824. *Studies in Aromatic Nucleophilic Replacement. Part VI.* Some Effects of Alkyl Groups.*

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The influence of *ortho-*, *meta-*, and *para*-methyl and -*tert.*-butyl groups on the rate of replacement by methoxide ion of the fluorine of *m*-fluoronitrobenzene has been studied. The fluorine was activated by a *meta*-nitro-group to limit steric effects at the reaction centre to those attributable to an alkyl group. Reaction rates and Arrhenius parameters are recorded. The results are discussed in terms of the polar and steric effects of alkyl groups and the marked steric effect of an *ortho-tert.*-butyl group is noted. The preparation and characterisation of certain new alkylfluoronitrobenzenes are recorded.

The polar and steric effects of alkyl groups have been extensively studied.[1] The effects of alkyl groups on halogenation in *ortho-* and *para*-positions have been investigated by de la Mare and Robertson [2] and by Berliner and Berliner,[3] and the activating effects of methyl and *tert.*-butyl groups on all three positions in nitration have been discussed by Cohn, Hughes, Jones, and Peeling.[4] Recently, Berliner, Berliner, and Nedilow,[5] have evaluated the relative effects towards iodination of alkyl groups in the *meta*-position. The deactivating influence of *para*-alkyl groups on aromatic nucleophilic replacement has been noted by Bevan, Hughes, and Ingold [6] and by Berliner and Monack; [7] recently, analogous effects of *ortho-* and *para*-methyl groups have been recorded by Bolto, Miller, and Williams.[8]

A series of alkyl-substituted *m*-fluoronitrobenzenes † have been prepared, and their rates of reaction with methoxide ion in absolute methanol measured. The objects were to obtain information as to the effect of *ortho-*, *meta-*, and *para*-substitution by alkyl groups on the rate of nucleophilic replacement of an activated fluorine atom, to compare the effects of methyl and *tert.*-butyl groups in the *meta*-position, and possibly to obtain information as to the mode of transmission of the inductive effect through the benzene ring. The fluorine atom removed as fluoride ion was activated by a *meta*-nitro-group in order

Table 1. k_2 *(in l. sec.$^{-1}$ mole^{-1}) for reaction of alkyl-substituted* 3-*fluoro*-1-*nitrobenzenes with methoxyl ion in absolute methanol.*

Unsubstituted [9]		4-Methyl		5-Methyl		6-Methyl	
T	10^5k_2	T	10^5k_2	T	10^5k_2	T	10^5k_2
97·87°	5·73	100·0°	0·798	100·00°	3·05	109·95°	1·92
112·45	25·0	109·95	2·15	109·95	8·26	120·1	5·05
119·92	51·3	120·1	5·64	120·1	20·6	130·4	12·7
129·4	123	130·4	13·3	130·4	53·9		

4-*tert.*-Butyl		5-*tert.*-Butyl		6-*tert.*-Butyl	
T	10^5k_2	T	10^5k_2	T	10^4k_2
130·2°	2·63	99·80°	2·12	100·0°	0·690
		110·2	5·84	109·6	1·84
		130·2	39·9	120·1	5·28
				130·4	14·3

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* Part V, *J.*, 1956, 469.

† For convenience of discussion all substituted nitrobenzenes are numbered from $NO_2 = 1$ in this section.

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

[2] Robertson, de la Mare, and Swedlund, *J.*, 1943, 279; *J.*, 1953, 782, and other papers in this series.

[3] Berliner and Berliner, *J. Amer. Chem. Soc.*, 1949, **71**, 1195.

[4] Cohn, Hughes, Jones, and Peeling, *Nature*, 1952, **169**, 291.

[5] Berliner, Berliner, and Nedilow, *J. Amer. Chem. Soc.*, 1954, **76**, 507; Berliner and Berliner, *ibid.*, p. 6179.

[6] Bevan, Hughes, and Ingold, *Nature*, 1953, **171**, 301.

[7] Berliner and Monack, *J. Amer. Chem. Soc.*, 1952, **74**, 1574.

[8] Bolto, Miller, and Williams, *J.*, 1955, 2929.

[9] Bevan and Bye, *J.*, 1954, 3091.

to eliminate from the reaction centre steric effects other than those due to alkyl groups. Rate constants and Arrhenius parameters are summarised in Tables 1 and 2.

TABLE 2. *Comparison of* 10^6k_2 (*in l. sec.*$^{-1}$ *mole*$^{-1}$) *at* 130·4° *and Arrhenius parameters* ($k_2 = Be^{-E/RT}$) *for alkyl-substituted* 3-*fluoro*-1-*nitrobenzenes with methoxyl ion in absolute methanol.*

	Unsub.	4-Me	5-Me	6-Me	4-Bu	5-Bu	6-Bu
10^6k_2 ………………	1350	133	539	127	26	407	143
$\log_{10} B$ ………………	12·8	11·2	12·1	11·5	—	12·1	12·3
E (kcal.) ……………	28·9	27·8	28·3	28·4	—	28·6	29·8

Discussion.—Relative rate constants for the 5-alkyl-3-fluoro-1-nitrobenzenes show that deactivation of this type of nucleophilic displacement follows the order $\mathrm{Bu^t} > \mathrm{Me} > \mathrm{H}$. This corresponds with the electron-release effects found by Hughes *et al.*[4] in the *para*-nitration of alkylbenzenes and by Berliner *et al.*[5] in the *meta*-iodination of *p*-alkylphenols and -anilines. It is noteworthy that the ratio of rates of *meta*-nitration—found by the former authors—though in the reverse direction corresponds rather closely with those noted here:

$k(m\text{-Me})/k(m\text{-Bu}^t) = 0{\cdot}63$ for nitration

$k(m\text{-Bu}^t)/k(m\text{-Me}) = 0{\cdot}74$ for nucleophilic replacement of fluorine

At all temperatures at which comparative rate constants were measured it is seen that deactivation by 6- and 4-methyl substituents is about equal and about four times greater than that effected by 5-methyl groups. This corresponds with a more effective transfer of charge from the *ortho*- and the *para*-position by resonance or with the operation of hyperconjugation or both. The fact that deactivation from the *meta*-position is more effective in the case of a *tert.*-butyl group, whereas here and in previous cases investigated [6, 7] the methyl group is most effective from the *para*-position, indicates that hyperconjugation is certainly operative.

Unfortunately, examination of the *tert.*-butyl case, in which C–H hyperconjugation would not arise, is complicated by the possibility of steric interaction between the 6-*tert.*-butyl group and the activating nitro-group which would lead to a decrease in the activating influence of the latter by its being forced out of coplanarity with the benzene ring. The activation energy for the present case, *viz.*, ~30 kcal., is significantly greater than for others and for the unsubstituted compound which are all 28—29 kcal. Deactivation due to steric inhibition of resonance would of course be superposed on retardation owing to electron release to the reaction site. The ratio of the effects, *p*-*tert.*-butyl : *p*-methyl, has been determined in aromatic nucleophilic displacement by Bevan, Hughes, and Ingold [6] as 1·76 and by Berliner and Monack [7] as 1·17. The former found that in no circumstance in a bimolecular nucleophilic displacement does the effect on the rate constant of a *para*-methyl group exceed twice that of a *tert.*-butyl group and even in the strongly electron-demanding unimolecular solvolysis of diphenylmethyl chloride in aqueous acetone [10] the ratio of rate constants is 2·32. We may therefore safely take this figure as an upper limit in the present case. If it is assumed that the rate for the 6-methyl compound is unaffected by steric inhibition of resonance, the value for the 6-*tert.*-butyl compound would, in the absence of this latter influence, be not more than

$$2{\cdot}32 \times 1{\cdot}27 \times 10^{-4} = 2{\cdot}92 \times 10^{-4}\ \text{l. sec.}^{-1}\ \text{mole}^{-1}$$

This value is considerably lower than that for the 5-*tert.*-butyl compound, showing that the polar influences of a *tert.*-butyl group are more effectively transferred from the *para*- than from the *meta*-position. This could be ascribed to C–C hyperconjugation.

In positions *para* to those at which occur aromatic nucleophilic displacements, which are inhibited by electron release, methyl groups have a greater retarding effect than *tert.*-butyl groups,[6, 7] whereas in the *para*-nitration of alkylbenzenes,[4] which is accelerated by electron release, the *tert.*-butyl group has a greater facilitating influence than the methyl group. This apparent contradiction can be considered on the following basis.

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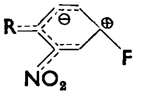
[10] Hughes, Ingold, and Taher, *J.*, 1940, 949.

In aromatic nitration the nitronium ion which is a powerful electrophile can attach itself to the π-electron system of the reactive carbon atom during the process of rehybridisation to the sp^3-like bonds of the transition state at a much earlier stage than, say, a methoxide ion can form a partial bond with the nucleus of a reactive aromatic carbon atom. Thus it is reasonable to suppose that the creation of the former transition state is largely influenced by the permanent polarisation effects, both inductive and hyperconjugative, which are set up by alkyl groups. Evidence from the dipole moments of alkylbenzenes and from the effects of *meta*-alkyl groups in both electrophilic and nucleophilic displacements indicates a permanent electron release in the order *tert.*-butyl > methyl > hydrogen.

It is generally agreed that the transition state of activated aromatic nucleophilic displacements takes place *via* a transition state (or transition states if an intermediate is postulated) in which benzenoid resonance is lost and the reactive carbon atom has a tetrahedral disposition of valencies. Thus in a reaction such as the one considered here, the transition state of the replacement cannot be formed until the molecule being attacked has to a considerable extent been polarised to the form shown inset. It has been clearly established that the order of mesomeric effects of alkyl groups is methyl > *tert.*-butyl > hydrogen.[10a] Thus the development of a positive charge at the reactive carbon atom will involve a greater loss of resonance energy in the case of *ortho*- and *para*-methyl groups than occurs with corresponding *tert.*-butyl groups, so that in the absence of steric effects alkyl groups should inhibit activated aromatic nucleophilic replacements in the order methyl > *tert.*-butyl > hydrogen. This is in fact the order always found.[6, 7]



(R = alkyl group)

Finally, the marked deactivating influence of an *ortho-tert.*-butyl group shown by the rate constants in Table 2 confirms the interpretation by Hughes *et al.*[4] of the influence of this group on nitration as being largely steric in origin.

EXPERIMENTAL

Materials.—All solids used in the kinetic measurements were recrystallised to constant m. p. from the appropriate solvent; liquids were purified by repeated distillation at reduced pressure.

1-*Fluoro*-2-*methyl*-5-*nitrobenzene*.—Commercial 2-methyl-5-nitroaniline was acetylated, and the acetyl compound crystallised to constant m. p., hydrolysed with 70% sulphuric acid, and reconverted into the amine with ammonia. The recrystallised amine was converted by Stech and Fletcher's modification[11] of the Schiemann reaction into the diazonium fluoroborate which decomposed to the required compound; b. p. 77°/4 mm., m. p. 35°.

1-*Fluoro*-4-*methyl*-3-*nitrobenzene*.—Prepared from commercial 4-methyl-5-nitroaniline by a method analogous to the above, this had b. p. 71°/3 mm., s. p. −8·8° to −8·9°.

1-*Fluoro*-3-*methyl*-5-*nitrobenzene*.—*p*-Toluidine was acetylated, nitrated, hydrolysed, and deaminated to 3 : 5-dinitrotoluene, which was reduced with potassium polysulphide to 3-amino-5-nitrotoluene. This was converted *via* the diazonium fluoroborate into the required *fluoro-compound*, m. p. 40·0—40·5° (from aqueous methanol) (Found: C, 54·4; H, 4·38; N, 9·0. $C_7H_6O_2NF$ requires C, 54·2; H, 3·9; N, 9·0%).

1-tert.-*Butyl*-2-*fluoro*-4-*nitrobenzene*.—*tert.*-Butylbenzene, prepared from benzene and *tert.*-butyl chloride, was nitrated. 2- and 4-*tert.*-Butylnitrobenzene were isolated by fractionation at 12 mm. and reduced to the corresponding amines. 2-*tert.*-Butylaniline (20 g.) was dissolved in concentrated sulphuric acid (200 g.) cooled to −10°, and the solution stirred vigorously while dry, finely powdered potassium nitrate (20 g.) was added gradually (1 hr.). The product was poured on a small quantity of ice at −10°, allowed to remain for 3 min., and the thick mass of nitro-amine sulphate was drained from excess of acid. The sulphate was basified with ammonia, and the base crystallised from aqueous alcohol; it had m. p. 71·5—72·5°. Some of these crystals were deaminated by using hypophosphorous acid, the nitro-compound reduced, and the acetyl derivative of the amine formed; m. p. 161—162°. Craig[12] gives for 4-*tert.*-butylacetanilide, m. p. 161—162°. Hence, by the above method nitration of 2-*tert.*-butylaniline

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[10a] Baker and Hemming, *J.*, 1942, 191.

[11] Stech and Fletcher, *J. Amer. Chem. Soc.*, 1948, **70**, 439.

[12] Craig, *J. Amer. Chem. Soc.*, 1935, **57**, 195.

afforded the 5-nitro-derivative. The latter was converted *via* the diazonium fluoroborate into the desired *fluoro-compound*, b. p. 103·5—104°/3 mm., m. p. 12·5—13° (Found: C, 61·0; H, 6·5; N, 6·8. $C_{10}H_{12}O_2NF$ requires C, 60·9; H, 6·1; N, 7·0%).

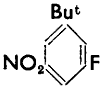
1-tert.-*Butyl-4-fluoro-2-nitrobenzene*.—4-*tert*.-Butyl-5-nitroaniline hydrochloride was prepared by Shoesmith and Mackie's method[13] and converted into the named *compound* in the usual way; it had b. p. 90—92°/7 mm. (Found: C, 61·0; H, 6·4; N, 6·6. $C_{10}H_{12}O_2NF$ requires C, 60·9; H, 6·1; N, 7·1%).

1-tert.-*Butyl-3-fluoro-5-nitrobenzene*.—*p*-Amino-*tert*.-butylbenzene was acetylated and nitrated; to avoid extensive decomposition of the product the following procedure was used. Finely powdered *p*-*tert*.-butylacetanilide (20 g.) was added during 15 min. to well-stirred fuming nitric acid (200 ml.) at 5°. The mixture was cooled to −10° and poured into much crushed ice and salt with vigorous stirring. The light yellow solid was collected on a spatula and placed in ice-cold ether over sodium hydrogen carbonate and ice, the mixture stirred and filtered, and the solid washed with dilute hydrochloric acid and much water, giving 4-acetamido-3 : 5-*tert*.-butyldinitrobenzene, m. p. 132—133° (yield 53%). This compound was deacetylated and then deaminated by Cohen and McCandlish's method,[14] giving 1-tert.-*butyl*-3 : 5-*dinitrobenzene*, m. p. 99·5—100·5° (Found: C, 53·4; H, 5·3; N, 12·8. $C_{10}H_{12}O_4N_2$ requires C, 53·6; H, 5·4; N, 12·5%). This was reduced by the same authors' method to 3-tert.-*butyl*-5-*nitroaniline*, m. p. 73° (Found: C, 61·7; H, 7·2; N, 14·8. $C_{10}H_{14}O_2N_2$ requires C, 61·8; H, 7·3; N, 14·4%). Acetyl derivative, m. p. 159·5—160°. The amine was converted in the usual way *via* the diazonium fluoroborate into the required *fluoro-compound*, b. p. 76°/1 mm. (Found: C, 60·9; H, 6·2; N, 7·2. $C_{10}H_{12}O_2NF$ requires C, 60·9; H, 6·1; N, 7·1%).

Analysis of Products.—It is known[15] that *o*- and *p*-nitrotoluene and their derivatives develop deep colours on treatment with concentrated methanolic potassium hydroxide in the presence of air or other oxidising agent. The reactions under discussion were therefore carried out under an atmosphere of nitrogen and in most cases rate constants were determined over the range 10—20% of reaction; in this range the falling off in rate constants, attributable to side reactions, was negligible. The products of the reaction between methoxide ion and 1-fluoro-4-methyl-3-nitrobenzene, the case in which colour production was most pronounced, were analysed in order to confirm that the process being measured was the replacement of fluorine by methoxide ion.

Four portions, each 250 ml., of 0·03M-1-fluoro-4-methyl-3-nitrobenzene and 0·0507N-sodium methoxide in absolute methanol were heated under nitrogen in sealed ampoules for 13 days at 100·1°. The tubes were cooled, the contents made slightly acid with methanolic hydrogen chloride, and the methanol removed by slow distillation from a water-bath until the residual volume was 50 ml. The mixture of sodium fluoride and sodium chloride which crystallised during the evaporation was weighed, and the chloride estimated by Volhard's method. This, together with a correction for the solubility of sodium fluoride in methanol, showed that 0·004427 mole of sodium fluoride had been formed. Hence, if the replacement of fluorine by methoxide ion is the only reaction taking place, the amount of 4-methoxy-2-nitrotoluene formed would be 0·7401 g. The remaining methanol was distilled off, and diethyl phthalate (2 ml.) added as a chaser; the mixture was then fractionated through a good column at 22 ± 0·1 mm. The following fractions were obtained: (i) b. p. 105°/22 mm. (2 ml.), (ii) b. p. 105—148°/22 mm. (0·1 ml.), (iii) b. p. 148—150°/22 mm. (0·92 g.), (iv) b. p. 172°/22 mm. (chaser). Fraction (iii) had b. p. 265—267°/760 mm. (Found: OMe, 20·8. Calc. for $C_8H_9O_3N$: OMe, 18·6%). Knecht[16] gives for 4-methoxy-2-nitrotoluene, b. p. 266—267°. The only substance present that can give a methoxyl analysis other than the expected product is diethyl phthalate, and on this basis the product isolated contained 76·4% of 4-methoxy-2-nitrotoluene which corresponds to 95% of the fluoride ion liberated.

Evidently up to 30% of reaction, for practical purposes, the only reaction taking place is that with which this communication is concerned.



(A)

Kinetic Measurements.—Thermostat temperatures were steady to within ±0·05°. The reactions were carried out in sealed tubes under nitrogen, and their progress was followed as in previous papers in this series except that the indicator used was bromocresol-green–methyl-red.

[13] Shoesmith and Mackie, *J.*, 1928, 2334.

[14] Cohen and McCandlish, *J.*, 1905, **87**, 1257.

[15] Green and Baddiley, *J.*, 1908, **93**, 1721.

[16] Knecht, *Annalen*, 1882, **215**, 88.

Determination of k_2(*l. sec.*$^{-1}$ *mole*$^{-1}$) *for reaction of* 1-tert.-*butyl*-3-*fluoro*-5-*nitrobenzene* (*A*) *with methoxyl ion in absolute methanol.*

Initially, [Halide] = 0·0300M, [OMe$^-$] = 0·06678M. Temp. 130·2°. Concns. in ml. of 0·02131N-NaOH solution per 9·01-ml. sample.

t (hr.) ...	0	3	3·5	4·0	4·5	5·1	5·5	6·5	7·5	9	10	11	12	12·5
[NaOH]	27·65	25·12	24·82	24·50	24·10	23·75	23·56	23·03	22·60	21·74	21·40	21·13	20·79	20·59
[Halide]	12·11	9·58	9·28	8·96	8·56	8·21	8·01	7·49	7·06	6·20	5·86	5·59	5·25	5·05
10^4k_2 ...	—	3·48	3·41	3·41	3·52	3·50	3·48	3·46	3·41	3·60	3·55	3·46	3·47	3·51

Mean k_2 = 3·48 × 10^{-4}. Duplicate = 3·42 × 10^{-4}.
Corrected for solvent expansion, k_2 = 3·99 × 10^{-4}.

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