

The Kinetics and Mechanisms of Aromatic Halogen Substitution. Part XXXII.¹ The Directive Power of the Acetoxy-group

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The rates and products of chlorination of acetoxybenzene, the diacetoxybenzenes, and 4-acetoxyacetanilide by molecular chlorine in acetic acid at 25° have been examined. The results allow calculation of partial rate factors for chlorination directed by the acetoxy-group to the *ortho*-, *meta*- and *para*-positions. The extent to which the observed rates and products for chlorination of the diacetoxybenzenes accord with estimates calculated by using the 'additivity principle' is discussed. The response of change in rate to change in structure for the chlorination of 4-substituted anilides (4-RC₆H₄NHAc, where R is an electron-withdrawing group) is less than would be expected from the rates of chlorination of monosubstituted benzenes containing electron-releasing groups. Possible reasons for this difference are discussed in terms of factors which may affect the electron-releasing power of activating substituents. Further evidence that molecular chlorination of simple aromatic compounds is accompanied by minor, but significant, contributions from sequences initiated by addition of chlorine is presented. Little indication of contributions from chlorodeacylation has been found under the conditions used in the present investigation.

ALTHOUGH a good deal is known concerning the way in which acetylation of the amino-group influences the effect of this substituent on the rate and orientation of attack by electrophiles on the aromatic nucleus, corresponding information concerning the effect of acetylation of the hydroxy-group is incomplete. Acyloxy-groups have been generally accepted as being *ortho*, *para*-directing and activating for aromatic substitution, and

¹ Part XXXI, P. B. D. de la Mare, M. A. Wilson, and O. M. H. El Dusouqui, *J.C.S. Perkin II*, 1974, 634.

² P. W. Robertson, P. B. D. de la Mare, and B. E. Swedlund, *J. Chem. Soc.*, 1953, 782.

the influence of the closely related benzyloxy-group is shown by the fact that phenyl benzoate is chlorinated by molecular chlorine more rapidly than benzene, but less rapidly than toluene,² but more extensive quantitative information concerning the directive power of the acetoxy-group is not available. The accepted values of σ_p and σ_m for the acetoxy-group are 0.3 and 0.39 respectively;³ they show that the acetoxy-group is quite powerfully electron-withdrawing from both the

³ D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, 1958, 23, 420.

para- and *meta*-positions as shown by its effect on the strengths of substituted benzoic acids. Since σ_m and σ_m^+ values are usually quite similar,⁴ it might be thought to be a reasonable approximation to use the value σ_m^+ *ca.* 0.39 to estimate the rate of an aromatic substitution directed to the *meta*-position by the acetoxy-group, but σ_p^+ is expected to have a negative value, and no experimental estimate of this quantity is available as far as we are aware, either from studies of the rates of aromatic substitution or from the rates of solvolysis of substituted aralkyl halides.

We have shown recently⁵ that some aryl acetates are chlorinated by way of unusual reaction paths and intermediates, with sequences involving stages of addition and chlorodeacylation as well as normal substitution. To interpret these results properly, it is necessary to know more about the normally expected directive power of the acetoxy-group; and consequently we have examined the rates and products of chlorination of acetoxybenzene and of a number of its analogues, molecular chlorine in acetic acid at 25° being used to enable comparison with studies by other investigators.

EXPERIMENTAL

Acetates were prepared by standard methods from the corresponding phenols. Phenyl acetate had b.p. 43° at 0.11 mmHg, 193—194° at 744 mmHg (lit.,⁶ 195° at 764 mmHg), and its purity was checked by g.l.c. before use. 1,2-Diacetoxybenzene, purified by chromatography on silica gel and recrystallised from aqueous ethanol, had m.p. 62.5—63° (lit.,⁶ 64—65°). 1,3-Diacetoxybenzene had b.p. 276—277° at 750 mmHg (lit.,⁶ 279° at 753 mmHg); its purity was checked by g.l.c. 1,4-Diacetoxybenzene had m.p. 122—122.5° (lit.,⁶ 123—124°). *p*-Acetoxyacetanilide was prepared by treating *p*-aminophenol (8 g, m.p. 183—185°) with acetic anhydride (8 g). When the reaction mixture had become hot, acetyl chloride (6.5 g) was added and the mixture was heated at 100° for 15 min. The product was poured into water, the precipitate was treated with charcoal in hot water, filtered, and allowed to crystallise, m.p. 155° (lit.,⁶ 155—156°).

Most of the expected products of substitution were prepared as reference samples for g.l.c., and were purified by distillation *in vacuo*; *o*-chlorophenyl acetate, n_D^{22} 1.512 6 (lit.,⁷ n_D^{30} 1.512 8); *m*-chlorophenyl acetate, n_D^{22} 1.511 9 (lit.,⁷ n_D^{30} 1.512 2); *p*-chlorophenyl acetate, b.p. 225—226° at 760 mmHg (lit.,⁷ 226—227° at 760 mmHg); 2,4-dichlorophenyl acetate, b.p. 243—245° at 760 mmHg (lit.,⁸ 244—245° at 760 mmHg); 2,4,6-trichlorophenyl acetate, b.p. 259—261° (lit.,⁸ 261—262°).

1,3-Diacetoxy-4-chlorobenzene was prepared from 4-chlororesorcinol (a gift from Ivon Watkins-Dow Ltd., whom we thank), and was purified by chromatography and recrystallised from aqueous ethanol: m.p. 44—46° (lit.,⁹ 46—47°). 1,4-Diacetoxy-2-chlorobenzene, prepared simi-

⁴ Y. Okamoto and H. C. Brown, *J. Org. Chem.*, 1957, **22**, 485.

⁵ P. B. D. de la Mare and B. N. B. Hannan, *Chem. Comm.*, 1971, 1324.

⁶ F. D. Chattaway, *J. Chem. Soc.*, 1931, 2495.

⁷ V. Baliah and K. Ganapathy, *Trans. Faraday Soc.*, 1963, **59**, 1784.

⁸ F. Fischer, *Annalen Supp.*, 1870, **7**, 184 (through Beilstein's 'Handbuch der Organischen Chemie,' 4th edn., vol. VI, pp. 190, 192).

larly from 2-chlorohydroquinone, had m.p. 69—70° (lit.,¹⁰ 71°).

4-Acetoxy-2-chloroacetanilide is the principal product of chlorination of 4-acetoxyacetanilide with chlorine (one molecular equivalent) in acetic acid. After recrystallisation from ethanol it had m.p. 126—126.5° (Found: C, 52.8; H, 4.1; N, 6.1. $C_{10}H_{10}ClO_3N$ requires C, 52.7; H, 4.4; N, 6.2%). τ [(CD₃)₂SO] 0.5 (1 H, s, NH), 2.3 (1 H, d, $J_{5,6}$ 8 Hz, H-6), 2.6 (1 H, d, $J_{3,5}$ 3 Hz, H-3), 2.9 (1 H, dd, $J_{5,6}$ 8, $J_{3,5}$ 3 Hz, H-5), 7.7 (3 H, s, OCOCH₃), and 7.9 (3 H, s, NCOCH₃).

Its isomer, 4-acetoxy-3-chloroacetanilide, was prepared from 4-nitrophenol, which was chlorinated to give 2-chloro-4-nitrophenol. This was reduced (Na₂S₂O₄) to 4-amino-2-chlorophenol which was acetylated with acetic anhydride. The resulting 4-acetoxy-3-chloroacetanilide was recrystallised from aqueous ethanol and had m.p. 120° (lit.,¹¹ 124°). (Found: C, 52.8; H, 4.2; N, 6.2%). τ [(CD₃)₂SO] —0.2 (1 H, s, NH), 2.1 (1 H, d, $J_{3,5}$ 2.5 Hz, H-2), 2.5 (1 H, dd, $J_{3,5}$ 2.5, $J_{5,6}$ 8.5 Hz, H-5), 2.8 (1 H, d, $J_{5,6}$ 8.5 Hz, H-6), 7.6 (3 H, s, OCOCH₃), and 7.9 (3 H, s, NCOCH₃). The isomers are clearly differentiated by these spectra.

2-Methylacetanilide and 1,4-diacetamidobenzene, used to interpolate into earlier series of rate comparisons, were samples prepared as described before.¹² Rates of chlorination were also determined essentially as before,¹² and rate coefficients have been calculated by using the standard second-order formula. Results for a typical kinetic run are as follows. [*p*-Acetoxyacetanilide (0.007 99M) and chlorine (0.003 55M) were allowed to react in acetic acid at 25°; aliquot parts (10.0 cm³) were removed at intervals, added to aqueous KI, and titrated with 0.004 06N-Na₂S₂O₃.] The

Time/s	336	936	1 680	2 532	3 735
Titre/cm ³	16.50	15.05	13.80	11.95	10.00
$k_2/l \text{ mol}^{-1} \text{ s}^{-1}$	0.022 4	0.020 8	0.018 6	0.020 5	0.021 0
Time/s	5 160	6 990	7 590	11 460	11 640
Titre/cm ³	8.40	6.25	6.0	3.8	3.7
$k_2/l \text{ mol}^{-1} \text{ s}^{-1}$	0.020 6	0.022 3	0.020 9	0.021 6	0.021 7

results of the measurements made in this and in other investigations^{12,13} are collected in Table 1.

Products were recovered after completion of the chlorination by removal of the bulk of the acetic acid under reduced pressure. If electrolytes were present, these were then precipitated by adding freshly distilled diethyl ether. The ether was then removed under reduced pressure; benzene was added, and it, together with the remaining traces of acetic acid, were removed *in vacuo*. The products were normally analysed by g.l.c., Varian Aerograph (series 1800 or model 1532) instruments being used. For the reaction of phenyl acetate, products were separated at 125° on a 5 ft × $\frac{1}{8}$ in aluminium column coated with 5% Carbowax 20M on acid-washed 100—120 mesh Chromosorb. A flame-ionisation detector was used, and appropriate corrections were made for the response of the various products from results obtained by using known mixtures of the reference materials. The results are given in Table 2.

When the chlorination of phenyl acetate (0.18M) with chlorine (0.13M) in the absence of added electrolytes was

⁹ P. A. Petyunin, *J. Gen. Chem. (U.S.S.R.)*, 1944, **14**, 203 (*Chem. Abs.*, 1945, **43**, 2285).

¹⁰ G. A. Varvoglis, *Ber.*, 1937, **70**, 2391.

¹¹ F. Kehrman and H. Grab, *Annalen*, 1898, **303**, 5.

¹² P. B. D. de la Mare and M. Hassan, *J. Chem. Soc.*, 1958, 1519.

¹³ K. J. P. Orton and A. E. Bradfield, *J. Chem. Soc.*, 1927, 986; B. Jones, *ibid.*, 1934, 210; 1938, 1414.

interrupted at *ca.* 88% consumption of chlorine, the product contained no 2,4-dichlorophenyl acetate, but rather more phenyl acetate than would have been expected was found by g.l.c. analysis. It was suspected, therefore, that some chlorine had been used up in the formation of adducts, as has been established also for the chlorination of biphenyl

TABLE I

Rates of chlorination of some aromatic compounds in acetic acid or aqueous acetic acid

Compound	Added substance	Temp./°C	$k_2/1 \text{ mol}^{-1} \text{ s}^{-1}$ (Note a)
Phenyl acetate	NaOAc, 0.2M	25	$4.8 \times 10^{-5}^b$
1,2-Diacetoxybenzene	NaOAc, 0.2M	25	$7.3 \times 10^{-6}^c$
1,3-Diacetoxybenzene		25	2.5×10^{-4}
1,3-Diacetoxybenzene	NaOAc, 0.2M	25	4.8×10^{-4}
1,4-Diacetoxybenzene	NaOAc, 0.2M	25	$1.0 \times 10^{-6}^c$
4-Acetoxy-acetanilide		25	0.021 4
1,4-Diacetamidobenzene		25	0.213 (lit., ¹² 0.230)
2-Methylacetanilide		25	0.190 (lit., ¹² 0.193)
4-Acetamidobiphenyl		25	0.248 ¹²
Benzene		25	$1.5 \times 10^{-6}^d, 12$
Acetanilide		25	0.93 ¹²
Acetanilide	1% H ₂ O	20	1.04 ¹³
<i>p</i> -Fluoroacetanilide	1% H ₂ O	20	$6.0 \times 10^{-3}^{13}$
<i>p</i> -Chloroacetanilide	1% H ₂ O	20	$6.0 \times 10^{-3}^{13}$
<i>p</i> -Bromoacetanilide	1% H ₂ O	20	$7.0 \times 10^{-3}^{13}$
<i>p</i> -Carboxyacetanilide	1% H ₂ O	20	$6.0 \times 10^{-3e, 13}$
<i>p</i> -Nitroacetanilide	1% H ₂ O	20	$1.5 \times 10^{-4}^{13}$

^a Except where otherwise noted, standard deviations for individual kinetic runs were in the range 1–3% with good agreement between duplicate runs. ^b In the absence of added NaOAc the reaction was autocatalytic (initial value of k_2 , *ca.* $4 \times 10^{-5} \text{ l mol}^{-1} \text{ s}^{-1}$); it was catalysed by added HCl; with added HCl (0.154M), $k_2 = 8.2 \times 10^{-5} \text{ l mol}^{-1} \text{ s}^{-1}$. With added LiCl (0.18M), autocatalytic behaviour was still observed; k_2 (initial) = $5.8 \times 10^{-5} \text{ l mol}^{-1} \text{ s}^{-1}$. ^c For the very slow reactions (in each case one kinetic run only) of 1,2- and 1,4-diacetoxybenzene in the presence of added NaOAc, substantial correction was required for the chlorination of acetic acid, determined in a 'blank' measurement. For the latter compound, this amounted to about half the measured rate, and the initial value of k_2 (5% reaction) is reported. ^d After correction for the solvent effect of the high concentration of benzene used. ^e Estimated¹³ from results for other *para*-substituted anilides.

TABLE 2

Products of chlorination of phenyl acetate in acetic acid at 25°

[PhOAc]/ M	[Cl ₂]/ M	[Added electrolyte]/ M	Substituted phenyl acetates (% total product)		
			2-Chloro	4-Chloro	2,4-Dichloro
0.20	0.12		8.5	54.8	36.7
0.20	0.14	NaOAc, 0.10	12.9	84.3	2.8
0.20	0.12	NaOAc, 0.20	12.6	87.4	
0.22	0.11	NaOAc, 0.20	13.0	87.0	
0.29	0.11	NaOAc, 0.20	12.6	87.4	
0.21	0.19	NaOAc, 0.20	13.2	86.8	
0.20	0.11	NaOAc, 0.28	14.0	86.0	
0.21	0.15	LiOAc, 0.20	12.7	87.3	
0.21	0.11	HCl, 0.15	8.0	36.3	55.7
0.21	0.11	LiCl, 0.18	12.5	84.5	3.0

and a number of its analogues.^{14,15} This was confirmed by examination (a Varian T60 instrument being used) of the ¹H n.m.r. spectrum of the product in CCl₄ (signals reported relative to tetramethylsilane as internal reference). This spectrum contained signals expected for the known products together with several additional signals near τ 7.8 (OCOCH₃) and a complex multiplet in the alicyclic region (τ 5.6–4.7),

mainly centred around τ 5.4. Integration of these signals relative to the total acetoxy-signal indicated that *ca.* 17% of the chlorine consumed had given adduct material; if, as with biphenyl,¹⁴ this material is mainly a mixture of tetrachlorides, then *ca.* 9% of the phenyl acetate consumed had given adduct. Treatment of this product with methanolic sodium methoxide in the n.m.r. tube, followed by addition of D₂O, removed these alicyclic signals.

For the diacetoxybenzenes, a similar column coated with 3% SE 30 on 100–120 mesh Varaport 30 was used, with temperature programming starting from an initial column-temperature of 120° (1,4-diacetoxybenzene) or 140° (1,3-diacetoxybenzene). For 1,4-diacetoxybenzene, the only product detected was 1,4-diacetoxy-2-chlorobenzene. 1,3-Diacetoxybenzene gave 96% 1,3-diacetoxy-4-chlorobenzene, together with small amounts of other products which were not identified; presumably one of these was 1,3-diacetoxy-2-chlorobenzene. 1,2-Diacetoxybenzene after *ca.* 9% reaction gave a major component, 1,2-diacetoxy-4-chlorobenzene (98%), together with minor amounts of two other components (each *ca.* 1%), one of which is presumed to be the 3-chloro-derivative.

Proportions of adduct similar to those found from the chlorination of phenyl acetate were detected in the products of chlorination of 1,3- and 1,4-diacetoxybenzene by treating the total product after removal of solvent in the usual way with excess of ethanolic sodium ethoxide at 78° for 90 min. The liberated chloride ion was estimated by using the standard Volhard method, and corresponded with the consumption of 18% of the chlorine to form an adduct from 1,3-diacetoxybenzene, and 22% from 1,4-diacetoxybenzene.

The 2- and 3-chloro-derivatives of 4-acetoxyacetanilide were separated clearly by g.l.c. on a 2 m column using OV 101 at 180°. The product of chlorination, an equimolar mixture of reactants being used, contained 4-acetoxy-2-chloroacetanilide (99.6%) and 4-acetoxy-3-chloroacetanilide (0.4%). Very little, if any, product of disubstitution was present; examination by mass spectrometry, a Varian CH7 instrument being used, showed that the ratio of peaks

TABLE 3

Products (% of total) of chlorination of phenol and of some chloro-substituted phenols with excess of chlorine in acetic acid containing acetyl chloride (0.09M) at 25°

Product	Aromatic compound chlorinated			
	Phenol	2-Chloro-phenol	4-Chloro-phenol	2,4-Dichloro-phenol
2-Chlorophenyl acetate		6.4		
4-Chlorophenyl acetate	0.2		1.4	
2,4-Dichlorophenyl acetate	1.0	0.5	0.7	1.0
2,4-Dichlorophenol		0.4		
2,4,6-Trichlorophenyl acetate	1.0	11.2	3.8	1.5
2,4,6-Trichlorophenol	96.2	63.5	94.0	97.5
Unidentified products	1.6	17.6		

at *m/e* 261 and 237 was < 0.02. We are indebted to Dr P. D. Woodgate for this measurement.

A number of control experiments were performed with a view to confirming or excluding possible routes to the formation of 2,4-dichlorophenyl acetate and other polychlorinated substances from phenyl acetate and chlorine. In a typical

¹⁴ G. H. Beaven, P. B. D. de la Mare, M. Hassan, E. A. Johnson, and N. V. Klassen, *J. Chem. Soc.*, 1961, 2749.

¹⁵ P. B. D. de la Mare, *Accounts Chem. Res.*, 1974, 7, 361.

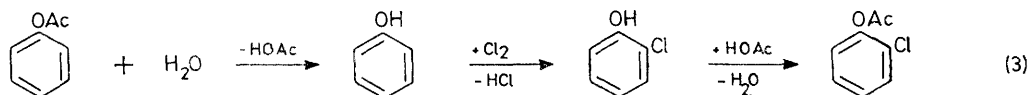
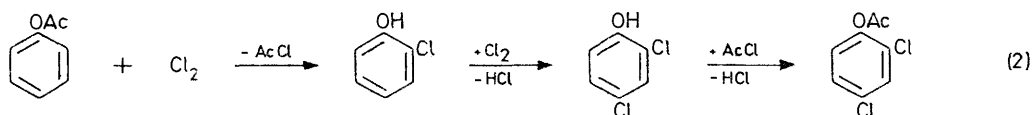
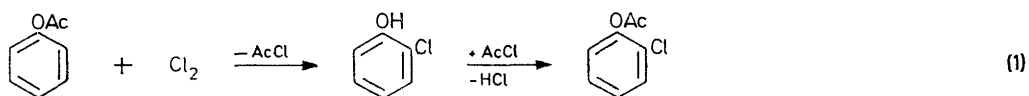
experiment, to *o*-chlorophenol (0.000 93M) in acetic acid containing acetyl chloride (0.099 8M), chlorine (0.085 7M) was added. The products were then recovered in the usual way and analysed by g.l.c. Results are given in Table 3.

In a further experiment, a solution of chlorine (0.19M) and HCl (0.055M) in acetic acid was treated with successive quantities of acetyl chloride and phenol in approximately equimolar amounts; in each addition, the initial concentrations of phenol and acetyl chloride were approximately equimolar and ranged from 0.000 5—0.014M. The products analysed by g.l.c. after each addition contained no 2,4-dichlorophenyl acetate, and were mainly (>90%) 2,4,6-trichlorophenol.

Neither 2- nor 4-chlorophenyl acetate with chlorine in acetic acid under the conditions used for the chlorination of phenyl acetate gave significant amounts of adduct or of 2,4-dichlorophenyl acetate.

DISCUSSION

(a) *Products of Chlorination of Phenyl Acetate.*—The chlorination of phenyl acetate by molecular chlorine in



acetic acid containing sodium acetate is substantially faster than that of benzene, and gives as primary products mainly 2- and 4-chlorophenyl acetates in the ratio 13:87 as estimated by g.l.c.; no 3-chlorophenyl acetate was detected. For reactions in acetic acid, in which hydrogen chloride was allowed to accumulate, mildly autocatalytic behaviour was noted; and such reaction mixtures allowed to run to completion and worked up after some time gave some 2,4-dichlorophenyl acetate. This product was not found if the reaction mixture was worked up carefully after partial reaction, nor was it obtained for reactions carried out in the presence of excess of sodium or lithium acetate.

Careful examination of the total product of chlorination, with or without added sodium acetate, and isolated with minimum decomposition, showed that it contained adducts detected from the ^1H n.m.r. spectrum and comprising material involving the consumption of *ca.* 17% of the reacting chlorine. If, therefore, as with biphenyl,¹⁴ these materials are tetrachlorides, they account for the consumption of *ca.* 8.5% of the reacting aromatic compound. The ^1H n.m.r. spectrum of the mixture suggests that more than one such compound is formed; the material is decomposed by g.l.c., when under our conditions it appears to revert to phenyl acetate and

chlorine rather than to products of substitution. On treatment with base, on the other hand, hydrogen chloride is eliminated, and both 2,4-dichlorophenyl acetate and a trichlorophenol are produced, so these adducts may include both tetra- and hexa-chlorides.

Several routes [equations (1)—(3); and the corresponding reactions at the 4-position] which conceivably could lead to the formation of the observed products of chlorination were considered.

In subsidiary experiments it was shown, however, that the chlorination of phenol or of any of the chlorophenols in acetic acid with small or large amounts of acetyl chloride, with and without added hydrogen chloride, always gave, as major product of chlorination, 2,4,6-trichlorophenol, expected because when formed in small amount in the presence of excess of chlorine it would react very much more rapidly than phenyl acetate at all the available positions activated by the hydroxy-group. Furthermore, reacylation of any phenol formed as an

intermediate occurs only slowly in the presence of acetyl chloride, and cannot compete significantly with chlorination of the phenol.

It is believed, therefore, that under the conditions used in the present experiments 2- and 4-chlorophenyl acetate are formed by conventional processes of electrophilic substitution in which a chlorine molecule attacks the aromatic substrate. Side-reactions involving chloro-deacylation appear to be absent; but *ca.* 17% of the reacting chlorine is consumed to give a mixture of adducts, probably including tetra- and hexa-chlorides and acetoxytri- and penta-chlorides.

The formation of a relatively large amount of 2,4-dichlorophenyl acetate from chlorination in the presence of developing or added hydrogen chloride may arise from the fact that reaction under these conditions gives an increased amount of adduct by capture of chloride ion. or through reversible disproportionation of the products of chlorination when these are left to stand in the presence of hydrogen chloride.

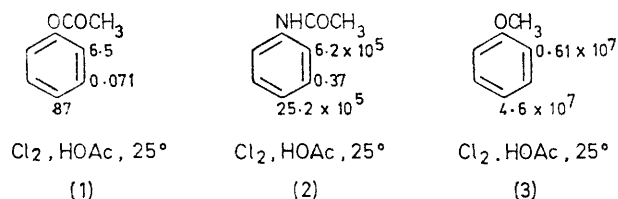
(b) *Products of Chlorination of the Diacetoxybenzenes.*—Analysis by g.l.c. showed that the chlorination of 1,3- and of 1,4-diacetoxybenzene both gave a single major product of substitution, identified by g.l.c. as 1,3-diacetoxy-4-chloro- and 1,4-diacetoxy-2-chloro-benzene,

respectively. The products of these chlorinations included also significant proportions of adducts which released hydrogen chloride on treatment with excess of sodium methoxide. Quantitatively, the amount of chlorine consumed in this way was for all these compounds quite similar to that obtained in the chlorination of biphenyl and its analogues;^{14,15} it would seem that, of the carbocationic intermediates involved in these aromatic substitutions, a proportion in the range 5–10% is captured by chloride ions to give adducts which then because of their non-aromatic character react rapidly with a further one or two equivalents of the chlorine.

(c) *Products of Chlorination of 4-Acetoxyacetanilide.*—The principal and almost exclusive product of chlorination of 4-acetoxyacetanilide is the 2-chloro-derivative, expected because the acetamido-group is much more strongly activating than the acetoxy-group.

(d) *Calculations of Partial Rate Factors for Molecular Chlorination directed by the Acetoxy-group.*—The proportions of products found in these various chlorinations can be put together with the rates of chlorination to give partial rate factors for chlorination directed by the acetoxy-group, and to enable an assessment to be made of the extent to which rates and products accord with the 'additivity principle', *viz.*, that substituent groups affect the free energy of activation for chlorination at the various ring positions independently and additively. For such a treatment to be valid even approximately, the mechanisms of all the chlorinations compared must be the same. For these aryl acetates, the kinetic form of chlorination in acetic acid is of the second order ($-d[\text{ArH}]/dt = k_2[\text{ArH}][\text{Cl}_2]$), as found for other aromatic chlorinations; and, apart from the autocatalytic behaviour observed in the presence of hydrogen chloride, is affected by other electrolytes as expected by analogy with other aromatic chlorinations,^{16,17} being accelerated through an ionic strength effect. This autocatalytic behaviour was observed only for the relatively slowly reacting acetates; so we have used the rates of chlorination of the more reactive 1,3-diacetoxybenzene in the presence and absence of sodium acetate to interpolate the rates for our other acetoxy-compounds into the series for which measurements have been made earlier.

Derived corrected partial rate factors for chlorination of acetoxybenzene and of acetanilide¹² are given in formulae (1) and (2).



(e) *Applicability of the Additivity Principle to Chlorination of the Diacetoxybenzenes.*—These partial rate factors

¹⁶ P. B. D. de la Mare, A. Singh, E. A. Johnson, R. Koenigsberger, J. S. Lomas, V. Sanchez del Olmo, and A. M. Sexton, *J. Chem. Soc. (B)*, 1969, 717.

can be used to calculate rates and products of chlorination of the diacetoxybenzenes, the additivity principle being assumed. The results are compared with experiment in Table 4.

TABLE 4

Found and calculated rates and products of chlorination of the diacetoxybenzenes by molecular chlorine in acetic acid at 25°

Compound	1,2-Diacetoxy- benzene	1,3-Diacetoxy- benzene	1,4-Diacetoxy- benzene
Corrected rate of molecular chlorination ($k_2/1 \text{ mol}^{-1} \text{ s}^{-1}$)			
Found	3.8×10^{-8}	2.5×10^{-4}	5.2×10^{-7}
Calculated	3.3×10^{-8}	2.9×10^{-4}	4.6×10^{-7}
Proportion of 4-chloro-isomer in substitution product			
Found	0.98	0.96	
Calculated	0.93	0.96	

Agreement between experiment and the predictions based on additivity of substituent effects is better than could have been expected. Although this type of treatment has been used with some success for description of the effects of alkyl,¹⁸ alkoxy,¹⁹ acetamido,¹⁹ aryl,²⁰ and now acetoxy-substituents, its theoretical applicability involves a number of assumptions, including the proposition that every event involving attack on any single nuclear position gives the product of substitution at that position. This condition is, as we have commented earlier, not satisfied when the products are partly those of addition, and this results in a degree of uncertainty in the values of partial rate factors estimated in the conventional way. Such uncertainties are unlikely, however, to affect the conclusions which will be drawn in the following discussion.

From the partial rate factors given in formulae (1) and (2), it can be calculated also that the product of chlorination of 4-acetoxyacetanilide should contain only 0.005% of the 3-chloro-isomer. In fact, the formation of *ca.* 0.4% was detected by g.l.c. Probably this arises from the decomposition of a small proportion of adduct material; a similar discrepancy arises in the *m*-chlorination of biphenyl.²⁰

(f) *Directive Power of the Acetoxy-group; Comparison with Other Substituents.*—The partial rate factor for chlorination *para*- to the acetoxy-group is 87 whereas that for the methoxy-group¹⁸ is 4.6×10^7 [compare structures (1) and (3)]; so the activating power of lone pairs of electrons of oxygen is profoundly reduced by the presence of the adjacent acetoxy-group. The related result is well known for the comparison of aniline with acetanilide.² The acetoxy-group is still, however, an *ortho*-, *para*-directing group; *ortho*-substitution is rather less important in acetoxybenzene ($f^{\text{OAc}_o} : f^{\text{OAc}_p}$ 0.07) than in anisole¹⁸ (0.13), probably because of the direct

¹⁷ P. B. D. de la Mare and P. W. Robertson, *J. Chem. Soc.*, 1943, 279.

¹⁸ L. M. Stock and H. C. Brown, *Adv. Phys. Org. Chem.*, 1963, 1, 35.

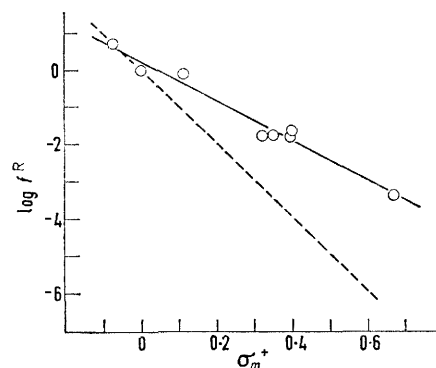
¹⁹ A. E. Bradfield and B. Jones, *Trans. Faraday Soc.*, 1941, 37, 726.

²⁰ P. B. D. de la Mare, D. M. Hall, M. M. Harris, M. Hassan, E. A. Johnson, and N. V. Klassen, *J. Chem. Soc.*, 1962, 3784; P. B. D. de la Mare and E. A. Johnson, *ibid.*, 1963, 4076.

electrostatic effect of the electron-withdrawing acetyl fragment; the steric effects of the two substituents would probably be similar, since the methyl group in anisole and the acetyl group in acetoxybenzene can dispose themselves in a conformation which does not interfere with electrophilic attack.

By using the partial rate factor for *para*-chlorination of acetanilide, the ρ value for molecular chlorination of -10 given by Stock and Brown,¹⁸ and the relationship $\log_{10} f = \rho\sigma^+$, the value of σ^+ for the *para*-acetoxy-group can be estimated to be -0.19 . The usefulness of this value depends on the precision of correlation between the rates of chlorination and the rates of solvolysis of the aryl dimethylcarbinyl chlorides used for defining σ^+ . The fact that it is of the sign opposite to that of the corresponding value of $\sigma(+0.31)$ ³ illustrates, of course, the fact that electron release from lone pairs conjugated with the aromatic system is more important relative to the opposing inductive effect in facilitating aromatic substitution than in weakening the strength of substituted benzoic acids.

of these *p*-substituted anilides are compared in Table 5 with experimental values of σ_m^+ , where these are known,



Plot of σ_m^+ against $\log f^R$ for chlorination of acetoxybenzenes

and of σ_m . Comparison with the former quantities corresponds with the best linear fit of the points for those substituents (Me, H, Ph, F, Cl, Br, CO₂H, NO₂) for which values of σ_m^+ are experimentally known (correlation

TABLE 5

Partial rate factors, f_m^R , and values of σ_m^+ derived from rates of substitution of 4-substituted acetanilides; and some related data

Substituent (R)	f_m^R (from rate of chlorination of 4-RC ₆ H ₄ NHAc)	$\log_{10} f_m^R$	σ_m^+ (from rate of chlorination of 4-RC ₆ H ₄ NHAc) (using $\rho = -5.3$)	σ_m^+ (from rate of solvolysis of 3-RC ₆ H ₄ CMe ₂ Cl) (ref. 4)	σ_m (from dissociation constant of 3-RC ₆ H ₄ CO ₂ H) (ref. 3)
Me	5.1	0.71	-0.09	-0.07	-0.07
H	1.0	0.00	0.05	0.00	0.00
Ph	0.82	-0.086	0.06	0.11	0.06
NHAc	0.35	-0.46	0.13	Not known	0.21
OCOCH ₃	0.071	-1.15	0.26	Not known	0.39
F	0.018	-1.74	0.37	0.35	0.34
Cl	0.018	-1.74	0.37	0.40	0.37
Br	0.021	-1.68	0.36	0.40	0.39
CO ₂ H	0.018	-1.74	0.37	0.32	0.37
NO ₂	0.000 44	-3.36	0.68	0.67	0.71

The ρ value (-10) used for the above estimation has been derived from studies of rates of chlorination of mono-substituted benzenes. If it could be used with confidence, in conjunction with the additivity principle, for discussion of the rates of chlorination of all disubstituted benzenes, effects of steric hindrance being allowed for where necessary, then a corresponding treatment could be used to deduce a value of σ_m^+ for acetoxy-groups and others for which direct measurements of the proportion of *meta*-substitution are impracticable, but the rates of substitution of 4-substituted anilides can be measured. Such a treatment was used earlier to obtain approximate values of σ_m for the phenyl and acetamido-groups. In the Figure, however, are plotted the values of $\log_{10} f_m^R$ determined in this way against σ_m^+ , the results of earlier investigations by Orton, Jones, and their co-workers¹⁸ being included with our own. It is clear that the results accord in a general way, though imperfectly, with a linear free-energy treatment, but that the value of ρ appropriate to these data is not -10 , but instead -5.3 . By using this value, the values of σ_m^+ for a number of substituents as determined from the rates of chlorination

coefficient r 0.988). The values of σ_m^+ thus determined for the other substituents (NHAc, OAc) are reasonable, but both of them deviate more from the experimental values of σ_m than do the σ_m^+ values determined by either method for any of the other substituents.

To discuss the results more closely, it is necessary first to consider possible reasons why the value of ρ found for the present structural situation seems to be so different from that for monosubstituted benzenes. Several possibilities exist. One is that plots of this kind should be expected to curve, because the transition-state structure changes with consequent change in ρ through the series of compounds investigated. This seems unlikely because of the additivity of substituent effects observed for the alkylbenzenes. A second is that for this reaction the σ_m^+ values for the substituents examined are genuinely much higher than expected because of enhanced electron release from these substituents to the *meta*-position, so that major and progressive deviations from the line having slope -10 (shown dotted in the Figure) are obtained. This is considered to be unlikely, because the required change in power of electron release

to, or withdrawal from, the aromatic ring is much larger than plausibly could be manifest at a position *meta* to the substituent.

Much more probable, in our opinion, is that the very high power of the acetamido-group to release electrons to the *ortho*-position can be modified by *para*-substituents, by an amount which depends on the effective electron-withdrawing power of the substituent. This is equivalent to saying that an electron-withdrawing substituent (R) in 4-RC₆H₄NHCOCH₃ increases the power of the NHCOCH₃ group to release electrons to the 2-position; so that the NHCOCH₃ group has a value of σ_o^+ which is variable, and depends in part on the electron-withdrawing power of R. In terms of a linear free-energy treatment, 'additivity' requires that equation (4) be satisfied. If, then, σ_{o-NHAc}^+ varies as in equation (5), equation (4) can be rewritten as in equation (6).

$$\log_{10}k_2 = \rho(\sigma_{m-R}^+ + \sigma_{o-NHAc}^+) \quad (4)$$

$$\sigma_{o-NHAc}^+ = (a + b\sigma_{m-R}^+) \quad (5)$$

$$\begin{aligned} \log_{10}k_2 &= a\rho + \rho(1 + b)\sigma_{m-R}^+ \\ &= a\rho + \rho'\sigma_{m-R}^+ \end{aligned} \quad (6)$$

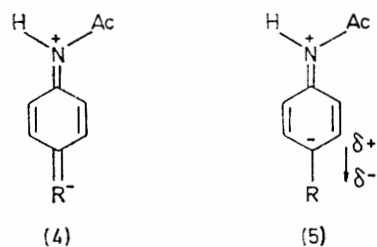
Here $a = \sigma_{o-NHAc}^+$ (R = H) and $\rho' = -5.3$ if $b = -0.47$. Under these circumstances a linear free energy relationship between $\log_{10}k_2$ and σ_{m-R}^+ will be found, but with a value of ρ' reduced from that of ρ because of progressive modification of σ_{o-NHAc}^+ by the electronic effect of the group R.

Whether equation (5) (here chosen for simplicity) or some other function of the electronic properties of R (e.g., σ_{m-R} ; σ_{p-R}) should be used could be a matter for argument. We do not think that the results are sufficiently extensive to warrant more detailed discussion except in qualitative terms, but the following matters are relevant. First, a treatment of the kind given above illustrates that ρ values can be composite quantities, and can be determined not only by the nature of the transition state for the reaction but also by structural details of the molecular environment in which reaction is occurring. A related point has been made by Schofield and his co-workers in a different context.²¹

²¹ C. D. Johnson and K. Schofield, *J. Amer. Chem. Soc.*, 1973, **95**, 270.

Secondly, the physical description of how the 4-substituent modifies the electron-releasing power of the acetamido-group is likely to be complex and involve several factors. Structure (4) illustrates how conjugative electron withdrawal could be effective in this way; in the present examples it could be of particular significance for the Ph, CO₂H, and NO₂ groups. Structure (5) shows that inductive electron withdrawal would be similarly effective, as for the OAc and halogen substituents.

Thirdly, some deviations from additivity recorded for nitration of substituted anilinium ions²² may be explicable in related terms.



Fourthly, it should be asked whether, if the 4-acetoxy-group modifies the electron-releasing power of the acetamido-group, it also similarly affects the electron-releasing power of the acetoxy-group. Although such an influence would be expected qualitatively, it certainly need not be so great for a much less powerfully electron-releasing substituent; the agreement between observed and calculated rates of chlorination of the acetoxy-benzenes (Table 4) suggests that the effect is relatively small in this case. For chlorination directed by the methoxy-group, however, the data given by Bradfield and Jones (ref. 19, Table 5) can be used to illustrate that the 2-nitro- and the 2-chloro-substituent deactivate the 4-position in anisole by amounts substantially less than expected from the σ^+ values of these groups taken in conjunction with a ρ value of -10 .

[5/1110 Received, 9th June, 1975]

²² R. S. Cook, R. Phillips, and J. H. Ridd, *J.C.S. Perkin II*, 1974, 1166.