624. *Kinetics of the Demethylation of Some Fluorophenyltrimethylammonium Iodides by Sodium Methoxide in Absolute Methanol.*

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The kinetics of the demethylation of R-phenyltrimethylammonium iodides by sodium methoxide in absolute methanol has been studied where R is *o*-F, *m*-F, *p*-F, H, and *p*-Me. Arrhenius parameters are recorded and the polar influences of the fluoro-group are discussed.

WHILE investigating the influence of various groups on aromatic nucleophilic replacement it was found that when the three isomeric fluorophenyltrimethylammonium iodides react with methoxide ion the result is demethylation and not replacement of fluorine.[1] Rate constants and Arrhenius parameters ($k_2 = B \exp -E/\boldsymbol{R}T$) are assembled in Tables 1 and 5.

TABLE 1. *Rate constants at* 80·91° *and Arrhenius parameters for aryltrimethylammonium iodides and sodium methoxide.*

Aryl	10^4k_2 (l. sec.$^{-1}$ mole^{-1})	E (kcal. mole^{-1})	$10^{-16}B$ (l. sec.$^{-1}$ mole^{-1})	Relative rates
o-C_6H_4F	53·0	30·51	3·6	12·1
m-C_6H_4F	17·1	31·76	6·8	3·90
p-C_6H_4F	7·74	32·55	9·5	1·76
Ph	4·39	32·70	6·7	1·00
p-C_6H_4Me	2·67	33·33	9·8	0·61

TABLE 2. *Effect of variation of initial concentrations of the reactants on second-order rate constants.*
Reaction between m-*fluorophenyltrimethylammonium iodide and sodium methoxide at* 80·91°.

Ionic strength	0·060	0·060	0·082	0·117
Initial molarities (approx.):				
[NaOMe]	0·040	0·020	0·041	0·080
[Halide]	0·020	0·040	0·041	0·037
10^3k_2 (l. sec.$^{-1}$ mole^{-1})	1·71	1·71	1·38	1·25

The reactions are of the type investigated some time ago by Hughes, Ingold, and their collaborators,[2] and second-order kinetics were established in the usual way (cf. Experimental section and Table 2). Activation energies are ~10 kcal. mole^{-1} and frequency

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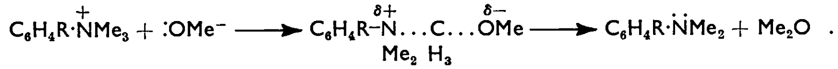
[1] Bunnett, Noble, Ryason, Tonkin, and Zahler, *J. Amer. Chem. Soc.*, 1953, **75**, 642; Bye, Ph.D. Thesis, London, 1954.

[2] *E.g.*, Hughes, Ingold, and Patel, *J.*, 1933, 526.

factors ~10^5 times greater than values for a reaction between an ion and a neutral molecule; these effects and the sensitivity to ionic strength of the medium would be expected

$$-C_6H_4F{\cdot}NMe_3{}^+I^- + OMe^- \longrightarrow C_6H_4F{\cdot}NMe_2 + Me_2O + I^- \quad . \; . \; . \; . \; . \; . \quad (1)$$

(cf. Frost and Pearson [3]) since the reaction involves the formation of a neutral transition state from two ions, as in (2) :



$$C_6H_4R{\cdot}\overset{+}{N}Me_3 + {:}OMe^- \longrightarrow C_6H_4R{-}\underset{Me_2}{\overset{\delta+}{N}}\ldots\underset{H_3}{C}\ldots\overset{\delta-}{O}Me \longrightarrow C_6H_4R{\cdot}\ddot{N}Me_2 + Me_2O \quad . \; . \quad (2)$$

In support of this mechanism the electron-releasing methyl group retards the reaction. It is reasonable to assume that from all three positions fluorine facilitates the reaction by electron-attraction. The possible electronic effects of fluorine which reach the quaternary nitrogen atom by an inductive displacement in the bond which links it to the phenyl nucleus are as follows: (1) A combined inductive and inductomeric effect damped in the usual way by passage along the carbon skeleton.[4] (2) An inductive development on the carbon atom linked to fluorine of a positive charge which is transmitted to the nucleus by a tautomeric mechanism with second-order relay to *meta*-positions. (3) Mesomeric release, producing negative charge at *ortho*- and *para*-positions with again second-order relay to *meta*-positions. This effect will be more important in the ground than in the transition state where the positive nitrogen is partially neutralised (cf. Baker and Hopkins: $+E$ effect [5]). (4) The fluorine atom exerts a field effect,[6] consequent on the small degree of screening of the fluorine nucleus, and this would produce positive charges decreasing in the order *ortho* > *meta* > *para*.

From the results it may be inferred that the electron-attracting power of fluorine falls off progressively as it is moved further away from the seat of reaction, as it would if only effects (1) and/or (4) operated. Evidently effect (2) is approximately cancelled by effect (3), for if the former predominated the sequence of activating power on the basis of reaction rates would be *o*-F > *p*-F > *m*-F or even *o*-F ~ *p*-F > *m*-F, but not the observed clear-cut sequence *o*-F > *m*-F > *p*-F. It seems reasonable to assume that effect (1) will become less intense by a constant factor after transmission through each bond. Therefore if, as Roberts and his collaborators suggested,[7] effect (2) does not exist and effect (1) operates alone, then the ratio $k_{o\text{-F}}/k_{m\text{-F}}$ should be equal to $k_{m\text{-F}}/k_{p\text{-F}}$. The existence of the mesomeric effect (3) makes this impossible since it will reduce the reactivity at the *ortho*- and *para*-positions by about the same amount and affect the *meta*-position to a smaller extent; therefore the ratio $k_{o\text{-F}}/k_{m\text{-F}}$ should be less than the ratio $k_{m\text{-F}}/k_{p\text{-F}}$. In fact in these reactions the former ratio at 80·91° ($53{\cdot}0/17{\cdot}1 = 3{\cdot}10$) is greater than the latter ($17{\cdot}1/7{\cdot}74 = 2{\cdot}21$), indicating that the *para*-position is more activated than would be expected on the basis of effects (1) and (3) only, acting in competition, and therefore that the inductive effect is, in part, transmitted by a conjugative mechanism.

Alternatively, as suggested by Ingold,[6] these results may be explained as due to the existence of a short-range field effect exerted by the fluorine atom which would have a greater influence on the reaction rate in *o*-fluorophenyltrimethylammonium iodide than in the *m*- and *p*-isomers and would increase the ratio $k_{o\text{-F}}/k_{m\text{-F}}$ to a value greater than that which it would have if only chain-transmitted effects operated.

EXPERIMENTAL

Materials.—*o*-, *m*-, and *p*-Fluorophenyltrimethylammonium iodide were prepared from the primary amines. A mixture of freshly distilled amine (1·2 g.), sodium hydroxide (1·3 g.),

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[3] Frost and Pearson, "Kinetics and Mechanism," Wiley, New York, 1953, pp. 138—139.

[4] Kenner, *Proc. Roy. Soc.*, 1946, **185**, *A*, 119.

[5] Baker and Hopkins, *J.*, 1949, 1089.

[6] Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell and Sons Ltd., London, 1953.

[7] Roberts, Clement, and Drysdale, *J. Amer. Chem. Soc.*, 1951, **73**, 2181.

methyl iodide (2·2 ml.), and water (2·0 ml.) was cooled in ice–salt and sealed in a Pyrex tube. After the initial reaction, started by allowing the mixture to warm to 20°, had subsided, the tube was placed in boiling water for 4 hr. After being cooled the mixture was filtered and the crystals of quaternary iodide were recrystallised once from water and twice from 95% methanol. Results are summarised in Table 3.

TABLE 3. *Aryltrimethylammonium iodides.*

Aryl	Yield (%) *	Decomp. † at	Found (%) C	H	N	F	Reqd. (footnote)
o-C_6H_4F	56	230°	38·4	4·8	5·1	7·3	*a*
m-C_6H_4F	69	183	38·8	4·7	—	7·1	*a*
p-C_6H_4F	76	240	38·3	4·5	4·85	6·9	*a*
p-C_6H_4Me	63	220	43·3	5·6	—	—	*b*

* After first recrystn. † At 1 atm.

(*a*) C_9H_9NIF requires C, 38·5; H, 4·7; N, 5·0; F, 6·8%. (*b*) $C_{10}H_{12}NI$ requires C, 43·3; H, 5·8%

TABLE 4. *Determination of rate constants. Reaction of* o-*fluorophenyltrimethylammonium iodide with sodium methoxide in absolute methanol.*

Initially [Halide] = 0·020M, [NaOMe] = 0·040M. Temp. 90·85°.

Concns. expressed in ml. of 0·01095N-NaOEt per 4·75 ml. of solution. Rate constants (k_2) in l. sec.$^{-1}$ mole^{-1}.

t (min.)	0	8·00	10·00	12·0	14·0	17·0	20·0	23·0
[NaOMe]	16·18	14·45	14·13	13·84	13·52	13·18	12·85	12·43
[Halide]	7·33	5·60	5·28	4·99	4·67	4·33	4·00	3·58
10^2k_2	—	1·60	1·57	1·56	1·58	1·55	1·53	1·61
t (min.)	26·0	29·0	32·0	35·0	38·0	41·0		
[NaOMe]	12·24	11·93	11·74	11·54	11·32	11·13	8·85	
[Halide]	3·39	3·08	2·89	2·69	2·47	2·28	0·00	
10^2k_2	1·55	1·58	1·56	1·55	1·57	1·58	—	

Mean k_2 = 1·57 × 10^{-2}.

Corr. for solvent expansion (17—91°), k_2 = 1·73 × 10^{-2}.

TABLE 5. *Rate constants for aryltrimethylammonium iodides and sodium methoxide in absolute methanol.*

Initial concns.: [NaOMe] = ~0·040M, [Halide] = ~0·020M.

Aryl	Ph		*p*-C_6H_4F			
Temp.	69·77°	95·29°	58·58°	68·91°	80·69°	91·93°
k_2	9·71 × 10^{-5}	2·69 × 10^{-3}	3·44 × 10^{-5}	1·52 × 10^{-4}	7·50 × 10^{-4}	3·13 × 10^{-3}

Aryl	*m*-C_6H_4F				*p*-C_6H_4Me	
Temp.	58·27°	69·15°	80·91°	91·39°	69·68°	95·24°
k_2	7·80 × 10^{-5}	3·59 × 10^{-4}	1·71 × 10^{-3}	6·22 × 10^{-3}	5·66 × 10^{-5}	1·68 × 10^{-3}

Aryl	*o*-C_6H_4F			
Temp.	58·37°	69·60°	80·63°	90·85°
k_2	2·77 × 10^{-4}	1·28 × 10^{-3}	5·14 × 10^{-3}	1·73 × 10^{-2}

Trimethylphenylammonium iodide was obtained by refluxing dimethylaniline with an equivalent amount of methyl iodide in methanol, recrystallised twice from 95% methanol, and then decomposed at 230° (Found : C, 41·5; H, 5·35. Calc. for $C_9H_{14}NI$: C, 41·1; H, 5·4%).

Methanol was dried as described by Vogel,[8] and stored under dry nitrogen.

Thermostat temperatures were constant within ±0·02°.

Kinetic Methods.—The method of sealed tubes was used and reactions were followed by analysing samples for residual methoxide. Sample tubes were rapidly cooled after known times. Their contents were washed with carbon dioxide-free distilled water into a definite excess of standard hydrochloric acid. Excess of acid was determined by titration with standard sodium ethoxide solution, in an atmosphere of nitrogen, to bromothymol-blue. In view of the sensitivity of these reactions to the ionic strength of the medium, solutions used in runs for the

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[8] Vogel, " Textbook of Practical Organic Chemistry," Longmans, Green, London, 1948, p. 168.

determination of Arrhenius parameters were made up to give the same initial concentrations of reactants, and samples were taken over the same range of reaction (30—70%).

" Infinity tubes " were used to ascertain that, with reagent concentrations as in the Tables, one mole of quaternary iodide consumed one mole of methoxide in a time equal to twelve times the measured half-life of each reaction.

Analyses of Products.—Analyses were carried out on contents of some of the " infinity tubes." The contents were just acidified with hydrochloric acid and concentrated on a water-bath, then a hot concentrated solution of picric acid in methanol was added. After cooling, the picrate was filtered off and recrystallised from methyl alcohol. *o*-Fluorophenyltrimethylammonium iodide yielded *o*-fluorodimethylaniline picrate, m. p. 126—128° (Braun and Rudolph [9] recorded 131°) (Found : C, 45·8; H, 3·8; N, 15·4; F, 5·1. Calc. for $C_9H_{13}NFI$: C, 45·7; H, 3·6; N, 15·2; F, 5·2%). *m*-Fluorophenyltrimethylammonium iodide yielded *m*-fluorodimethylaniline picrate, m. p. 184—186° (Found : C, 46·0; H, 3·6; N, 15·3; F, 4·9%). *p*-Fluorophenyltrimethylammonium iodide yielded *p*-fluorodimethylaniline picrate, m. p. 150° (Schiemann and Winkelmüller [10] recorded 151·5°) (Found: C, 46·4; H, 3·7; N, 15·0; F, 5·0%). Trimethylphenylammonium iodide yielded dimethylaniline picrate, m. p. and mixed m. p. 159° (Hodgson and Kershaw [11] recorded 159°). Trimethyl-*p*-tolylammonium iodide yielded *NN*-dimethyl-*p*-toluidine picrate, m. p. and mixed m. p. 127° (Hodgson and Kershaw [11] recorded 128°).

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[9] Braun and Rudolph, *Ber.*, 1931, **64**, 2469.
[10] Schiemann and Winkelmüller, *Ber.*, 1933, **66**, 731.
[11] Hodgson and Kershaw, *J.*, 1930, 277.