LIX.—*The Nature of the Alternating Effect in Carbon Chains. Part XXXII. The Directive Influence of ψ-Basic Systems in Aromatic Substitution. Nitration of Benzylidene*-m-*nitroaniline.*

By John William Baker and Christopher Kelk Ingold.

The study of orientation by neutral and by ionic substituents has a natural sequel in the consideration of directive action by the intermediate class of " ionogenic " groups, that is, neutral systems which tend to acquire an ionic charge by interaction with the reagent employed for further substitution. This category comprises not only simple acidic and basic substituents with a single potentially ionic centre (*e.g.*, OH, NR_2), but also ψ-acidic and ψ-basic groups, the ionic forms of which are regarded as possessing a distributed charge; and in Part XXXI (Baker, J., 1928, 2257) it was shown, by reference to the nitration of some ψ-acidic phenylnitromethanes, that the anionic charges, which are developed in the side chains of these substances under certain conditions, dominate nuclear substitution, consistently with their assumed partial location on the atom adjoining the ring (I). Here the aromatic nucleus occupies the ψ-position of a ψ-acidic system, and ionisation leads to *op*-substitution; similarly, when the nucleus occupies the ψ-position in a ψ-base, ion-formation with partial transference of the charge to the α-atom of the side chain should produce strong *m*-orientation (II).

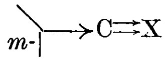
(I.)

(anion of ψ-acid)

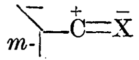
(II.)

(kation of ψ-base)

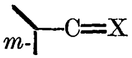
One of the simplest series of cases in which illustrations of this effect are to be expected is furnished by the substitution in acid media of the Schiff's bases derived from benzaldehyde. It has, indeed, long been known that these bases yield essentially *m*-nitro-products on nitration with nitric acid in concentrated sulphuric acid. Recently, however, Flürscheim and Holmes (J., 1928, 2230), whose estimate (87·5%) of the proportion of *m*-nitro-derivative formed from benzylidene-*m*-nitroaniline, $C_6H_5\cdot CH{:}NR$, is definitely *higher* than the corresponding figure for benzaldehyde, $C_6H_5\cdot CH{:}O$, claimed to have proved that this high proportion is formed, not from the kation, but from the free base. The point is one of some importance, for, if it were true, only Flürscheim's theory could consistently explain it. All theories of aromatic substitution (even the less acceptable varieties) which are based on, or allied to, the electronic theory of valency, unite in requiring that, in the absence of salt formation, the *m*-orienting effect of $\cdot CH{:}NR$ should be less than that of $\cdot CH{:}O$ (III, IV); the theory of affinity-demand alone reverses that order (V) (compare *loc. cit.*, p. 2236). Indeed, the example may fairly be described as the remaining *pièce de résistance* of the affinity-demand theory of orientation, and Flürscheim and Holmes, who clearly realise the importance of the instance, conclude that their work appears strongly to support a non-electronic interpretation of aromatic substitution as opposed to an interpretation based on the electronic theory of valency.



(III. O>NR)



(IV. O>NR)



(V. NR>O)

The first step in Flürscheim and Holmes's alleged demonstration that nitration proceeds through the free base consists in their statement that the base is "proved" to be largely present as such in their sulphuric acid solvent. We cannot find in their paper any clear evidence for this assertion, although a reference is made to the "intensely yellow colour" of the sulphuric acid solutions.

" Intensely yellow " is certainly a correct description; but the base itself is almost colourless and forms colourless solutions in dry alcohol. It is true that Flürscheim and Holmes prepared a " colourless " solid hydrochloride by precipitation with hydrogen chloride in dry benzene, but this might well be a non-ionised form, such as a ψ-salt, Ph·CHCl·NHR, which (like triphenylchloromethane and many other substances) might develop colour in suitable ionising solvents (see below); it does, indeed, form a strongly yellow solution in dry alcohol. Our experiments lead us to suggest that, on the contrary, the free base, for all practical purposes, is absent, and that the compound exists entirely as a sulphate in the sulphuric acid medium. This conclusion is based largely on partition experiments. When a solution of the base in ligroin is shaken with the acid, the whole of the base passes into the acid (with development of the usual strong colour). When a saturated solution of the base in the acid is shaken repeatedly with ligroin, or even with carbon tetrachloride, in which the base is very soluble, none is removed.* Finally, when a warm concentrated solution of the base in the acid is cooled to the ordinary temperature and kept, the *hydrogen sulphate* separates. This salt, when dry, is almost colourless; but it gives the usual strong colour on solution in sulphuric acid.

Flürscheim and Holmes's second argument is that the high proportion of *m*-isomeride cannot be due to nitration of the ammonium kation, which " fact," according to them, is " established " by the observations that the *m*-ratio remained nearly the same when ammonium sulphate was added to the nitration solvent, whereas in the nitration of diethylbenzylamine (*idem*, J., 1926, 1569), admittedly a reaction of the kation, the addition of ammonium sulphate caused the *m*-ratio to be strongly depressed. Our observations compel us to challenge this conclusion also. It is true that, under the conditions used by Flürscheim and Holmes for the nitration of the Schiff's base, the addition of ammonium sulphate makes no great difference to the proportion of *m*-isomeride; but we find that precisely the same is true of the nitration of diethylbenzylamine. Furthermore, although careful observation shows that there is a small difference, which will be considered later, between the two cases, the direction of the disparity is the opposite of that suggested by Flürscheim and Holmes.

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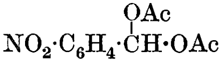
* Neither is benzaldehyde extracted, which proves the absence of hydrolysis, since added benzaldehyde is readily removed. Indeed, if benzaldehyde and *m*-nitroaniline are brought together in the solvent, rapid combination occurs with formation of the anhydro-base, which, since it is present as sulphate, cannot be partitioned with neutral solvents, but can be recovered in good yield by pouring the acid solution into excess of ice-cold sodium hydrogen carbonate solution.

In seeking confirmatory evidence of the theory that nitration of the Schiff's base proceeds through the salt, we first studied its nitration with a nearly neutral reagent, namely, acetyl nitrate, the expectation being that salt formation would occur only to a small extent or not at all, and that, consequently, the proportion of *m*-isomeride would be found to be below the value, 79%, given by benzaldehyde in mixed acids. This was confirmed, the proportion found being 41%; but it soon transpired that the result could not justly be regarded as evidence on the question at issue, since at least one derivative of the Schiff's base other than its salt was almost certainly present in the nitration medium. From a solution of *m*-nitrobenzylidene-*m*-nitroaniline in this medium we have isolated an unstable crystalline compound which may have the constitution (VI), and it is possible, therefore, that nitration of benzylidene-*m*-nitroaniline takes place at least partly through a similar addition compound with acetyl nitrate. In this connexion the following analogy also seems to have some value: when benzaldehyde was nitrated with acetyl nitrate in excess of acetic anhydride, it was found possible to isolate the *p*-nitro-additive compound (VII); and the proportion of *m*-nitro-product in the mononitro-compounds was only 37%.

(VI.)

$$NO_2 \cdot C_6H_4 \cdot \overset{\overset{\large O \cdot NO_2}{|}}{C}H \cdot NAc \cdot C_6H_4 \cdot NO_2$$



$$NO_2 \cdot C_6H_4 \cdot \overset{\overset{\large OAc}{|}}{C}H \cdot OAc$$

(VII.)

We therefore resumed the comparative study of the nitration of benzyldiethylamine and the Schiff's base in sulphuric acid with and without ammonium sulphate, on the basis of the following considerations. First, we concur with Flürscheim and Holmes in assuming that, *if* the Schiff's base is nitrated essentially as such, the depression in the *m*-ratio caused by sulphate ions should be negligible in comparison with that observed in a corresponding experiment with benzyldiethylamine, in which it is known that nitration occurs through the kation of the salt and that sulphate ions cause electrostriction equivalent to a certain amount of change in the direction, dissociated kation → undissociated salt; this difference, *if established*, would, we agree, constitute strong evidence that the azomethine is nitrated as base. Secondly, we suggest that if, on the other hand, the Schiff's base, like benzyldiethylamine, is nitrated through the kation of its salt, then, if there is any observable difference of behaviour, it should be the Schiff's base which should exhibit the larger repression of *m*-substitution when nitrated in the presence of sulphate ions. The reason is that the Schiff's base is a pseudo-base and that any association of the ions of the true (electrovalent) salt should be succeeded by partial conversion of this into the pseudo-(covalent) salt; in other words, whilst any depression of the *m*-ratio in the nitration of benzyldiethylamine is dependent on the loss of *m*-orienting power represented by the change, ion ⟶ salt, *i.e.*, pole ⟶ dipole, in the case of the Schiff's base a further *m*-repressing influence exists in the second stage of the change, ion ⟶ salt ⟶ *ψ*-salt, *i.e.*, pole ⟶ dipole ⟶ neutral form. A difference in this direction would therefore be strong evidence in favour of the theory that the nitration of the azomethine, leading to the high proportion of *m*-isomeride, takes place through the ion of the salt. The details of our nitrations are given in the experimental portion, but Table I constitutes a summary of the results relating to the point at issue. The figures represent the mean values of the percentage of *m*-isomeride, together with the mean deviations from the mean to give an indication of consistency.

TABLE I.

Diethylbenzylamine.		Benzylidene-*m*-nitroaniline.	
Conditions.	meta (%).	Conditions.	meta (%).
Without $(NH_4)_2SO_4$ ...	61·0 ± 1·3	Without $(NH_4)_2SO_4$ ...	89·1 ± 0·3
With $(NH_4)_2SO_4$ ...	61·9 ± 0·3	With $(NH_4)_2SO_4$ ...	83·7 ± 0·2
Diff.	+0·9 ± 1·6	Diff.	−5·4 ± 0·5

The difference here recorded for benzyldiethylamine is within the experimental error; no importance can be attached to it, and the only possible conclusion is that any alteration of the *m*-ratio caused by ammonium sulphate cannot be detected in the experiments we have conducted. On the other hand, the difference for benzylidene-*m*-nitroaniline, although not large, is well beyond the limits of precision, and affords clear evidence of nitration through the kation of the salt, confirming the indications of the experiments described earlier in this paper.

Thus it transpires that a reinvestigation of this crucial nitration reverses the theoretical situation in the direction favourable to those theories of aromatic substitution which are directly or indirectly related to the electronic theory of valency; and the same investigation shows that the theory of the distributed charge in *ψ*-basicity, as well as in *ψ*-acidity, is to be seriously regarded in its application to orientation by ionogenic systems.*

EXPERIMENTAL.

Materials.—The benzylidene-*m*-nitroaniline employed had m. p. 72°, and was almost colourless (very pale greenish-yellow) (Found :

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* The application of this theory to the nitration of benzylidene-*m*-nitroaniline was made by the undersigned shortly after the appearance of Flürscheim and Holmes's publication, despite their claim to have proved the contrary (*Ann. Reports*, 1928, **25**, 140).—C. K. I.

C, 68·8; H, 4·2. Calc.: C, 69·0; H, 4·4%). Following Flürscheim and Holmes's procedure, the sulphuric acid used for nitration contained a small excess of sulphur trioxide as a precaution against hydrolytic fission; for the same reason, the nitric acid employed was rendered anhydrous by distillation with excess of sulphuric acid.

*Salts of Benzylidene-*m*-nitroaniline.*—The base formed a colourless solution in alcohol dried with calcium, but a yellow solution in concentrated or fuming sulphuric acid. The hydrochloride, prepared by Flürscheim and Holmes's method, gave a yellow solution in calcium-dried alcohol and a yellow solution in concentrated or fuming sulphuric acid. The *hydrogen sulphate* was obtained as follows: The base (3·5 g.) was added in small portions with shaking to sulphuric acid (10 g.) containing 2·7% excess sulphur trioxide. The warm suspension was filtered through asbestos with precautions against access of moisture from the atmosphere, and the saturated solution of the sulphate kept in a sealed vessel at the ordinary temperature for several days, crystals slowly separating; these were collected and washed with ethyl sulphate and dry ether successively, or with ether only. A further quantity was precipitated from the mother-liquor by dilution with dry ether. The salt (Found: SO_4'', 32·4. $C_{13}H_{10}O_2N_2,H_2SO_4$ requires SO_4'', 29·6%) is very pale yellow, is comparatively stable in air, has m. p. 225° (decomp.) with previous darkening, and gives a yellow solution in fuming sulphuric acid.

Partition Experiments.—The ligroin (b. p. 110—120°) and carbon tetrachloride used were purified by repeated and prolonged shaking, first with concentrated and finally with fuming sulphuric acid (5% sulphur trioxide). The solvent for the second phase was sulphuric acid containing 2·7% excess of sulphur trioxide. The temperature was that of the room and the mixtures were shaken for periods varying from 1 to 24 hours. The results are summarised in the introduction.

Formation of Azomethines in Sulphuric Acid.—The acid used as solvent and condensing agent contained 2·7% excess of sulphur trioxide. The formation and isolation of benzylidene-*m*-nitroaniline have already been described; a similar experiment with *m*-nitrobenzaldehyde in place of benzaldehyde yielded *m*-nitrobenzylidene-*m*-nitrobenzylamine, which was similarly isolated. The product in each case was identified by m. p. and mixed m. p. with authentic specimens.

Side-chain Transformations of an Azomethine and of Benzaldehyde with Nitric Acetic Anhydride.—(Nitration 3). Benzylidene-*m*-nitroaniline (2·3 g.) was added in small portions at 35° to a mixture prepared at 0° of absolute nitric acid (6·0 g.) and acetic anhydride, and the mixture was kept at room temperature over-night. The product was poured on ice and excess of potassium hydrogen carbonate and extracted with ether and benzene after decomposition of the acetic anhydride. Qualitative separation of the residue showed that substances other than nitrobenzylidene-*m*-nitroanilines were present, but the mixture was too complex to admit of the isolation of a pure individual. The whole process was therefore repeated with *m*-nitrobenzylidene-*m*-nitrobenzylamine in place of the original azomethine, except that the separation by means of ether and alkali was replaced by evaporation to constant weight at the ordinary temperature in an oil-pump vacuum with passage of a limited stream of dry air. The gain in weight was 42·4%, whereas the gain required for the addition of 1 mol. of acetyl nitrate is 38·8%. The material was not crystalline, but a product which remained crystalline for a short time was obtained as follows. A moderately concentrated solution of *m*-nitrobenzylidene-*m*-nitroaniline in a similarly prepared mixture of nitric acid and acetic anhydride was cooled in liquid ammonia for several hours; the liquid then became filled with a mass of colourless crystals. These rapidly dissolved if the temperature was raised, and were therefore collected at −30° in jacketed apparatus and washed with ethyl nitrate and ligroin at the same temperature. The crystals had m. p. 50—55° (decomp.) when rapidly heated in a sealed tube, but quickly decomposed at the ordinary temperature, either in the air or in sealed tubes, giving nitrous gases and a red gum. The freshly prepared crystals when warmed with dilute sulphuric acid gave nitric acid (nitron precipitate) in addition to the normal hydrolysis products. These experiments are regarded as proving the formation, rather than the constitution, of an addition product of the azomethine with the reagent used.

(Nitration 5). Benzaldehyde (5·0 g.) was added during 2 hours at 35° to a nitration solution prepared at 0° from absolute nitric acid (18 g.) and acetic anhydride (30 c.c.). After being kept overnight, the mixture was poured on ice and excess of potassium hydrogen carbonate, and, after decomposition of the acetic anhydride, extracted twice with ether and once with benzene. The residue obtained after removal of the solvents partly crystallised, and the crystals were drained and washed with ether–ligroin. They then had m. p. 118—120°, and one crystallisation from ether raised this to 125—127°, alone or in admixture with an authentic specimen of *p*-nitrobenzylidene diacetate.

*Nitration of Benzylidene-*m*-nitrobenzylamine and of Benzaldehyde in Acetic Anhydride.*—The numerical particulars, except analyses, relating to these nitrations are given in Table II; the analytical details and results are in Table IV.

The products of the nitration of the azomethine were isolated as described for nitration 3 above, and hydrolysed by boiling with dilute sulphuric acid. The aldehydes were isolated by extraction with ether and benzene successively, and oxidised with permanganate to acids, which were isolated and analysed by reduction and bromination as usual.

The nitration product of benzaldehyde was isolated in the same way, and the subsequent treatment was the same except for the omission of the hydrolysis.

TABLE II.

Nitration No.	Substance nitrated.	Weight taken (g.).	HNO_3 (g.).	Ac_2O (g.)	Temp.	Time (hrs.).	Product (g.).	Treated (g.).	Acids (g.).
1	PhCH:NR	2·00	6·08	25	0° room	2·2 0·8	2·68	2·18	0·916
2	,,	2·29	7·0	11·5	35° room	2·5 24·0	2·640	2·037	1·002
4	PhCH:O	4·98	18·0	30	35° room	2·0 20·0	10·40	4·682	2·480

The heading "Treated" should be interpreted, "Product hydrolysed and oxidised" for nitrations 1 and 2, and "Product oxidised" for nitration 4.

In nitration 1 the azomethine was previously dissolved in half the acetic anhydride, and the solution was slowly added to a mixture of the nitric acid and the other half.

In nitration 2 the solid azomethine was added in small portions to the nitration mixture.

In nitration 4 the benzaldehyde was run into the nitration solution. Part of the solution of the acids obtained by oxidation was lost and the weight recorded is that of the residue from the remaining solution.

Nitration of Benzyldiethylamine and Benzylidene-m-*nitroaniline in Sulphuric Acid with and without Addition of Ammonium Sulphate.*—The numerical particulars, except analyses, relating to these nitrations are recorded in Table III; the analytical details and results will be found in Table IV.

The benzyldiethylamine, b. p. 105—107°/20 mm., was in all cases run into the nitration solution. The product was poured on ice, basified with potassium hydroxide, and extracted with chloroform. Owing to the difficulty of removing the last traces of this solvent from the residual oil, some of the recorded yields of nitro-bases may be slightly too high. The products were oxidised, and the acids analysed, as usual.

The solid benzylidene-*m*-nitroaniline was in all cases added little by little without solvent to the nitration solution. The product was poured on ice and excess of potassium hydrogen carbonate and extracted successively with ether and benzene. The material obtained was subjected to the usual routine of hydrolysis, oxidation, reduction, and bromination.

TABLE III.

Nitration No.	Substance nitrated.	Weight taken (g.).	Am_2SO_4 (g.).	HNO_3 (g.).	H_2SO_4 (g.).	SO_3 % in H_2SO_4.	Temp.	Time (hrs.).	Product (g.).	Aldehydes (g.).	Treated (g.).	Acids (g.).
6	$PhCH_2 \cdot NEt_2$	3·00	—	3·06	66	1·5	0° room	2·0 2·0	2·817	—	2·268	1·321
7	,,	2·66	—	1·50	38	2·7	0° room	1·5 2·0	3·253	—	2·005	1·173
8	,,	3·01	—	1·60	20	5·0	0° room	2·0 2·0	3·795	—	3·131	0·908
9	,,	3·00	35	3·06	66	1·5	0° room	2·0 2·0	3·581	—	2·654	1·209
10	,,	3·98	26	2·00	57	2·7	0° room	1·5 2·0	4·751	—	3·379	2·380
11	,,	3·03	6	1·8	20	5·0	0° room	2·0 2·0	3·795	—	2·843	1·414
12	PhCH:NR	3·00	—	2·45	71	1·5	35–40° room	4·0 22·0	—	1·824	1·824	1·321
13	,,	3·00	—	0·60	16·5	2·7	10° room	1·0 21·0	3·410	—	2·254	1·198
14	,,	3·00	21	2·40	40	2·7	40° room	3·0 21·0	—	1·968	1·968	1·062
15	,,	3·00	21	2·40	40	2·7	35–40° room	4·0 20·0	—	1·601	1·601	1·264

The heading " Treated " should be interpreted " Product oxidised " for nitrations 6—11, " Product hydrolysed and oxidised " for nitration 13, and " Aldehydes oxidised " for nitrations 12, 14, and 15. The corresponding figures for nitrations 6—11 may be somewhat too high owing to the difficulty, mentioned above, of completely freeing the oily nitration product from chloroform.

In nitration 8, part of the solution of the acids obtained by oxidation was lost and the weight recorded is that of the residue from the remainder.

In nitration 13, the 2·254 g. of nitration product yielded 1·645 g. of aldehydes and the whole of this was oxidised.

In nitrations 12, 14, and 15, the nitration products were hydrolysed without weighing, but the aldehydic product was weighed and the whole of it oxidised.

Analytical Results relating to the Nitrations.—The analytical data and the proportions of isomeride calculated therefrom are given in Table IV.

Table I (p. 435) shows the mean values (and mean deviations) of the proportion of *m*-nitro-isomeride formed from benzyldiethylamine and from benzylidene-*m*-nitroaniline in mixed acids, together with difference figures indicating the effect of ammonium sulphate on the meta-ratio; in the latter case, the mean deviations are obtained by subtracting one from another the individual results taken in pairs.

It should be stated that the experimental conditions (temperature, proportions of reagents, etc.) relating to the individual nitrations of which the results are averaged are not exactly the same (Table III); nevertheless, the internal consistency of the results of each of the several sets so treated is such as to show that any differences due to the varied conditions referred to are too small to be detected by the experiments here recorded.

TABLE IV.

		Recovered (g.).			Composition. Acids. R·CO$_2$H (mols. %):			Percentage nitro-isomerides.	
Nitration No.	Acids analysed (g.).	$C_6H_5 \cdot CO_2H$	$C_6H_2Br_3 \cdot NH_2$	$C_6HBr_3 <^{NH_2}_{CO_2H}$	R = C_6H_5.	op- $NO_2 \cdot C_6H_4$.	m- $NO_2 \cdot C_6H_4$.	op-.	m-.
1	0·725	0·550	0·041	0·046	95·0	2·5	2·5	(50*ca.*)	(50*ca.*)
2	0·862	0·015	0·815	0·624	2·8	57·6	39·6	59·3	40·7
4	0·9115	0·015	1·047	0·773	2·3	59·1	38·6	62·6	37·4
6	0·805	0·012	0·600	0·998	2·1	39·7	58·2	40·4	59·6
7	0·835	0·014	0·601	1·030	2·4	38·8	58·8	39·6	60·4
8	0·734	0·048	0·483	0·928	9·0	33·7	57·3	37·0	63·0
9	0·777	0·025	0·550	0·984	4·6	37·0	58·4	38·7	61·3
10	1·008	0·066	0·662	1·223	9·1	34·5	56·4	38·0	62·0
11	0·720	0·009	0·497	0·930	1·8	37·2	61·0	37·7	62·3
12	0·903	0·014	0·175	1·573	3·2	10·8	86·0	11·2	88·8
13	0·681	0·209	0·090	0·845	40·4	6·5	53·1	10·7	89·3
14	0·790	0·260	0·136	0·799	45·5	8·8	45·7	16·1	83·9
15	0·857	0·473	0·063	0·360	77·2	3·8	19·0	16·5	83·5

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