287. *Studies of the* ortho-*Effect. Part IV. Kinetics of the Formation of* o-*Substituted Phenyltrimethylammonium Iodides in Methyl-alcoholic Solution.*

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The velocities of reaction of methyl iodide with seven *o*-substituted dimethylanilines have been measured, and the results analysed on the basis of the equation $k = PZe^{-E/RT}$. Six of the seven groups studied cause an increase both in E and in PZ, but *o*-F leads to no change in PZ. The largest effects are observed with *o*-Me and *o*-Ph, and it is suggested that, in the transition complex, the group becomes " linked " to the nitrogen of NMe_2 by a hydrogen bond. Effects of smaller magnitude are found in the *o*-OPh, *o*-OMe, *o*-NO_2 and *o*-Cl derivatives, and these are regarded as due to an interaction between the unshared electrons of the nitrogen and the group in the *o*-position whereby, without the formation of an actual " linkage," the former are subjected to a constraint. The interactions here postulated would raise E by decreasing the electron-availability of the nitrogen, and would also increase PZ by conferring a charge on the reactive portion of the complex. The interaction is not possible in *o*-fluorodimethylaniline, since fluorine cannot expand its valence group; the lack of any " *ortho*-effect " in the *o*-fluoro-compound is, in fact, the key to the interpretation of the observations, as it was in previous work on the hydrolysis of benzoic esters.

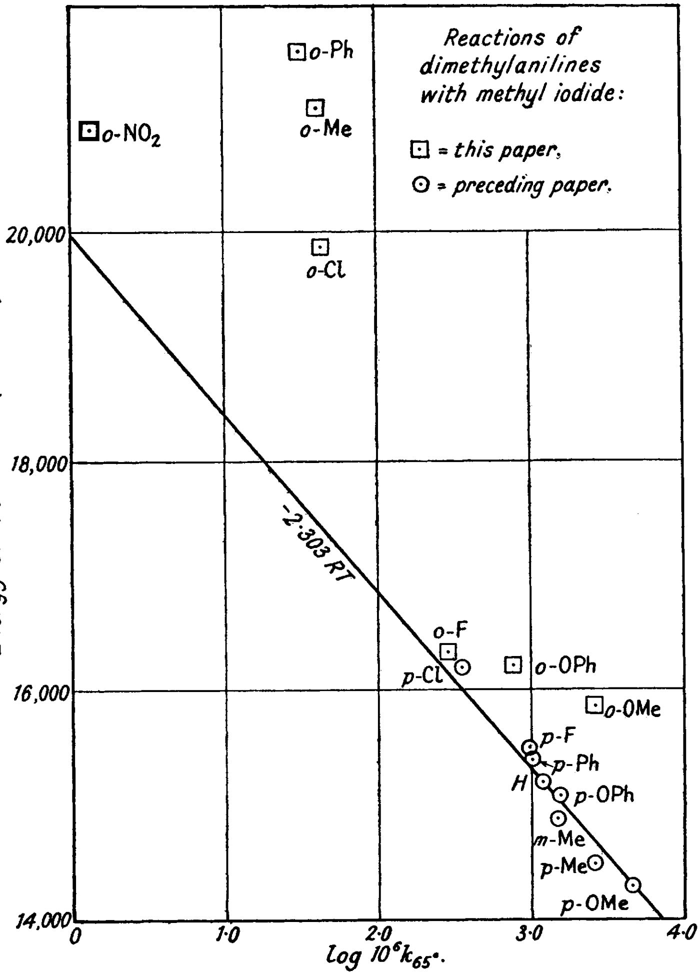
The lack of reactivity displayed by *o*-substituted tertiary bases is among the earliest recorded examples of " steric hindrance," and has been the subject of numerous investigations. In 1872, Hofmann failed to prepare quaternary iodides by heating certain di-*o*-substituted dimethylanilines with methyl iodide at 150°, and Fischer and Windaus found later (*Ber.*, 1900, **33**, 345) that of the six isomeric xylidines only dimethyl-*m*-2-xylidine gave no quaternary iodide at 100°; the reaction was greatly retarded by a single *o*-methyl group, and inhibited by methyl and bromine in the two *ortho*-positions (*ibid.*, p. 1967). The low velocity of reaction of dimethyl-*o*-toluidine with allyl bromide was observed by Thomas (J., 1913, **103**, 594). Similarly, von Braun (*Ber.*, 1916, **49**, 1101) obtained only poor yields of quaternary salts by the interaction of methyl iodide with dimethyl-*o*-toluidine and with *o*-chloro- and *o*-bromo-dimethylanilines, although *o*-anisidine reacted vigorously and completely; he suggested (von Braun, Arkuzewski, and Kohler, *Ber.*, 1918, **51**, 282) that in the first three cases the residual affinity of the nitrogen is partly satisfied by the *o*-substituent.

We have now carried out a kinetic study of the reactions of a number of *o*-substituted dimethylanilines with methyl iodide in methyl-alcoholic solution. The energies of activation and the values of log PZ of the equation $k = PZe^{-E/RT}$ are recorded below. The quantities $E_o - E_p$ and P_o/P_p in the final columns represent respectively the differences in the energies of activation and the ratios of the non-exponential terms for the reactions of the isomeric *o*- and *p*-substituted compounds (the figures relating to the latter are from the preceding paper).

Reaction of MeI *with* *o*-$X{\cdot}C_6H_4{\cdot}NMe_2$.

X.	E(cals.).	log PZ.	$E_o - E_p$.	P_o/P_p.
o-F	16,300	7·0	800	1
o-OPh	16,200	7·4	1,100	3
o-OMe	15,900	7·7	1,600	6
o-NO_2	20,900	7·7		6
o-Cl	19,900	8·5	3,700	40
o-Me	21,100	9·3	6,600	250
o-Ph	21,600	9·5	6,200	400

All the results recorded in this and the preceding paper are shown graphically in the figure, where E is plotted against log k_{65°. The straight line drawn through the point for the unsubstituted compound has the theoretical slope $-2{\cdot}303RT$, and reactions having a constant value for PZ give points falling on this line. The six points standing above the line indicate larger values of PZ.



An inspection of the results for the seven *o*-substituted bases studied shows that they form a series with the *o*-fluoro- and the *o*-phenyl compounds as extreme members. The relative magnitudes of the effects are quite unconnected with the weights, volumes, or chemical characters of the groups; this is not unusual, of course, for substituents in the *o*-position.

Like groups standing in the *m*- or *p*-positions, *o*-F causes no change in the value of the PZ term. The rather higher value of E for the *o*- than for the *p*-fluoro-derivative ($E_o - E_p = 800$ cals.) may be ascribed to the shorter distance from which the inductive effect operates; the relative strengths of the *o*- and *p*-substituted fluorobenzoic acids and fluoroanilines are capable of a similar interpretation (Jenkins, this vol., p. 640, 1137). It is clear, therefore, that *o*-F exhibits no features which are not also observed in *p*-F, and in this respect the reaction now under consideration shows a complete analogy with the alkaline hydrolysis of ethyl benzoates (Evans, Gordon, and Watson, J., 1937, 1430).

The $E_o - E_p$ values for the phenoxyl and methoxyl groups are perceptibly higher than for fluorine. The difference of 1,600 cals. between the energies of activation for the *o*- and *p*-methoxy-derivatives is certainly too large to be explained on the basis of the inductive effect of the group; this is evident, for example, from the fact that, whereas the ratio K_o/K_p of the dissociation constants of the *o*- and *p*-fluorobenzoic acids is 7·5, K_o/K_p is only 2·4 for the *o*- and *p*-methoxybenzoic acids (values of dissociation constants are due to Dippy and Lewis, J., 1937, 1426). A further significant observation is the appreciable increase in the value of *PZ* for the *o*-OPh and *o*-OMe compounds, methoxyl again having the larger effect. Comparison of the P_o/P_p ratio for the *o*- and *p*-methoxyl derivatives with the small variations observed among the compounds where *PZ* can justifiably be regarded as constant (preceding paper) indicates that these increases in *PZ*, though not large, are real. The kinetic data thus lead us to conclude that the reactions of *o*-phenoxy- and *o*-methoxy-dimethylanilines are influenced, though not very powerfully, by some factor which does not operate in the *p*-substituted bases or in *o*-fluorodimethylaniline. The *o*-nitro-compound is similar, showing an increase in *PZ* although $E_o—E_p$ cannot here be computed since data for the *p*-nitro-derivative are not available.

In the chlorodimethylanilines, we find a very much larger increase both in *E* and in *PZ* in passing from the *p*- to the *o*-derivative. The difference in the energies of activation has the relatively high value of 3,700 cals., as contrasted with only 800 cals. for the fluoroanilines. The ratio of the dissociation constants of *o*- and *p*-chlorobenzoic acids ($K_o/K_p =$ 10·9), on the other hand, is not so markedly greater than that for the fluoro-acids ($K_o/K_p = 7·5$), and in the chloroanilines and chlorophenols the transfer of the substituent from the *p*- to the *o*-position has a *smaller* effect than in the corresponding fluorine compounds (K_o/K_p for phenols, Cl 7·7, F 16·4; K_p/K_o for anilines, Cl 21·3, F 40·7; *K* values are due to Bennett, Brooks, and Glasstone, J., 1935, 1821). In the reactions of the tertiary bases with methyl iodide, chlorine in the *o*-position leads also to a 40-fold increase in the *PZ* term, whereas, as pointed out above, fluorine has no such effect.

The largest "*ortho*-effects" observed in this system are, however, those of methyl and phenyl; the energies of activation for the *o*-derivatives are here more than 6,000 cals. above those for the isomeric *p*-compounds, and *PZ* is increased by factors of 250 and 400 respectively. There is a striking contrast between the effect of *o*-methyl observed here and in the relative strengths of the isomeric dimethyltoluidines. The latter differ but little, that of the *o*-substituted base being actually the larger (Davies and Addis, J., 1937, 1622); there is therefore no "*ortho*-effect," although the strengths of *o*-toluidine and methyl-*o*-toluidine (both *lower* than the values for the *p*-isomerides; Hall and Sprinkle, *J. Amer. Chem. Soc.*, 1932, **54**, 3469), and still more that of *o*-toluic acid (appreciably higher than *p*-toluic; Dippy and Lewis, *loc. cit.*), may indicate the operation, though less powerfully, of a factor of the same type as that observed in our study of quaternary salt formation. The marked difference observed in this system between the *o*-phenyl and *o*-phenoxy-derivatives also contrasts with the proximity of the values of the dissociation constants of the corresponding benzoic acids (Dippy and Lewis, *loc. cit.*).

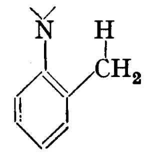
The order of the energies of activation found for dimethyl-*o*-toluidine, *o*-chlorodimethylaniline and dimethyl-*o*-anisidine is in agreement with the relative yields of quaternary iodide obtained by von Braun (*loc. cit.*) from these compounds under standard conditions, *viz.*, *o*-CH_3 7·6, *o*-Cl 15·6, *o*-OMe 100%.

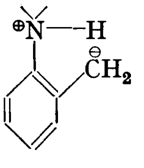
All the *o*-substituents which we have examined, with the sole exception of fluorine, have the effect of increasing both the energy of activation and the *PZ* term, and similar influences have been observed in the esterification of acids (Hinshelwood and Legard, J., 1935, 587) and the acid-catalysed hydrolysis of esters (Timm and Hinshelwood, J., 1938, 862). In alkaline hydrolysis, on the other hand, groups in the *o*-position (F again excepted) reduce the value of *PZ* (Evans, Gordon, and Watson, *loc. cit.*). In order to interpret these influences upon the esterification and hydrolysis processes, interaction between the doubly-linked oxygen (acting as electron donor) and the group in the *o*-position has been postulated (Dippy, Evans, Gordon, Lewis, and Watson, J., 1937, 1421; compare *Ann. Reports*, 1938, **35**, 245); such interaction, which is regarded as occurring in the transition complex and not in the normal state of the acid or ester, is not possible in the case of fluorine which cannot expand its valence group. As far as we are aware, there is no other satisfactory explanation of these phenomena, in spite of the fact that the relative strengths of the halogeno- and nitro-benzoic acids, phenols, and anilines are interpretable on the basis of inductive and mesomeric effects alone (Jenkins, *loc. cit.*; the " interaction " hypothesis is still necessary for the *o*-Me and *o*-OH derivatives).

In the reactions of *o*-substituted dimethylanilines with methyl iodide, the *o*-fluoro-derivative stands apart from the others in that it exhibits no peculiar features. The remaining groups which we have studied provide the following order of increasing *ortho*-effects: OPh < OMe (NO_2) < Cl < Me < Ph. Not only is this order quite unrelated to the volumes of the groups, but a geometrical effect of the Victor Meyer type would lead to a decrease and not an increase in *PZ*. The strengths of the corresponding benzoic acids or anilines do not, as a rule, indicate the operation of the same influences in equilibria as in reactions, *i.e.*, the definite and often large effects which have been recorded above appear to be the manifestation of some factor which is peculiar to the highly-energised transition state. We suggest, therefore, that the interpretation already put forward for hydrolysis and esterification is applicable here also, *viz.*, that simultaneously with the formation of the transition complex (*i.e.*, while the system ascends the energy valley to the pass) there is an interaction between the unshared electrons of the nitrogen and the substituent. This is really the expression, in modern language, of von Braun's suggestion (*loc. cit.*) that the free affinity of the nitrogen is to some extent saturated by the group attached to the *o*-carbon atom.

It is reasonable to suppose that such interaction may take place to an extent which varies from compound to compound, and it is possible to envisage a series of groups which, when suitably placed with respect to the electron-donating nitrogen atom, will give a steadily increasing " degree of interaction." The extreme members of this series would be fluorine, where interaction is zero, and carboxyl, which under normal conditions transfers a proton completely to nitrogen, forming an electrovalent bond. Intermediate between these would be groups capable of forming a hydrogen bond with the nitrogen, and we suggest that examples are found in the *o*-methyl and *o*-phenyl derivatives of dimethylaniline (when they enter into a transition complex). In order to make the hydrogen-bonding process possible, the atoms must be so placed that the proton can be attached to either, and it would appear that this condition is here fulfilled (the hydrogen bond " completes " a five-membered " chelate ring " with one double bond; compare the analogous case of propiophenone, Evans, J., 1936, 785). The unperturbed forms for dimethyl-*o*-toluidine are as written in (I) and (II), and the participation of (II) in the resonance state causes the electrons of the nitrogen to be less available for reaction with the methyl group of methyl iodide, and hence raises *E* to a marked degree. It also confers a charge upon the reactive portion of the complex, the life of which is thus increased (compare *Ann. Reports*, 1938, **35**, 247), with a resulting rise in the value of the *PZ* factor. The effect should perhaps be expressed as an increase in the ratio (average life of transition complex)/(average life of transition complex + time required for stabilisation of the ionic product) as suggested by Norrish (*Trans. Faraday Soc.*, 1937, **33**, 1521).

(I.)

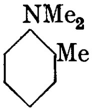




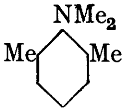
(II.)

In the above examples, the proton may be regarded as shared between the carbon and nitrogen atoms, since it is linked to one or the other in the unperturbed structures; but it is not unlikely that there may sometimes be an interaction between the electrons of the nitrogen and the group in the *o*-position, by which the former are subjected to a constraint, without the formation of an actual " bond." This may be supposed to occur if the atoms are not placed suitably for chelation, if the hydrogen with which the electrons interact is not sufficiently " loose " to permit the formation of an ionised structure, or perhaps if a hydrogen atom is not concerned. We suggest that something of this kind occurs in *o*-phenoxy-, -methoxy-, -nitro-, and -chloro-dimethylanilines, where the observed effects are smaller than in the methyl and the phenyl compounds. The extent of such interaction, as indicated by the results of our kinetic studies, increases in the series OPh$<$OMe(NO_2)$<$Cl, and all these groups have much smaller effects than those which we believe to form an actual hydrogen bond. It is not possible to determine whether an interpretation of this kind, rather than the postulate of an actual co-ordinate bond, should be applied to the alkaline hydrolysis of *o*-chloro- and *o*-nitro-benzoic esters; the positions of the atoms are here not unsuitable for ring completion, however.

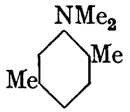
Von Braun (*loc. cit.*) finds that groups in the *o*-position make the *p*-position of dimethylaniline less reactive also, the effects being in the order $CH_3$$>Cl>$OMe. For instance, the yields of substituted benzyl alcohols obtained by reaction with formaldehyde under stated conditions were *o*-Me 6, *o*-Cl 36, *o*-OMe 60%, and similar phenomena were observed in other reactions involving the *p*-position; but if an additional methyl group was introduced in a position *m* to the dimethylamino-group, the reactivity of the *p*-position was *increased* (von Braun, Arkuzewski, and Kohler, *loc. cit.*); *e.g.*, although (IV) was *less* reactive than (III), (V), and (VI) were *more* reactive [especially (VI), where the nitrogen was more reactive with methyl iodide also].



(III.)



(IV.)



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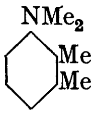

(VI.)

Clearly, the interaction of the unshared electron pair with the *o*-substituent will reduce the electromeric effect of the dimethylamino-group, thus rendering the *p*-position less reactive towards electrophilic reagents, and two methyl groups as in (IV) will be more effective than one; but if an additional methyl group be placed as in (V) or (VI), it will activate the position *ortho* to itself, and hence in (V) and (VI) the positions *para* to dimethylamino- will be more reactive than they are in (III) or (IV). In addition, the *m*-methyl group in (VI) (by its $+I$ effect) will render the protons of the *o*-methyl group more strongly bound, and thus reduce the hydrogen-bond formation, rendering (VI) more reactive than (V). The absence of any indication of an " *ortho*-effect " in the strength of dimethyl-*o*-toluidine, whereas there appears to be such an effect in methyl-*o*-toluidine and in *o*-toluidine, is probably due to a similar cause (compare *Ann. Reports*, 1938, **35**, 248).

EXPERIMENTAL.

o-Nitrodimethylaniline, obtained by Hodgson and Kershaw's method (J., 1930, 280), was purified by treatment with acetic anhydride followed by fractionation. The remaining tertiary amines were prepared by methylation of the appropriate anilines with methyl sulphate (Evans and Williams, this vol., p. 1199). In each case, primary and secondary bases were removed by treatment with acetic anhydride, and the tertiary base was isolated and purified by suitable means. The boiling points of the pure amines were as follows:

o-Me	87°/30 mm.	*o*-Ph	145·5°/11 mm.	*o*-Cl	85·5°/10 mm.
o-OMe	113/28 mm.	*o*-F	75 /20 mm.	*o*-NO_2	146 /20 mm.
		o-OPh, m. p. 34·5°			

The kinetic determinations were carried out as described in the preceding paper. The reactions between the *o*-substituted dimethylanilines and methyl iodide are bimolecular, but the plot of $1/(a-x)$ against time is not always linear: the *o*-F, *o*-OMe, and *o*-OPh compounds gave a straight line up to 40% or 50% of the change, but for *o*-chloro- and *o*-nitro-dimethylanilines the reversed reaction causes a falling off with time. Dimethyl-*o*-toluidine and 2-dimethylaminodiphenyl are peculiar in exhibiting slight autocatalysis, and the plot of $1/(a-x)$ against t shows an upward trend. In each of these four cases, however, the tangent at zero time is easily and accurately drawn, and the plot of log k against $1/T$ gives a good straight line.

o-Nitrodimethylaniline was studied at 110°, 125°, 135°, and 145°, and although the equilibrium point lay at about 16% change, the velocity coefficients at zero time could be reproduced with fair accuracy for the two highest temperatures. At the lower temperatures, however, the curve obtained by plotting $1/(a—x)$ against t did not permit of extrapolation. The results for this compound, depending on measurements at two temperatures only, are therefore subject to some error. There is no reason to suppose that the conclusions drawn regarding this compound are in any way affected thereby, however; the *o*-nitro-group certainly causes a very large increase in the energy of activation, and it would be necessary to decrease the observed value by 1000 cals. in order to eliminate the change in *PZ*.

The velocity coefficients are summarised below, R being the *o*-substituent in *o*-$R{\cdot}C_6H_4{\cdot}NMe_2$.

R = Me.		R = OMe.		R = OPh.		R = F.		R = Cl.		R = NO_2.		R = Ph.	
T.	10^4k.	*T*.	10^4k.	*T*.	10^4k.	*T*.	10^4k.	*T*.	10^4k.	*T*.	10^4k.	*T*.	10^4k.
65°	0·417	35°	2·46	35°	0·714	45°	0·710	65°	(0·434)*	65°	(0·0135)*	65°	0·301
90	3·39	44·95	5·50	45	1·60	55	1·50	75	1·02	135	2·15	85·9	1·99
100	7·99	55	12·3	55	3·57	65	3·09	85·25	2·33	145·1	4·01	101	6·74
		65	25·2	65·05	7·47	74·8	5·96	98·9	6·53				

* Calculated.

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