The Kinetics and Mechanisms of Aromatic Halogen Substitution. Part XXXI.[1] The Reaction Pathway involved in the Chlorination of *N*-Acetylcarbazole

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We have confirmed that the chlorination of *N*-acetylcarbazole in anhydrous acetic acid involves direct electrophilic chlorination, contrary to a recent proposal.

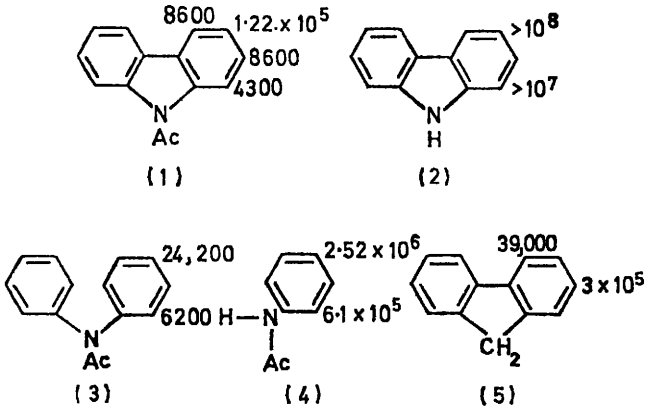
In an earlier paper,[2] we described the chlorination of *N*-acetylcarbazole in anhydrous acetic acid as being a conventional aromatic chlorination, kinetically of the second order, involving in the rate-determining transition state the *N*-acetylcarbazole molecule and molecular chlorine, giving all the possible chloro-*N*-acetylcarbazoles. 3-Substitution was found to be predominant, and from the rate of chlorination and the product proportions, partial rate factors for chlorination in the various nuclear positions were described as in structure (1). Comparison was made with corresponding partial rate factors for carbazole (2), *N*-acetyldiphenylamine (3), acetanilide (4), and fluorene (5).

It was concluded that the 1- and 3-positions in

[1] Part XXX, G. W. Burton, P. B. D. de la Mare, L. Main, and B. N. B. Hannan, *J.C.S. Perkin II*, 1972, 265.

[2] P. B. D. de la Mare, O. M. H. El Dusouqui, and E. A. Johnson, *J. Chem. Soc.* (*B*), 1966, 521.

carbazole are, as expected, very powerfully activated by the lone pair of electrons on the nitrogen atom; and that as far as the corresponding positions in *N*-acetylcarbazole are concerned, these are (a) as expected,



very much less activated; (b) as expected, still powerfully activated relative to benzene; and (c) quantitatively of the order of magnitude expected by treatment of the *N*-acetylcarbazole system as a disubstituted benzene, the 1- and 3-positions being affected by the *N*-acetyl group on the one hand and the attached aryl group on the other, comparison being made with the known reactivities of (3)—(5). The uncertainties in any such treatment were discussed; it was concluded that any special influence derived from resonance within the five-membered ring [3] must be small relative to the other factors involved in activation for the substitution, though it may be significant.

Recently, Kricka and Ledwith [4] have found that 1-chlorobenzotriazole, which chlorinates carbazoles,[5] does not chlorinate *N*-acetylcarbazole in dichloromethane at room temperature. From this, they deduce that *N*-acetyl-3-chlorocarbazole, isolated from the reaction of *N*-acetylcarbazole with chlorine in acetic acid, does not arise *via* electrophilic substitution of *N*-acetylcarbazole. As an alternative, they suggest that under our conditions the adventitious water present in our nearly anhydrous acetic acid hydrolyses *N*-acetylcarbazole to produce an equilibrium concentration of carbazole, which then is chlorinated and then reacetylated to give *N*-acetyl-3-chlorocarbazole.

Kricka and Ledwith's proposal is (a) inconsistent with the information available to them in our earlier paper,[3] (b) not supported by theory, (c) not supported by the experiments they adduce in support of their contention, and (d) not supported by information supplied by results for other electrophilic substitutions. We now deal with these points *seriatim*.

[3] C. Eaborn and J. A. Sperry, *J. Chem. Soc.*, 1961, 4921; R. Baker and C. Eaborn, *ibid.*, p. 5077.
[4] L. J. Kricka and A. Ledwith, *J.C.S. Perkin I*, 1973, 859.
[5] P. M. Bowyer, D. H. Iles, and A. Ledwith, *J. Chem. Soc.* (*C*), 1971, 2775.

(*a*) The reaction pathway (1) suggested by Kricka and Ledwith,[4] has the kinetic form of equation (2).

$$Ar_2NAc + H_2O \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Ar_2NH + HOAc;$$

$$Ar_2NH + Cl_2 \xrightarrow{k_2} \text{products} \qquad (1)$$

$$\frac{-d[Cl_2]}{dt} = \frac{k_1k_2[Ar_2NAc][H_2O][Cl_2]}{k_{-1}[HOAc] + k_2[Cl_2]} \qquad (2)$$

This reduces to the observed kinetic form of equation (3)

$$-d[Cl_2]/dt = k_{obs}[Ar_2NAc][Cl_2] \qquad (3)$$

only if $k_{-1}[HOAc] \gg k_2[Cl_2]$; with the reverse inequality the measured rate is independent of the chlorine concentration, and the rate of disappearance of chlorine is kinetically of the first order in aromatic compound and of the first order in water [equation (4)]. The

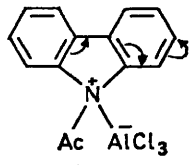
$$-d[Cl_2]/dt = k_1[Ar_2NAc][H_2O] \qquad (4)$$

observed kinetic form therefore requires that the rate of *N*-acetylation of carbazole in acetic acid be very much greater than the rate of chlorination of carbazole in acetic acid. The latter is, however, very fast; and the fact that it can be measured after dissolution of carbazole in the solvent means that the former must be much slower. So Kricka and Ledwith's interpretation is inconsistent with our published results. It is inconsistent also with our report of the products of chlorination. Thus 2-chlorocarbazole is easily detected by t.l.c. in the products of chlorination of *N*-acetylcarbazole by chlorine in acetic acid, followed by hydrolysis; it is absent in the product of chlorination of carbazole.

(*b*) Kricka and Ledwith assume that the electron-withdrawing power of the acyl group will sufficiently reduce the activating power of the lone-pair of electrons on nitrogen to ensure that orientation would, if *N*-acetylcarbazole were the substrate, be dominated by activation from the adjacent aryl ring. Our original analysis of the factors which may be involved in determining orientation in these compounds gives sufficient warning of the complexities involved in theoretical predictions relating to substitution in such systems, but our own results show that orientation in the chlorination of carbazole has been changed in that of *N*-acetylcarbazole towards 2- and 4-substitution (which now make a significant contribution to the products) but not enough to make this mode of substitution dominant; and that this result is perfectly consistent with our knowledge of related systems.

(*c*) The fact that 1-chlorobenzotriazole in dichloromethane chlorinates carbazole, but not the much less reactive *N*-acetylcarbazole, is not unexpected; it establishes that 1-chlorobenzotriazole in dichloromethane is less reactive as an electrophile than chlorine in acetic acid. That *N*-acetylcarbazole can be partly hydrolysed by acetic acid containing aqueous hydrogen chloride is also not unexpected, and is irrelevant to the situation existing in our experiments. That

N-acetylcarbazole is acetylated and benzoylated under Friedel–Crafts conditions to give the 2-derivative [6] is *not unexpected*; under these conditions, the lone pair of electrons must be heavily complexed with the catalyst, as Kricka and Ledwith note, and this would probably allow activation from the adjacent aryl ring to become dominant [structure (6)].



(6)

(*d*) Kricka and Ledwith [4] state that electrophilic substitution in *N*-acetylcarbazole is 'apparently confined to Friedel–Crafts acylation, the one reported exception being chlorination by chlorine in acetic acid'. In fact it is clear from the relevant volumes of Beilstein's Handbuch, and from refs. 7—9 quoted in our paper,[2] that there are several other examples. Thus *N*-acetylcarbazole has been reported as reacting with bromine in carbon disulphide to give the 3-bromo-derivative,[7] and with two molecules of bromine in chloroform to give 3,6-dibromo-*N*-acetylcarbazole.[8] Tucker [9] records that *N*-acetylcarbazole is iodinated in acetic acid to give the 3-iodo-derivative, and that carbazole can also be iodinated similarly to give 3-iodocarbazole, a result which also confirms that carbazole is not acetylated rapidly in acetic acid. Even nitrations of *N*-acetylcarbazoles have been reported [8,10] to give the 3-nitro-derivatives; other workers [11] have been less successful in obtaining useful products by nitration of *N*-acetylcarbazole, but have shown that this reaction in acetic acid takes a course different from that involved in the nitration of carbazole, thus confirming that in this solvent, even in the presence of water and of acids, the separate reactions of carbazole and of its *N*-acetyl-derivative can be recognised.

We conclude, therefore, that Kricka and Ledwith's suggested interpretation of our results on the chlorination of *N*-acetylcarbazole is incorrect, being unsoundly based both experimentally and theoretically. In the Experimental section we give some supporting and amplifying information relating to the hydrolysis of *N*-acetylcarbazole, to the acetylation of carbazole, and to the chlorination of *N*-acetylcarbazole and of carbazole.

EXPERIMENTAL

Carbazole (B.D.H.; recrystallised from ethanol; m.p. 245—246°), and *N*-acetylcarbazole, m.p. 68—69°, agreed in properties with those previously reported.[2,4] We have confirmed that the reaction of carbazole both with one and with two mol. equiv. of chlorine in acetic acid is complete within 1 min. We have confirmed also that over a concentration range [ArH] = 0·019—0·0025M, [Cl_2] = 0·013—0·005M, and [HCl] = 0·003—0·0003M the initial rate of chlorination of *N*-acetylcarbazole in acetic acid has the kinetic form given in equation (3); as expected, the measured rate rises towards the end of the reaction, since (as we reported earlier) the chloro-*N*-acetylcarbazoles produced in the reaction are themselves chlorinated at a rate which cannot be neglected. The mean second-order rate coefficient under our conditions was 3·9 l mol^{-1} min^{-1} at 25·0° (value reported previously, 4·3 l mol^{-1} min^{-1}). The rate of reaction was measured also in the presence of water (1%). The rate was again of the second order, k_2 = 7·2 l mol^{-1} $min.^{-1}$ A similar rate increase when water is added to the solvent acetic acid has been recorded by other workers for other substrates.[12,13]

Table 1 gives an example of a typical kinetic run, with $[ArH]_{init}$ = 0·0104M and $[Cl_2]_{init}$ = 0·0100M in acetic acid containing 1% H_2O and 0·01M-HCl at 25·0°; aliquot parts (5 ml) were withdrawn at intervals for titration with 0·01M-$Na_2S_2O_3$.

TABLE 1

Typical rate data for chlorination of *N*-acetylcarbazole

t/min	0·00	0·66	4·17	7·75	10·66	13·75	15·50	17·58	21·83
Titre (ml)	10·00	9·32	7·42	6·30	5·48	4·80	4·50	4·12	3·50
k_2/l mol^{-1} min^{-1}			7·4	6·9	7·1	7·2	7·2	7·5	7·8

An experiment was performed in parallel with this, in which the *N*-acetylcarbazole solution had been left in the solvent for 5 days. Its u.v. spectrum (see below) showed that it had been hydrolysed incompletely ($[N\text{-acetylcarbazole}]_{init}$ = 0·0104M; carbazole formed after 5 days, $\gtrsim$0·0022M; hence the rate of hydrolysis, calculated as the rate of disappearance of *N*-acetylcarbazole, $k_1 = \gtrsim 3 \times 10^{-5}$ min^{-1}). The chlorination was then started by adding standarised chlorine, and the disappearance of chlorine was followed as before, with the results in Table 2. Comparison of the two kinetic runs shows that in the first the

TABLE 2

Rate data for chlorination of *N*-acetylcarbazole after 5 days in HCl–CH_3CO_2H

t/min	0·00	0·58	3·28	6·92	9·17	11·25	13·66	18·78	23·50
Titre (ml)	10·00	4·84	3·46	2·92	2·42	2·30	2·00	1·42	1·12

decrease in chlorine concentration shows very little abnormality over the first ½ min, whereas in the second there is a very rapid initial consumption of chlorine, using up more than two moles of chlorine per mole of carbazole formed by hydrolysis. Furthermore the rate of chlorination of *N*-acetylcarbazole in the first experiment, when calculated as an initial first-order rate coefficient based on the decrease in concentration of *N*-acetylcarbazole, is *ca.* 0·07 min^{-1}, very much slower than the chlorination of carbazole ($k_1 \gg 23$ min^{-1}) but very much faster (by a factor of *ca.* 10^3) than the rate of hydrolysis of *N*-acetylcarbazole in the same solution. Hence the chlorination

[6] S. G. P. Plant and S. B. C. Williams, *J. Chem. Soc.*, 1934, 1142; S. G. P. Plant, K. M. Rogers, and S. B. C. Williams, *ibid.*, 1935, 741; D. A. Kinsley and S. G. P. Plant, *ibid.*, 1954, 1341; L. Ruberg and L. Small, *J. Amer. Chem. Soc.*, 1941, **63**, 736.

[7] G. L. Ciamician and P. Silber, *Gazzetta*, 1882, **12**, 272.

[8] G. Mazzara and A. Leonardi, *Gazzetta*, 1895, **25**[II], 395.

[9] S. H. Tucker, *J. Chem. Soc.*, 1926, 546.

[10] B. Oddo, *Gazzetta*, 1914, **44**[I], 485.

[11] R. W. G. Preston, S. H. Tucker, and J. M. L. Cameron, *J. Chem. Soc.*, 1942, 500.

[12] A. E. Bradfield and B. Jones, *Trans. Faraday Soc.*, 1941, **37**, 726.

[13] P. B. D. de la Mare and P. W. Robertson, *J. Chem. Soc.*, 1943, 279; P. B. D. de la Mare and J. S. Lomas, *Rec. Trav. chim.*, 1967, **86**, 1082.

of *N*-acetylcarbazole under these conditions cannot involve prior hydrolysis to carbazole.

Measurements of u.v. spectra were made by using a Unicam SP 800 recording spectrophotometer, with 1 cm cells and appropriate controls. Extinction coefficients and wavelengths have been obtained directly from the scanned spectra; high precision is not claimed for them, but we regard them as being accurate enough to sustain our conclusions.

The u.v. spectrum of carbazole in 95% ethanol has $\lambda_{max.}$ 256 (ε 22,000), 293 (18,800), 323 (3660), and 336 nm (3230), with shoulders at 287 and 314 nm. The spectrum in acetic acid was similar; in particular, the maxima at longer wavelength [323 (ε 3600) and 336 nm (3200)] appeared clearly. No change in the spectrum was noted over 19 h.

The spectrum of *N*-acetylcarbazole in 95% ethanol was markedly different; absorption bands were noted in ethanol at 287 (ε 11,800), 301 (6600), and 314 nm (7350). In acetic acid, the same bands were observed; in particular, the maxima at longer wavelength [301 (ε 6400) and 313 nm (6800)] were well resolved, and there was no significant absorption at 336 nm. No significant change in the spectrum was noted after 10 h.

The hydrolysis of *N*-acetylcarbazole to carbazole could be forced to completion within a reasonable time by using a mixture of equal volumes of acetic acid and concentrated hydrochloric acid. Under these conditions the absorptions of *N*-acetylcarbazole were replaced by those of carbazole; good isosbestic points were apparent at 317 and at 287 nm. Under less extreme conditions, however, the hydrolysis of *N*-acetylcarbazole was found to be very slow. Thus in acetic acid, or in acetic acid containing 1% of water, or in acetic acid containing HCl (0·01M) prepared from acetic acid, aqueous HCl (1M), and the theoretically required amount of acetic anhydride, the production of carbazole was very slow indeed. For example, in acetic acid containing H_2O (1%) and HCl (0·01M), no carbazole was detected after 3 h, 3% after 23 h, and 6·6% after 47 h.

These results confirm (a) that carbazole is not appreciably acetylated in acetic acid, (b) that *N*-acetylcarbazole gives carbazole only very slowly (if at all) in acetic acid, in acetic acid containing water, and in acetic acid containing water and HCl. Only under very extreme conditions (50% acetic acid–5·5M-HCl) does the rate of deacylation approach that of the chlorination of *N*-acetylcarbazole in acetic acid.

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