D$ IN SODIUM METHOXIDE–METHANOL SOLUTION AT 70.0 ± 0.05°

| Time, sec. | Radioactivity, c./min.-mg.[a] | Mole % $II_D$ | $10^6 k_T$ | $10^6 k_D$ |
|---|---|---|---|---|
| 0 | 4614 | 88.6 | .. | .. |
| 64,500 | 3894 | 70.1 | 2.85 | 4.02 |
| 86,640 | 3722 | 65.1 | 2.70 | 3.96 |
| 108,960 | 3401 | 59.9 | 3.06 | 4.02 |
| 129,960 | 3258 | 55.6 | 2.93 | 4.03 |
| 151,140 | 3135 | 52.7 | 2.80 | 3.88 |
| 172,800 | 2942 | 49.2 | 2.86 | 3.86 |
| 194,580 | 2732 | 46.1 | 2.97 | 3.82 |
| 216,060 | 2658 | 42.9 | 2.82 | 3.85 |
| 1,670,400 | 331 | 9.4 | .. | .. |
| | | | 2.87 ± 0.08 | 3.98 ± 0.11 |

[a] Efficiency = 12.31%; actual counting level was 20–40 times higher.

2.7660 g. (0.0166 mole) of 9-tritiofluorene (prepared as described above) was diluted to 200 ml. in a volumetric flask. The solution was divided among ten sealed Pyrex vessels, and maintained at 69.3 ± 0.05° as described in method C, withdrawing samples every hour. Each sample was worked up by adding the red mixture to 30 ml. of water and 30 ml. of ether and washing the ether layer with 30-ml. portions of water until washings were no longer basic. The ether solution was then dried over anhydrous sodium sulfate, filtered, and evaporated to dryness in a stream of dry nitrogen. After recrystallization from 3–5 ml. of ethanol, each sample was dried at 50° under vacuum, and finally analyzed by scintillation counting.[46]

**Trapping Experiments: 1,1,1,2,2,3,3-heptafluoro-4-hexanol from 1-Hydroheptafluoropropane.**—To 38 g. (0.22 mole) of 1-hydroheptafluoropropane (prepared from perfluorobutyric acid[18]) in 120 ml. of dry ether cooled to −40° in an atmosphere of dry nitrogen was added simultaneously with rapid stirring over a period of 40 min., 120 ml. of a 0.2 *M* solution of methyllithium in ether (Foote Mineral Co., Exton, Pa.) and 23 g. (0.4 mole) of freshly distilled propionaldehyde in 120 ml. of ether; *ca.* 2 l. of methane evolved through a condenser cooled to −80°. After allowing the mixture to warm to 20° over *ca.* 2 hr., the solution was neutralized with 3 *N* sulfuric acid. The ether layer was separated, washed once with 30 ml. of water, and dried over sodium sulfate. Distillation after removal of the ether gave fraction 1, b.p. 35–80°; fraction 2, 9 g., b.p. 80–103°; and fraction 3, 5 g., b.p. 103–112°; leaving a residue of 7 g. Although fractions 2 and 3 were largely 2-butanol (7.7-min. v.p.c. peak), vapor phase chromatography[46] indicated they were *ca.* 10 and 15%, respectively, of the fluorinated hexanol. The product hexanol was isolated by preparative vapor phase chromatography.[46] The infrared spectrum, v.p.c. retention time (25.6 min.) and b.p. of this product was identical with that of an authentic sample of 1,1,1,2,2,3,3-heptafluoro-4-hexanol prepared from heptafluoro-*n*-propyl iodide.[45c]

**1,1,1,2-Tetrafluoro-2-trifluoromethyl-3-pentanol from 2-Hydroheptafluoropropane.**—In a manner similar to that described in the previous experiment, methyllithium and propionaldehyde were added to 2-hydroheptafluoropropane in ether at −70°. After the usual work-up, 13 g., b.p. 88–115°, containing *ca.* 15% of the fluorinated hexanol and 85% 2-butanol was obtained. The hexanol was isolated by preparative vapor phase chromatography[46] as above (23.0-min. peak) and found to be identical in the infrared spectrum, boiling point, and v.p.c. retention time with an authentic sample prepared from heptafluoroisopropyl iodide.[45c]

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# Chemistry of Aliphatic Disulfides. VI. Effect of α-Alkylation on the Cyanide Cleavage of Unsymmetrical Disulfides[1,2]

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The cyanide cleavage of several α-alkylated unsymmetrical disulfides of the type $RS-SCH_2CO_2CH_3$ have been studied to determine the nature of the equilibria between the disulfide and the primary cleavage products. Cyanide cleavage in the presence of N,N-diphenylcarbamyl chloride (DPCC) has been found to be a thermodynamically controlled reaction involving the unsymmetrical disulfide and the four primary cleavage products. The reactivity of the disulfide toward cyanide ion decreases as R is changed from isobutyl to isopropyl to *t*-butyl.

In previous experiments[4] the cyanide ion cleavage of methyl 4-phenyl-3,4-dithiabutanoate (I) was found to provide the four possible primary cleavage products II–IV as predicted[5] from the "$\Delta pK_a$" value of I (1.28). The more stable primary cleavage products sodium thiophenoxide (II) and methyl thiocyanoacetate (III) predominated over sodium carbomethoxymethyl mercaptide (IV) and phenyl thiocyanate (V). The cleavage of I was conducted in the presence of a single equivalent of N,N-diphenylcarbamyl chloride (DPCC) and the mercaptides were obtained as the N,N-diphenylcarbamate derivatives VI and VII.

However, when either II and III or IV and V were allowed to react in the presence of DPCC the same mixture of products as that obtained from the cyanide cleavage of I resulted. Thus it was concluded[4] that the products obtained from the cleavage of I, as well as the products obtained from the previous cleavage reactions[5] involving DPCC, resulted from thermodynamic control of the cleavage reaction.

These results are consistent with at least two mechanisms. Attack of cyanide ion on I would provide the primary cleavage products in either case. The primary cleavage products could then equilibrate *via* either: (a) the unsymmetrical disulfide by attack of the mercaptide on the sulfur atom of the thiocyanate (Fig. 1), or (b) nucleophilic addition of the mercaptide to the carbon atom of the thiocyanate to yield the intermediate VIII (Fig. 2). Decomposition of VIII would be expected to provide an excess of the mercaptide of greater anionic stability, in this case II,

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[2] Part V of this series R. G. Hiskey and W. P. Tucker, *J. Am. Chem. Soc.*, **84**, 4794 (1962).

[3] Abstracted in part from a thesis submitted by W. H. Bowers to the University of North Carolina in partial fulfillment of the requirements for the M.S. Degree, June, 1962.

[4] R. G. Hiskey and F. I. Carroll, *J. Am. Chem. Soc.*, **83**, 4647 (1961).

[5] R. G. Hiskey and F. I. Carroll, *ibid.*, **83**, 4644 (1961).