The Kinetics and Mechanisms of Aromatic Halogen Substitution. Part 35.[1] The Directive Effect of the Benzoyloxy-substituent

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The rates of chlorination of 4-acetamidophenyl benzoate, 1,3-bisbenzoyloxybenzene, and appropriate reference compounds by molecular chlorine in acetic acid at 25 °C have been determined. By using the additivity principle, partial rate factors for chlorination directed by the benzoyloxy-group have thence been calculated, *viz.* $f_{o\text{-O}\cdot\text{CO}\cdot\text{Ph}}$ 5.5, $f_{m\cdot\text{OCO}\cdot\text{Ph}}$ 0.059, $f_{p\cdot\text{O}\cdot\text{CO}\cdot\text{Ph}}$ 52. Comparison with analogous results obtained for the acetoxy-group allow estimates to be made of σ^+ values for the benzoyloxy-substituent. These values are used to discuss the course of halogenation of 2-benzoyloxynaphthalene.

ALTHOUGH benzoylation is a common procedure for protecting the hydroxy-group of a phenol, little is known quantitatively about the electronic effect of the benzoyloxy-group. We have, therefore, used rates of molecular chlorination to define in part the effect of this substituent by comparison with that of the acetoxy-group discussed in an earlier paper.[2]

EXPERIMENTAL

Materials and methods were generally those used in earlier work.[2] Rates are for chlorination by molecular chlorine in acetic acid at 25 °C. Phenyl benzoate, m.p. 69 °C (lit.,[3] 69 °C); 1,2-bisbenzoyloxybenzene, m.p. 85 °C (lit.,[3] 84 °C); 1,3-bisbenzoyloxybenzene, m.p. 115 °C (lit.,[3] 117 °C); 1,4-bisbenzoyloxybenzene, m.p. 204 °C (lit.,[3] 199 °C); 4-acetamidophenyl benzoate, m.p. 171 °C (lit.,[4] 171 °C); *o*-chlorophenyl benzoate, b.p. 312—315 °C, n_D^{23} 1.5781 (lit.,[5] b.p. 314—316 °C); and *p*-chlorophenyl benzoate, m.p. 87 °C (lit.,[6] 88—88.5 °C), were prepared by benzoylation of the corresponding phenols. All these compounds had the expected ^{1}H n.m.r. spectra. 2-Methylacetanilide, m.p. 112 °C, was used as a reference for interpolation of the results into our earlier series.[2,7]

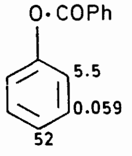
In our corresponding work on the acetoxybenzenes, kinetic disturbances resulting from the hydrogen chloride formed in the reaction affected the kinetic behaviour, and so the more slowly reacting compounds were examined in a medium containing added sodium acetate. In the present work, this difficulty was not encountered. The benzoyloxy-group is, however, less activating than the acetoxy-group, so our values for the rates of chlorination of phenyl benzoate and of 1,2- and 1,4-diacetoxybenzene required a large correction for consumption of chlorine by the medium. The results obtained for phenyl benzoate are included in the Discussion section, but for deriving conclusions relating to the effect of the benzoyloxy-group we have used the additivity principle associated with the rates of chlorination of the more rapidly reacting compounds, 4-acetamidophenyl benzoate (k_2 1.80 × 10^{-2} l mol^{-1} s^{-1}) and 1,3-bisbenzoyloxybenzene (k_2 1.42 × 10^{-4} l mol^{-1} s^{-1}). Rates are means of two concordant runs corrected for ' blank ' consumption of chlorine from the results of control experiments in which the aromatic compound had been omitted, and are considered to be reliable to within ±5 in the third significant figure. Control runs in which 2-methylacetanilide was used gave k_2 0.194 l mol^{-1} s^{-1} (lit.,[7] 0.193 l mol^{-1} s^{-1}).

For determining the *ortho* : *para* ratio for chlorination of phenyl benzoate, the product of reaction was recovered in the usual way and analysed by g.l.c. A Varian Aerograph series 14 instrument was used, with a stainless steel column of 4% Carbowax 20M on 100—120 mesh Chromosorb WHP at 230 °C and a flame ionisation detector. Standard mixtures of the pure isomers were used to calibrate the instrument. No peaks attributable to other products were detected. The resulting estimate of the *ortho* : *para* ratio for chlorination of phenyl benzoate under standard conditions is 0.21 ± 0.01.

Hazlet [8] obtained 2-benzoyloxy-1-bromonaphthalene from the bromination of 2-benzoyloxynaphthalene in hot acetic acid with iron as catalyst; more recently Prajer-Janczewska [9] reported the formation of both the 1- and the 8-bromo-derivative by a similar reaction in which a catalyst was not used. The proportions in which these products were formed was not recorded. By carrying out the reaction with initial concentrations of reactants *ca.* 0.07M in acetic acid containing 15% of water at *ca.* 50 °C and then diluting the reaction mixture with water, we have obtained nearly pure 1-bromo-2-benzoyloxynaphthalene, m.p. 99 °C (lit.,[8,9] 98.5—99.5, 100—101 °C) in 65% yield. The remaining product contained approximately equal amounts of the 1- and 8-bromo-isomers as judged by the ^{1}H n.m.r. spectrum of the mixture of acetates obtained from it. In further experiments we allowed 2-benzoyloxynaphthalene (0.024M) in 90% acetic acid to react with one mol. equiv. of bromine (a) at 30 °C and (b) at 118 °C under reflux. The products were recovered in quantitative yield. Hydrolysis (aqueous NaOH) gave mixtures of naphthols which were acetylated and examined by ^{1}H n.m.r. spectroscopy. Methyl signals at δ 2.25 and 2.15 were recorded in CCl_4 as solvent, the ratios being for (a) 3 : 1 and for (b) 1.25 : 1. Comparison with the spectrum of authentic 2-acetoxy-1-bromonaphthalene prepared from 1-bromo-2-naphthol, m.p. 84 °C (lit.,[8] 83 °C) established that the signal at δ 2.25 could be attributed to this compound. Had any unchanged starting material been left unbrominated, the derived 2-acetoxynaphthalene would have had a signal lying under that for the 1-bromo-derivative; integration of the aromatic signals relative to the methyl signals indicated, however, that very little of this possible component was present. Prajer-Janczewska's report [9,10] that the second component of the mixture of bromo-2-benzoyloxynaphthalenes is the 8-isomer being accepted, the proportion of 8-derivative formed in the bromination at 30 °C is therefore 0.25, and at 118 °C is 0.45. The change in ratio is a little more than would be expected if the energies of activation for 1- and for 8-substitution were responsible for the whole of the rate difference.

DISCUSSION

The additivity principle being assumed, the rates of chlorination of 4-acetamidophenyl benzoate and 1,3-bisbenzoyloxybenzene, together with the *ortho* : *para* ratio for chlorination of phenyl benzoate as determined in this paper, and the rate and product ratio for the chlorination of acetanilide described earlier,[7] give just sufficient information for calculation of partial rate factors for phenyl benzoate. The resulting calculated rate of chlorination of phenyl benzoate, on the basis that the rate of chlorination of benzene[7] is 1.5×10^{-6} l mol^{-1} s^{-1}, is 1.6×10^{-5} l mol^{-1} s^{-1}. Our two estimates of this rate coefficient were discordant, each requiring rather large corrections for consumption of chlorine by the solvent, but they agree semi-quantitatively: k_2 2.1 and 1.1×10^{-5} l mol^{-1} s^{-1}. Under more polar conditions, in acetic acid containing 1% water at 20 °C, a value of k_2 of 3.4×10^{-5} l mol^{-1} s^{-1} has been recorded by Bradfield and Jones,[11] in qualitative accord with our estimates.



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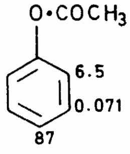

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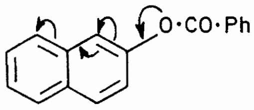


(3)

Both 1,2- and 1,4-bisbenzoyloxybenzene should by calculation react more slowly than benzene, too slowly for satisfactory measurement under our conditions. We have confirmed experimentally that these compounds are chlorinated very slowly.

The values obtained in this way are qualitatively reasonable. Comparison of partial rate factors with those determined for the acetoxy-group shows that the remote phenyl group behaves as if it were electron-withdrawing both in its inductive influence (as shown by the partial rate factors for *meta*-chlorination) and to a lesser extent in its effect on the conjugative power of the lone pairs of electrons on the oxygen atom attached to the ring (as shown by the partial rate factors for *para*-chlorination).

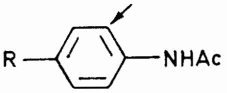
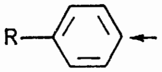
In correlating rates of different reactions by using linear free energy relationships involving single substituent parameters (σ, σ^+, or σ^-), it is usual to consider that *meta*- and *para*-substituents can be included in correlations involving a single reaction constant, ρ.[12a] It was pointed out earlier, however,[2] that for molecular chlorine a better correlation of rate with σ^+ is obtained if it is considered that the ρ values for *meta*- and *para*-substitution are different. This is particularly apparent if values of partial rate factors for *meta*-substitution are obtained by the indirect procedure used in the present work. On this basis, a ρ value of -5.3 should be used to estimate the value of $\sigma^+_{m\text{-O·COPh}}$ as $+0.23$. This accords to the expected degree of approximation with the accepted[12b] value of $\sigma_{m\text{-O·COPh}}$ $(+0.21)$ determined from the strengths of substituted benzoic acids. It is accepted conventionally[12c] that values of σ_m^+ for electron-withdrawing groups should be the same as the corresponding values of σ_m to a good approximation These values for the O·COPh group are rather less than that estimated for σ_I from the rates of third-order bromination of $RCH_2 \cdot CH{:}CH_2$ (σ_I^{OCOPh} $+0.36$).[13] In our view, this difference results from the fact that there is significant conjugative interaction between the lone-pairs of the oxygen atom (-O- in -O-COPh) and the *meta*-position in the attacked ring. Treatment of the same data set by using the dual substituent parameter equation (1)[14] gives values (Table

$$\log_{10}(k/k_0) = \rho_I\sigma_I + \rho_R\sigma_R^+ \qquad (1)$$

1) which accord with this conclusion, since ρ_R and hence σ_R^+ makes a marked contribution to the total electronic effect of any given substituent on the rate of chlorination, even when the substituent is *meta* to the point of attack.

TABLE 1

Dual substituent parameter treatment applied to molecular chlorination directed by *meta*- and by *para*-substituents

Reaction	ρ_I	ρ_R	Origin of data set
	−4.83	−1.21	Ref. 2 and papers therein cited
+ Cl_2 in 99% HOAc or in HOAc			
	−9.03	−10.33	Ref. 15

From the partial rate factor for substitution *para* to the benzoyloxy-group, a value $\sigma^+_{p\text{-O·CO·Ph}}$ of -0.17 can be estimated. By analogy with the corresponding results for the acetoxy-group, this value is likely to be rather more negative (probably by *ca.* 0.1) than that which would be obtained if the rate of solvolysis of m-PhCO·O·$C_6H_4CMe_2Cl$ were examined.

There exist only a very few substituents for which a direct determination of the much discussed ' selectivity factor '[16,17] for molecular chlorine has proved to be possible. With the results of the present work, however, there are now available eight indirect estimates made by comparison of the two reaction series shown in Table 1. These values, and the derived selectivity factors, are given in Table 2.

Selectivity factors tend to be higher for the more reactive substituents, because they include a large numerical component from $f_{p\text{-R}}$ values, which cover a wider range than that covered by $f_{m\text{-R}}$. There is, however, no obvious linear relationship between $\log_{10}f_{p\text{-R}}$ and $\log_{10}f_{m\text{-R}}$ as would have been expected[18] if the selectivity relationship held accurately. This is apparent in Table 2 from the fact that the phenyl substituent, which is more activating for the *para*-position than the acetoxy- or benzoyloxy-group, has a lower value of S_f.

TABLE 2

Selectivity factors in molecular chlorination

Substituent (R)	$\log_{10}f_{p\text{-R}}$ [a]	$\log_{10}f_{m\text{-R}}$ [b]	$S_f = \log_{10}(f_{p\text{-R}}/f_{m\text{-R}})$
NHAc	6.40	−0.46	6.86
Me	2.91	0.71	3.62
Ph	2.78	−0.09	2.87
OAc	1.94	−1.15	3.09
OBz	1.71	−1.24	2.95
F	0.59	−1.74	2.33
Cl	−0.40	−1.74	1.34
Br	−0.52	−1.68	1.16

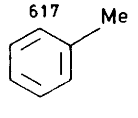
[a] From rates of chlorination of RC_6H_5 in HOAc or aqueous HOAc. [b] From rates of chlorination of *p*-RC_6H_4·NHAc in HOAc or aqueous HOAc.

The ratio $f_{o\text{-R}}/f_{p\text{-R}}$ for the benzoyloxy-group is within experimental error the same as that for the acetoxy-group; its low value (0.106) probably reflects a somewhat greater inductive influence at this position than elsewhere, since its steric effect would not be expected to be very large. The result is that the *o*-benzoyloxy-group is only modestly activating for molecular chlorination ($f_{o\text{-O·CO·Ph}}$ 5.5).

This result is useful in interpreting observations by Prajer-Janczewska[9] concerning the products of bromination of 2-benzoyloxynaphthalene. This reaction was shown to give not only the expected 1-bromo-derivative but also its 8-bromo-isomer. The 8-position, being conjugated with the 2-substituent, is expected to be more reactive than any other, excepting the 1-position, in molecules of this kind.[19] The extent of the expected activation of the various positions can be estimated by assuming that linear free energy relationships apply to these aromatic halogenations. Structures (4)—(7) show the necessary comparisons.

Of the estimated values in (7), the conclusion that the 1-position would be activated only very modestly depends only on the expected linear free energy relationships already well established.[16,19] The estimated value for the 8-position, however, depends also on the extent to which a linear free energy relationship between $\log_{10}f_{8\text{-R}}$ and $\log_{10}f_{1\text{-R}}$ is followed accurately. This has the justification that the 8-position is, like the 1-position, formally conjugated with the 2-substituent as shown by the arrows in structure (3). Its behaviour might therefore resemble that of the *ortho*- and *para*- rather than of the *meta*-positions in benzene.

The predicted values would allow for the formation of *ca.* 23% of the 8-bromo-derivative of (7). Experimentally, for reaction in 90% acetic acid at 30 °C, we estimate that *ca.* 25% is formed, and we have confirmed that most of the rest is the 1-bromo-isomer. For 2-methylnaphthalene,[19] small proportions of the products of 4- and 5-substitution were found also; but for 2-benzoyloxynaphthalene this would not be expected, since the substituent is not conjugated with these positions which therefore would be subject to the full deactivating influence of the substituent.



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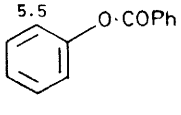
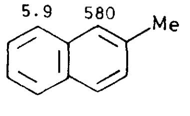


(5)

Experimental partial rate factors (one position in benzene = 1) for molecular chlorination in acetic acid (ref. 16 and this paper)



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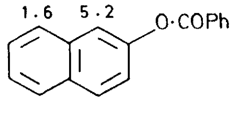

(7)

Experimental (6)[19] and estimated (7) partial rate factors (rate at a single 1-position in naphthalene = 1) for molecular bromination in acetic acid

Qualitatively, the change in product proportions with temperature is in the direction expected; the isomer formed in smaller proportion at 30 °C is formed in more nearly equal proportion at 118 °C. Quantitatively, however, a somewhat larger difference in energies of activation for substitution in the two positions than in free energies of activation is required to produce the observed change in proportions. A corollary is that the entropy of activation for substitution in the 1-position must be somewhat lower than that for the 8-position, as is consistent with its more congested nature.

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