

308. *Nucleophilic Displacement of Fluorine from Organic Compounds. Part II.* Kinetics of the Reactions of Alkyl Fluorides with Ethanolic Sodium Ethoxide.*

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With ethanolic sodium ethoxide primary alkyl fluorides undergo almost exclusively substitution, at rates 10^3 — 10^4 times smaller than those for the corresponding bromides. The reactions of primary fluorides and bromides differ little in energy of activation, the lower rates with the fluorides being due to low values of A . Both these facts are probably connected with a highly solvated transition state for fluorides. Secondary and tertiary fluorides undergo a predominating elimination at rates 10^5 — 10^6 times smaller than those for the corresponding bromides. The reactions of tertiary fluorides are characterised by increased energy of activation and diminished values of A relatively to bromides. The influence of structure of the alkyl group on the rates of substitution and elimination is roughly parallel for bromides and fluorides, but for fluorides the proportion of elimination decreases with increasing temperature, whereas the opposite is true for bromides.

IN Part I* of this series one of us discussed the ready displacement of fluorine from 1-fluoro-2:4-dinitrobenzene by weakly nucleophilic reagents. We now turn to alkyl fluorides where much more vigorous conditions are necessary to displace the fluorine. The reactions with nucleophilic reagents of alkyl halides other than fluorides have been extensively investigated during the last two decades: our object is to provide comparable results for alkyl fluorides and to elucidate the causes of their inertness.

The remarkable resistance of alkyl fluorides to alkaline hydrolysis has been known for some years (Swarts, *Bull. Acad. roy. Belg.*, 1921, 7, 438; Bockemüller, *Annalen*, 1933, 506, 25). Even secondary and tertiary alkyl fluorides, although often thermally unstable, display a relatively high stability towards alkali in solution. Recently Hoffmann (*J. Org. Chem.*, 1950, 15, 429) has studied quantitatively the reactions of ω -bromo- ω -fluoro- and $\omega\omega'$ -difluoro-alkanes with results confirming the difficulty of displacement of the fluorine.

There have been, however, very few kinetic studies. Cooper and Hughes (*J.*, 1937, 1183) briefly record the rate of hydrolysis of *tert.*-butyl fluoride—about 1000 times slower than that of the chloride. McCabe and Warner (*J. Amer. Chem. Soc.*, 1948, 70, 4031) report the relatively slow bimolecular hydrolysis of fluoroethanol by hydroxyl ions and by water; and Bernstein and Miller (*J. Amer. Chem. Soc.*, 1948, 70, 2312, 3600) report the bimolecular reactions of a series of substituted benzyl fluorides with ethanolic sodium ethoxide and with aqueous ethanol. Also the kinetics of the reactions of 2-fluorohexane and *sec.*-amyl fluoride with sodium iodide in acetone have been studied by Bergmann, Polanyi, and Szabo (*Trans. Faraday Soc.*, 1936, 32, 843). In all these reactions the fluoro-compounds reacted much more slowly than the corresponding chlorides. We now present the results of a systematic investigation of the kinetics of the reactions of primary, secondary, and tertiary alkyl fluorides, mainly fluorobutanes and fluoropentanes, with ethanolic sodium ethoxide. These have been chosen because they can be prepared from accessible starting materials, because, being liquids—lower alkyl fluorides are gases—they can, for the most part, be suitably purified by fractional distillation, and because the reactions of several of the corresponding bromides and chlorides have been carefully studied.

EXPERIMENTAL

Materials.—Alkyl fluorides were prepared (a) by the action of an alkyl bromide on potassium fluoride dissolved in ethylene glycol (Hoffman, *J. Org. Chem.*, 1950, 15, 430) or (b) by addition of anhydrous hydrogen fluoride to an olefin (McElvain and Langston, *J. Amer. Chem. Soc.*, 1944, 66, 1759). Method (b) was used for secondary and tertiary fluorides, and method (a) mainly

* Part I, *J.*, 1951, 3301.

for primary fluorides. In (a) the initial alcohols and bromides, and the final fluorides, were carefully fractionated through a 50-cm. Fenske column, the main fraction having a boiling range of less than 0.2°. Three samples of *n*-amyl alcohol were used: (i) *n*-amyl alcohol (at least 85% pure) from British Drug Houses Ltd., (ii) synthetic *n*-amyl alcohol from Messrs. Boots, and (iii) a sample prepared by the action of formaldehyde on *n*-butylmagnesium bromide. The physical properties of these and other fluorides are assembled in Table 1.

The olefins required for method (b) were prepared by dehydration of the corresponding alcohol, except for cyclohexene which was purchased from British Drug Houses Ltd. *tert.*-Amyl alcohol was dehydrated by warming it with dilute sulphuric acid, and *tert.*-butyl and *n*-amyl alcohol were dehydrated by passing the vapour over activated alumina at 200–300°.

*cyclo*Hexyl and *tert.*-amyl fluoride were distilled at reduced pressures to avoid thermal decomposition.

The ethanol used as solvent was dried by Lund and Bjerrum's method (*Ber.*, 1931, 64, 210) and fractionated. It was shown to contain between 0.04 and 0.07% of water by Karl Fischer

TABLE 1.

| Compound | B. p./mm. | B. p. range | n_D^{20} | n_D^{25} |
|--------------------------------------|------------|-------------|------------------|------------|
| <i>n</i> -Amyl fluoride (i) | 64.2°/761 | 0.2° | 1.3590 | — |
| " (ii) | 64.2°/754 | 0.03 | 1.3593 | 1.3569 |
| " (iii) | 64.0°/750 | 0.00 | 1.3593 | 1.3570 |
| <i>n</i> -Butyl fluoride | 32.2°/755 | 0.05 | — | — |
| 2-Methyl- <i>n</i> -butyl fluoride * | 56.2°/577 | 0.10 | 1.3570 | 1.3542 |
| <i>iso</i> Amyl fluoride | 56.1°/757 | 0.10 | 1.3572 | 1.3547 |
| <i>sec.</i> -Amyl fluoride (i) | 56.2°/756 | 0.15 | 1.3578 | 1.3550 |
| " (ii) | 56.3°/738 | 0.2 | 1.3588 | — |
| <i>sec.</i> -Butyl fluoride | 24.7°/765 | 0.3 | — | — |
| <i>cyclo</i> Hexyl fluoride | 43.2°/100 | 0.2 | 1.4149 | 1.4123 |
| <i>tert.</i> -Butyl fluoride | Unobserved | — | 1.3320 (1.5° c.) | — |
| <i>tert.</i> -Amyl fluoride | 22.0°/300 | 0.2 | 1.3481 | — |

* $[\alpha]_D^{0^\circ}$.

TABLE 2.

n-Amyl fluoride at 120.0°. Initial NaOEt = 1.017M; initial n -C₅H₁₁F = 0.877M. Concns. are expressed in ml. of 0.3700N-HCl per 4.07 ml. of reacting solution.

| | | | | | | | | |
|---------------------------------------|-------|-------|------|------|------|------|-------|-------|
| Time (secs.) × 10 ⁻⁴ | 0.00 | 0.80 | 1.81 | 2.60 | 4.47 | 6.86 | 10.09 | 18.36 |
| NaOEt | 11.20 | 10.18 | 9.29 | 8.63 | 7.54 | 6.55 | 5.76 | 4.34 |
| n -C ₅ H ₁₁ F | 9.66 | 8.64 | 7.75 | 7.09 | 6.00 | 5.01 | 4.22 | 2.80 |
| 10% k | — | 1.43 | 1.32 | 1.33 | 1.28 | 1.25 | 1.16 | 1.13 |

Mean $k = (1.27 \pm 0.08) \times 10^{-5}$. Corr. for solvent expansion, $k = (1.45 \pm 0.09) \times 10^{-5}$.

With initial NaOEt = 0.539M and initial n -C₅H₁₁F = 0.432M, mean $k = (1.26 \pm 0.02) \times 10^{-5}$. Corr. for solvent expansion, $k = (1.44 \pm 0.02) \times 10^{-5}$.

*cyclo*Hexyl fluoride at 139.1°. Initial NaOEt = 1.092M; initial C₆H₁₁F = 0.889M.

| | | | | | | | |
|----------------------------------|-------|-------|-------|-------|-------|-------|-------|
| Time (secs.) × 10 ⁻⁴ | 0.00 | 10.28 | 17.81 | 25.40 | 34.26 | 44.16 | 58.55 |
| NaOEt | 12.02 | 10.45 | 9.59 | 8.85 | 8.20 | 7.66 | 6.67 |
| C ₆ H ₁₁ F | 9.89 | 8.32 | 7.46 | 6.72 | 6.07 | 5.53 | 4.54 |
| 10% k | — | 1.66 | 1.63 | 1.64 | 1.60 | 1.55 | 1.67 |

Mean $k = (1.63 \pm 0.03) \times 10^{-6}$. Corr. for solvent expansion, $k = (1.95 \pm 0.04) \times 10^{-6}$.

tert.-Amyl fluoride at 119.7°. Initial NaOEt = 1.000M; initial *tert.*-C₅H₁₁F = 1.149M.

| | | | | | | | |
|--|-------|-------|-------|-------|-------|-------|-------|
| Time (secs.) × 10 ⁻⁴ | 0.00 | 5.47 | 9.27 | 14.28 | 22.88 | 32.57 | 46.35 |
| NaOEt | 12.62 | 11.86 | 11.51 | 10.95 | 10.08 | 9.59 | 8.58 |
| <i>tert.</i> -C ₅ H ₁₁ F | 10.98 | 10.22 | 9.87 | 9.31 | 8.44 | 7.95 | 6.94 |
| 10% k | — | 1.22 | 1.07 | 1.10 | 1.14 | 1.01 | 1.06 |

Mean $k = (1.11 \pm 0.06) \times 10^{-6}$. Corr. for solvent expansion, $k = (1.27 \pm 0.06) \times 10^{-6}$.

n-Butyl fluoride at 89.8°. Initial NaOEt = 1.141M; initial BuⁿF = 0.853M. (Concns. in ml. of 0.3710N-HCl per 4.07 ml.)

| | | | | | | | | |
|---------------------------------|-------|-------|-------|-------|-------|-------|-------|-------|
| Time (secs.) × 10 ⁻⁴ | 0.00 | 6.62 | 15.32 | 24.06 | 30.98 | 39.93 | 50.27 | 60.07 |
| NaOEt | 12.53 | 11.64 | 10.73 | 9.96 | 9.46 | 8.97 | 8.41 | 8.07 |
| Bu ⁿ F | 9.36 | 8.47 | 6.56 | 6.79 | 6.29 | 5.80 | 5.24 | 4.90 |
| 10% k | — | 1.39 | 1.33 | 1.32 | 1.31 | 1.26 | 1.25 | 1.20 |

Mean $k = (1.29 \pm 0.05) \times 10^{-6}$. Corr. for solvent expansion, $k = (1.41 \pm 0.05) \times 10^{-6}$.

titration. Ethanolic sodium ethoxide was prepared by dissolving clean sodium in ethanol purified as above.

Procedure.—Aliquot portions, usually 4.07 ml., of a standard solution of an alkyl fluoride and sodium ethoxide in anhydrous ethanol were enclosed in "Pyrex" tubes having a minimum vapour space. After being heated in a thermostat for a suitable time, the mixture was added to an excess of standard hydrochloric acid which was back-titrated potentiometrically with standard sodium hydroxide, a quinhydrone electrode and silver-silver chloride half-cell being used. It was shown that the end-point in acid-alkali titrations was not sensibly affected by molar concentrations of sodium fluoride. Olefins were estimated by the extraction method of Hughes and Ingold (*J.*, 1940, 910), but carbon tetrachloride was used as solvent in place of chloroform. Second-order rate coefficients were evaluated by using the equation $k = \frac{1}{(a-b)t} \ln \frac{b}{a} \cdot \frac{a-x}{b-x}$, where a = initial [NaOEt], b = initial [fluoride], x = moles of fluoride consumed, and t = time, rate coefficients being given in l. mole⁻¹ sec.⁻¹. The mean deviation from the mean is quoted after the mean rate coefficient. Table 2 shows examples, and all the results are collected in Table 3.

TABLE 3.

| Compound | Temp. | 10 ⁴ k | Mean deviation, Olefin, | | Compound | Temp. | 10 ⁴ k | Mean deviation, Olefin, | |
|-------------------------------|--------|-------------------|-------------------------|-----|--|--------|-------------------|-------------------------|------|
| | | | % | % | | | | % | % |
| <i>n</i> -Amyl fluoride (i) | 119.0° | 12.9 | 7.1 | — | 2-Methyl- <i>n</i> -butyl fluoride | 120.8° | 3.3 | 13 | 10 |
| " | 119.0 | 13.5 | 7.1 | — | | | | | |
| " | 89.8 | 1.25 | 4.3 | — | " " | 120.8 | 3.7 | 14 | — |
| " | 89.8 | 1.18 | 6.3 | — | " " | 100.0 | 0.89 | 15 | — |
| <i>n</i> -Amyl fluoride (ii) | 138.6 | 59.5 | 6.4 | — | " " | 89.8 | 0.33 | 23 | — |
| " | 120.9 | 16.0 | 6.5 | — | " " | 138.6 | — | — | 7.5 |
| " | 120.0 | 14.5 | 6.2 | 1.3 | <i>cyclo</i> Hexyl fluoride ... | 161.7 | 10.5 | 5.2 | 80.3 |
| " | 89.8 | 1.44 | 3.1 | 0.5 | " " | 160.8 | 10.0 | 8.3 | 75 |
| " | 89.8 | 1.39 | 3.2 | — | " " | 147.8 | 3.96 | 5.0 | — |
| " | 79.8 | 0.563 | 2.4 | 2.1 | " " | 139.1 | 1.95 | 2.1 | 90 |
| <i>n</i> -Amyl fluoride (iii) | 120.2 | 14.8 | 3.6 | — | " " | 138.3 | 1.92 | 2.2 | 94 |
| " | 89.8 | 1.40 | 2.4 | — | <i>sec.</i> -Amyl fluoride (i) | 139.1 | 3.9 | 12 | 83 |
| " | 79.8 | 0.578 | 3.4 | — | <i>sec.</i> -Amyl fluoride (ii) | 161.7 | 19 | 12 | 60 |
| <i>n</i> -Butyl fluoride ... | 120.8 | 15.1 | 3.8 | — | " " | 138.4 | 3.4 | 7.6 | 82 |
| " | 120.8 | 15.5 | 3.4 | — | <i>sec.</i> -Butyl fluoride ... | 120.0 | 0.94 | 4.4 | 71 |
| " | 104.9 | 4.54 | 4.4 | — | <i>tert.</i> -Butyl fluoride ... | 118.5 | 1.46 | 6.9 | 95 |
| " | 89.8 | 1.43 | 3.4 | — | " " | 138.5 | 6.9 | 7.8 | 96 |
| " | 89.8 | 1.41 | 3.8 | — | <i>tert.</i> -Amyl fluoride ... | 119.7 | 1.27 | 5.2 | 95 |
| <i>iso</i> Amyl fluoride ... | 119.0 | 4.3 | 15 | 12 | " " | 139.7 | 5.8 | 4.9 | 89 |
| " | 119.0 | 5.3 | 5.3 | — | | | | | |
| " | 119.0 | 5.0 | 5.1 | — | | | | | |
| " | 89.8 | 0.53 | 19 | — | | | | | |
| " | 89.8 | 0.52 | 4.2 | — | | | | | |
| " | 138.6 | — | — | 6.0 | | | | | |

DISCUSSION

The low specific rates of these reactions necessitate the use of relatively high temperatures (up to 160°) and approximately molar concentrations if the reactions are to occur with reasonable speeds. Heating molar ethanolic sodium ethoxide in "Pyrex" glass tubes at 140° for six days caused only negligible loss of alkali, possibly by very slight attack on the glass, so no difficulties arise on this account. In aqueous ethanol, however, the loss of alkali is considerable; consequently we have not been able to study these reactions in aqueous ethanolic media, although it was desirable to do so. Certain other complications, however, do arise, particularly the deviation from any integral-order rate law, especially noticeable at higher temperatures. Second-order rate coefficients tend to decrease as a reaction proceeds, more markedly at high temperatures. Nevertheless, except for 2-methyl-*n*-butyl and *iso*- and *sec.*-amyl fluoride, the mean deviation of observed values of second-order velocity coefficients at all but the highest temperatures does not often exceed 5%. We have found no evidence even with tertiary fluorides of first-order reactions under the conditions we employ. Consequently we believe the reactions studied to pursue the bimolecular mechanism found most typically with other primary halides in

reactions with ethanolic sodium ethoxide. At the higher temperatures it is possible that a significant proportion of the fluoride may be in the vapour phase. However, use of bulbs in which the "free" space was restricted to ~ 2 c.c. probably limits the amount of fluoride in the vapour phase to 3%, so no correction for this has been attempted. With *n*-amyl fluoride we took special steps to ensure that impurities were not vitiating the results: the fluoride was prepared from *n*-amyl alcohol from three sources, including a carefully purified synthetic specimen (cf. p. 1674). Two of the samples of fluoride gave virtually the same results, the third (from commercial *n*-amyl alcohol) showed slight differences, probably due to small amounts of impurities. With the other amyl fluorides, save *tert*-amyl fluoride, physical properties lie so close together that it is difficult to be certain of the purity of a given specimen; so the results with *iso*amyl and 2-methyl-*n*-butyl fluoride are of qualitative value only. With *sec*-amyl fluoride prepared by two independent methods, physical properties and rates of reaction were almost the same (Tables 1 and 3).

Table 4 summarises our results for the overall (combined substitution and elimination)

TABLE 4.

(k and A in l. mol.⁻¹ sec.⁻¹. E is accurate to ± 900 cal., A to ± 0.5 unit.)

| Alkyl | Temp. | Bromides | | Fluorides | | log A |
|---------------------------------|-------|-----------------------|---------------------|-------------|------------|---------|
| | | k^a | k^b | E (kcal.) | | |
| <i>n</i> -Amyl | 55° | 3.92×10^{-4} | 8×10^{-6} | 22.1 | 7.4 | |
| <i>n</i> -Butyl | 55 | 4.39×10^{-4} | 6×10^{-6} | 21.8 | 7.3 | |
| <i>sec</i> -Amyl | 25 | 3.43×10^{-6} | 1×10^{-11} | ~ 27 | ~ 8.7 | |
| <i>tert</i> -Amyl | 25 | 5.90×10^{-5} | 6×10^{-11} | 24.4 | 7.7 | |
| <i>tert</i> -Butyl | 25 | 3.00×10^{-5} | 6×10^{-11} | 24.8 | 8.0 | |
| <i>iso</i> Amyl | 55 | — | 2×10^{-6} | ~ 22 | ~ 6.9 | |
| 2-Methyl- <i>n</i> -butyl | 55 | — | 2×10^{-6} | ~ 21 | ~ 6.0 | |
| <i>cyclo</i> Hexyl | 55 | — | 4×10^{-10} | 26.4 | 8.2 | |

^a Except for Bu^tBr, taken from Hughes, Ingold, *et al.*, *J.*, 1948, 2038 *et seq.* ^b Extrapolated from values at higher temps. Only one significant figure is given because of the considerable extrapolation. See Table 3 for observed values.

TABLE 5. Elimination and substitution in alkyl fluorides and bromides.

(k_B is the velocity coefficient for bimolecular substitution, k_E for bimolecular elimination, in l. mole⁻¹ sec.⁻¹).

| Alkyl | Bromides at 55.0° ^a | | Fluorides at 120.0° | |
|---------------------------------|--------------------------------|------------|---------------------|--------------------|
| | $10^5 k_B$ | $10^5 k_E$ | $10^5 k_B$ | $10^5 k_E$ |
| <i>n</i> -Butyl | 39.6 | 4.3 | — | — |
| <i>n</i> -Amyl | 35.7 | 3.5 | 1.41 | 0.02 |
| <i>iso</i> Butyl | 5.8 | 8.5 | — | — |
| <i>iso</i> Amyl | — | — | 0.49 | 0.05 |
| 2-Methyl- <i>n</i> -butyl | — | — | 0.30 | 0.04 |
| <i>sec</i> -Butyl | 2.3 | 10.3^b | 0.027 | 0.067^b |
| <i>sec</i> -Amyl | 2.0 | 8.3^b | 0.014 | 0.060^b |
| <i>tert</i> -Butyl | 3 | 90^b | 0.007 | 0.139 |
| <i>tert</i> -Amyl | 6 | 177^b | 0.006 | 0.121 |
| <i>cyclo</i> Hexyl | — | — | 0.005 | 0.038 ^b |

^a Hughes, Ingold, *et al.*, *J.*, 1948, 2038 *et seq.* ^b Extrapolated from results at other temps.

reactions of alkyl fluorides with ethanolic sodium ethoxide: available overall velocity coefficients for the reactions of corresponding alkyl bromides are included. For the primary halides, where the predominating process at 55° is substitution (Table 5), the bromides react ~ 5000 — 7000 times faster than the fluorides. The most comparable value of the energy of activation is for substitution with *isobutyl* bromide, *viz.*, 23 kcal. (Hughes and Dostrovsky, *J.*, 1946, 173), and differs little from those of the primary fluorides, so that the large fall in rate of substitution is due to a fall in log A from 11.0 to ~ 7.4 . This suggests the conclusion that, as with 1-fluoro-2:4-dinitrobenzene (see Part I), in comparison with the corresponding bromides, solvation of the incipient fluoride ion in the transition state enables the reaction to pursue a course much more economical of activation energy than would otherwise be possible in view of the probable large dissociation energy of the carbon-fluorine bond. For tertiary halides the predominating reaction is elimination and the most comparable Arrhenius parameters are those for the elimination reaction of

tert.-butyl bromide (Hughes, Ingold, *et al.*, *J.*, 1948, 2050). Here again for the fluorides we observe a value of $\log A$ lower by two units than for the bromide, but the energy of activation is increased from ~ 20 to ~ 24 kcal., so that the rate ratio is even larger, *viz.*, 10^5 — 10^6 . Solvation of the incipient fluoride ion is again probably a major factor, but is apparently insufficient to reduce the energy of activation with the tertiary fluorides to a value as low as that for the bromides.

The influence of the structure of the alkyl group on the rates of substitution and elimination is roughly parallel for alkyl fluorides and bromides (Table 5). The features common to bromides and fluorides are those already well-known (Hughes, Ingold, *et al.*, *J.*, 1948, 2093), but there is one exception. With fluorides the rate of elimination is much less sensitive to alkyl structure than is the rate of substitution (Table 5). This difference in sensitivity does not seem so marked with bromides, but the rates of bimolecular substitution for tertiary bromides are only available as upper limits, so we pursue this point no further. With secondary fluorides, the predominating process is elimination, but the overall rates are less than for either tertiary or primary fluorides, so that we find for elimination the rate sequence primary < secondary < tertiary, and *vice versa* for substitution. Also, although our olefin determinations are subject to considerable uncertainty, Table 3 shows that the olefin proportions tend to decrease with increasing temperature, in notable contrast with the bromides where there is an increase.

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