937. *The Cumulative Effect of Substituents in an Aromatic Nucleus on Reactions of the Side-chain: The Effect of Chlorine as Substituent on the Reaction of Benzoyl Chlorides with Aniline, on the Alkaline Hydrolysis of Ethyl Benzoates, and on the Ionisation of Benzoic Acids.*

By J. G. MATHER and J. SHORTER.

Rate coefficients (usually at four temperatures) have been measured for the reactions of benzoyl chloride, three monochlorobenzoyl chlorides, and six dichlorobenzoyl chlorides with aniline in benzene, and for the alkaline hydrolysis of ethyl benzoate, three ethyl monochlorobenzoates, and all ethyl dichlorobenzoates except the 2,6-isomer, in aqueous ethanol containing 84·6% (w/w) of ethanol. Arrhenius parameters have been evaluated. Values of pK_a in water at 22° have been measured potentiometrically for all dichlorobenzoic acids, except the 3,4-isomer.

The relative effect of *m*-Cl and *p*-Cl on the reactivity of benzoyl chloride towards aniline is compared with their relative effect on alkaline ester hydrolysis and on acid dissociation. *o*-Chlorobenzoyl chloride is the most reactive of the three isomers, and there is no distinctive effect of *o*-Cl on the Arrhenius non-exponential factor (cf. alkaline ester hydrolysis), but a second *o*-Cl reduces the reactivity greatly. The relation between the effects of *o*-Cl, *m*-Cl, and *p*-Cl on reactivity in the benzoylation is examined in terms of a simple electrostatic theory.

The 3,5-, 2,4-, and 2,5-dichloro-compounds show strict additivity of substituent effects in ester hydrolysis and acid dissociation, but departures from additivity in the reaction of benzoyl chlorides with aniline are considerable. In the case of 3,4-dichloro-compounds there is a departure from strict additivity of substituent effects which is probably due to electrostatic interaction of the C–Cl dipoles. The 2,3-dichloro-compounds show an additional effect due to the three substituents' being adjacent on the ring. The ionisation of 2,6-dichlorobenzoic acid shows strict additivity, whereas in the other systems the 2,6-isomers show great departures.

DURING recent years attention has been paid to the combined effect of two or more nuclear substituents on the reactivity of aromatic side-chains, in order to discover the extent to which substituent effects are additive and to explain departures from strict additivity. Considerable variety and complexity of behaviour has been observed.[1-5] We felt that it would be valuable to study systematically the effect of a particular substituent in various types of reaction. The small monatomic substituent chlorine was chosen since it produces large changes in the reactivity of aromatic compounds. The reactions selected

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[1] (*a*) Stubbs and Hinshelwood, *J.*, 1949, S71; (*b*) Bose and Hinshelwood, *J.*, 1958, 4085.

[2] (*a*) Jones and Robinson, *J.*, 1955, 3845; (*b*) Crocker and Jones, *J.*, 1959, 1808; (*c*) Jones and Watkinson, *J.*, 1958, 4064.

[3] Shorter and Stubbs, *J.*, 1949, 1180.

[4] Peltier, *Bull. Soc. chim. France*, 1958, 994, and papers referred to therein.

[5] Dippy, Hughes, and Bray, *J.*, 1959, 1717, and papers referred to therein.

were that between substituted benzoyl chlorides and aniline, the alkaline hydrolysis of substituted ethyl benzoates, and the ionisation of substituted benzoic acids.

The kinetics of the reaction between benzoyl chloride and aniline in benzene solution were first studied by Hinshelwood and his colleagues.[6] The reaction takes place quantitatively according to the equations:

$$\mathrm{Ph{\cdot}COCl + NH_2Ph = Ph{\cdot}NH{\cdot}COPh + HCl}$$
$$\mathrm{PhNH_2 + HCl = Ph{\cdot}NH_3^+Cl^-}$$

the aniline hydrochloride being precipitated. The reaction is of the second order, the first stage being slow and the second very rapid. The second-order rate coefficients fall slightly with decrease in the initial concentration of the reactants. (In certain solvents such as hexane and carbon tetrachloride the kinetic behaviour is complicated,[6a] and the dilution effect in benzene is presumably a residuum of such complication.) In the early work the effect of *meta*- and *para*-substituents in the benzoyl chloride and aniline molecules was investigated. Stubbs and Hinshelwood [1a] studied the effect of *ortho*-substituents in the aniline molecule and also the cumulative effect of substituents in the aniline molecule. More recently Benkeser *et al.*[7] have studied the reactions of several *meta*- and *para*-substituted benzoyl chlorides with aniline in benzene; Bose and Hinshelwood [1a] have investigated the reaction in nitrobenzene and other polar solvents; Elliott and Mason [8] have examined kinetic isotope effects; and various aspects of the benzoylation of aniline have been investigated by Litvinenko and his colleagues.[9]

There have been many studies of the influence of nuclear substituents on the rate of alkaline hydrolysis of ethyl benzoate and the ionisation of benzoic acid, so only those concerned with the cumulative effect of two or more substituents will be mentioned here.

Blakey, McCombie, and Scarborough [10] measured the rates of hydrolysis of mono- and di-substituted ethyl benzoates in aqueous ethanol, including all ethyl dichlorobenzoates except the 2,6-isomer. For ethyl *o*-chlorobenzoate, however, they obtained two sets of rate coefficients differing by some 30% under the same experimental conditions; they were unable to explain this. Studies of the combined effect of two substituents *ortho* to each other on the saponification of ethyl benzoate have been made by Price and Lincoln, and by Westheimer and Metcalf in order to investigate steric inhibition of resonance.[11] Brynmor Jones and Robinson [2a] studied a variety of 3,4- and 3,5-disubstituted ethyl benzoates, including the dichloro-esters. The 3,5-compounds showed good additivity of substituent effects, but the 3,4-compounds showed appreciable departures from strictly additive behaviour.

Ten years ago few really accurate measurements of the dissociation constants of disubstituted benzoic acids had been made, although there was much accurate information on the dissociation constants of monosubstituted acids.[12] In 1949 Shorter and Stubbs [3] surveyed the available data for the classical dissociation constants of disubstituted benzoic acids. The change in the free energy of ionisation caused by two or more substituents in benzoic acid was shown in a number of cases to be very nearly the algebraic sum of the effects of the individual groups, but certain 2,3- and 2,6-disubstituted acids provided striking exceptions. In the last 10 years a number of accurate measurements of the dissociation constants of disubstituted benzoic acids have been made, mainly by Dippy [5] and by Peltier [4] and their colleagues. Considerable variety of behaviour in the cumulative effects of substituents has been observed. When the present work was started no value for the

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[6] (*a*) Grant and Hinshelwood, *J.*, 1933, 1351; (*b*) Williams and Hinshelwood, *J.*, 1934, 1079; (*c*) Newling, Staveley, and Hinshelwood, *Trans. Faraday Soc.*, 1934, **30**, 597.

[7] Benkeser, de Boer, Robinson, and Sauve, *J. Amer. Chem. Soc.*, 1956, **78**, 682.

[8] Elliott and Mason, *Chem. and Ind.*, 1959, 488.

[9] See, *e.g.*, Litvinenko and Aleksandrova, *Ukrain. khim. Zhur.*, 1960, **26**, 66.

[10] Blakey, McCombie, and Scarborough, *J.*, 1926, 2863.

[11] Price and Lincoln, *J. Amer. Chem. Soc.*, 1951, **73**, 5838; Westheimer and Metcalf, *J. Amer. Chem. Soc.*, 1941, **63**, 1339.

[12] Dippy, *Chem. Rev.*, 1939, **25**, 151.

dissociation constants of any dichlorobenzoic acids had been published. Davis and Hetzer[13] have recently presented values for 2,4-, 3,4-, and 2,6-dichlorobenzoic acid, measured by potentiometric titration or spectrophotometry, and Dippy, Hughes, and Bray[5] have studied 2,4-, 2,5-, and 2,6-dichlorobenzoic acid by conductivity measurements.

EXPERIMENTAL

Preparation and Purification of Benzoic Acids.—Commercial benzoic acid, the monochlorobenzoic acids, and 2,4-, 2,5-, and 3,4-dichlorobenzoic acid were crystallised to constant m. p. from aqueous ethanol, glacial acetic acid, and benzene. Ethyl esters made from these acids gave satisfactory second-order kinetics in alkaline hydrolysis.

2,3-Dichlorobenzoic acid was prepared from 2,3-dichloroaniline by diazotisation and a Sandmeyer reaction, followed by acid hydrolysis of 2,3-dichlorobenzonitrile. To obtain pure 2,3-dichlorobenzoic acid it was essential to purify 2,3-dichloroaniline carefully by fractional freezing, and to isolate the nitrile by steam-distillation and crystallise it from ethanol. The nitrile was hydrolysed by refluxing with 60% sulphuric acid for 1 hr. 2,3-Dichlorobenzoic acid was crystallised to constant m. p. from aqueous ethanol.

2,6-Dichlorobenzoic acid was prepared from 2,6-dichlorotoluene by Lehmstedt and Schrader's method.[14]

3,5-Dichlorobenzoic acid was prepared from anthranilic acid as described by Brynmor Jones and Robinson.[2a]

Preparation and Purification of Benzoyl Chlorides and Aniline.—The benzoyl chlorides were usually made from the pure benzoic acids by treatment with thionyl chloride, and were repeatedly distilled under reduced pressure. In certain cases carefully fractionated commercial samples of the benzoyl chlorides were used. Aniline was purified by distillation at atmospheric and finally under reduced pressure.

Preparation and Purification of Ethyl Benzoates.—The benzoic acids were usually esterified with ethanol and sulphuric acid. Liquid esters were fractionated under reduced pressure; solid esters were recrystallised from light petroleum (b. p. $<30°$). In each case the ester was purified until it gave consistent second-order kinetics in alkaline hydrolysis. It was necessary to redistil certain esters every few days to keep them in a condition to satisfy this kinetic criterion of purity.

In the case of ethyl 2,3-dichlorobenzoate it was found that the product of esterification by the action of ethyl iodide on the silver salt gave more consistent kinetics than that made by the usual method. Ethyl 2,6-dichlorobenzoate was made by the silver salt–ethyl iodide method.

Purification of Solvents.—"AnalaR" benzene was dried ($MgSO_4$) and fractionated through a Widmer column (b. p. 79·5—80°, lit., 80·1°; n_D^{20} 1·5007, lit., 1·5009). Williams and Hinshelwood[6b] showed that elaborate purification of benzene was unnecessary.

Ethanol was purified by the magnesium–iodine method. It was mixed with boiled-out conductivity water to give a mixture containing 84·6% (w/w) of ethanol.

Measurement of Rate Coefficients for the Benzoylation Reaction.—As in earlier work the reaction was followed by filtering-off the aniline hydrochloride produced, dissolving this in water, and estimating the chloride by Volhard's method.[1,6] Since there is a slight effect of dilution on the rate coefficients it was desirable for comparison of coefficients to be made at standard concentrations. The reaction between aniline and the chloro-substituted benzoyl chlorides being rapid, low concentrations of reactants were used: 0·005M-aniline and 0·0025M-benzoyl chloride. This is Williams and Hinshelwood's "Dilution III."[6b] If the initial concentration of benzoyl chloride is a and that of aniline $2a$ mole l.$^{-1}$, and x is the percentage change after t min., then $k = x/120a.t(100 - x)$, where k is the second-order rate coefficient in l. mole^{-1} sec.$^{-1}$. At temperatures other than 15° or 25°, rate coefficients were corrected for thermal expansion or contraction of the solvent.

Typical results are shown in Table 1. The mean deviation in k in most experiments was 1—2% over 80% of the course of the reaction.

Measurement of Rate Coefficients in Ester Hydrolysis.—Equal concentrations (0·05M) of ester and sodium hydroxide (carbonate-free) were used. The reaction was followed by running

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[13] Davis and Hetzer, *J. Phys. Chem.*, 1957, **61**, 123.

[14] Lehmstedt and Schrader, *Ber.*, 1937, **70**, 1526.

TABLE 1.

Aniline and 2,4-dichlorobenzoyl chloride at 15°.

t (min.)	5	10	15	25	40	60
x (%)	30·75	46·9	57·1	68·25	78·05	83·8
10^2k (l. mole^{-1} sec.$^{-1}$)	29·55	29·50	29·68	28·81	29·60	28·77

Mean value of $10^2k = 29{\cdot}32$ ($\pm 1{\cdot}2\%$).

Aniline and benzoyl chloride at 25°.

t (min.)	10	20	40	60	80	100	140	200
x (%)	16·6	28·75	45·4	55·4	61·9	66·5	74·1	80·5
10^2k (l. mole^{-1} sec.$^{-1}$)	6·67	6·71	6·92	6·91	6·77	6·63	6·81	6·91

Mean value of $10^2k = 6{\cdot}79$ ($\pm 1{\cdot}5\%$).

samples into ice-cold hydrochloric acid (measured excess) and titrating the excess of acid with standard sodium hydroxide solution (bromothymol Blue as indicator).[2a,15] The reaction was timed from the removal of the first sample and the analysis of this provided the initial concentration a for the second-order rate expression: $k = x/60a.t(a - x)$, where x is the concentration of ester or alkali (mole l.$^{-1}$) that has reacted after time t (min.), k being in units l. mole^{-1} sec.$^{-1}$.

Typical results are shown in Table 2. The mean deviation in k in most experiments was 1—2% over about 70% of the course of the reaction.

Measurement of Strengths of Benzoic Acids by Potentiometric Titration.—A direct-reading pH-meter (Electronic Instruments Ltd., model 23A) was used. The titration vessel was fitted with glass electrode, calomel reference electrode (saturated potassium chloride), and mechanical stirrer; a potassium hydrogen phthalate buffer solution was used for standardisation. Solutions of the benzoic acids (0·01, 0·001, or 0·0005M according to solubility) were made up in boiled-out conductivity water under nitrogen. 50 ml. portions were titrated with carbonate-free sodium hydroxide (0·04N for 0·01M-acid; 0·01N for 0·001 or 0·0005M-acid), the pH being read after each addition of 0·25 ml. of alkali. The titration was continued to the theoretical half-equivalence point. Strict temperature control was not necessary since pK_a varies only slightly with temperature; the experiments were made at 22° ± 0·5°. Values of pK_a were calculated by means of the following equations: [13]

TABLE 2.

Alkaline hydrolysis of ethyl 2,4-dichlorobenzoate at 25°.

t (min.)	0	15	30	45	60	80	100	120	150
10^3x (mole l.$^{-1}$)	0·0	9·9	16·5	20·4	23·5	26·7	28·8	30·8	32·6
10^3k (l. mole^{-1} sec.$^{-1}$)	—	7·33	7·57	7·26	7·25	7·30	7·15	7·36	7·22

$a = 0{\cdot}0440$ mole l.$^{-1}$. Mean value of $10^3k = 7{\cdot}31$ ($\pm 1{\cdot}2\%$).

Alkaline hydrolysis of ethyl 2,3-dichlorobenzoate at 15°.

t (min.)	0	10	20	40	80	130	220	300	360
10^3x (mole l.$^{-1}$)	0·0	2·6	5·1	8·9	15·4	20·9	26·9	30·3	32·0
10^3k (l. mole^{-1} sec.$^{-1}$)	—	2·02	2·10	2·01	2·09	2·11	2·07	2·05	2·00

$a = 0{\cdot}0476$ mole l.$^{-1}$. Mean value of $10^3k = 2{\cdot}06$ ($\pm 1{\cdot}8\%$).

$$\mathrm{p}K_\mathrm{a} = \mathrm{pH} - \log([\mathrm{B}^-]/[\mathrm{HB}]) - \log f_{\mathrm{B}^-}$$

$$-\log f_{\mathrm{B}^-} = 0{\cdot}5\sqrt{\mu}/(1 + 1{\cdot}32\sqrt{\mu}),$$

where $[\mathrm{B}^-]$ is the concentration of benzoate ion, [HB] is that of undissociated benzoic acid, and f_{B^-} is the activity coefficient of the benzoate ion at ionic strength μ. Table 3 shows a typical set of values of pK_a at different points in the titration. The mean deviation in such sets of values of pK_a was usually 0·01—0·02.

With a 0·01M-solution of benzoic acid itself pK_a was found to be 4·21, in good agreement with the value of 4·203 given by Dippy [12] (conductivity measurements, 25°) and that of 4·205 obtained by Jones and Parton [16] (E.M.F. measurements, 20°). At 0·001M-concentration,

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[15] Evans, Gordon, and Watson, *J.*, 1937, 1430.

[16] Jones and Parton, *Trans. Faraday Soc.*, 1952, **48**, 8.

TABLE 3.

Determination of pK_a for 2,5-dichlorobenzoic acid at 22°.

NaOH (ml.)	0·25	0·50	0·75	1·00	1·25	1·50	1·75	2·00
pH	3·16	3·18	3·21	3·24	3·27	3·30	3·34	3·38
pK_a	2·65	2·62	2·63	2·66	2·63	2·62	2·64	2·65

50 ml. of 0·001M-acid were titrated with 0·01N-sodium hydroxide. Mean value of pK_a = 2·64 ± 0·01.

however, the observed value was 4·30 and at 0·0005M it was 4·32. We attribute this apparent rise in pK_a with dilution to the failure of the saturated potassium chloride bridge to eliminate completely the liquid-junction potential at very low concentrations of organic acid and salt. We therefore express the results for the chloro-substituted acids as ΔpK_a values, *i.e.*, relative to benzoic acid under the same conditions of concentration. Thus the ΔpK_a value for 2,5-dichlorobenzoic acid, calculated from the results in Table 3, is 4·30 − 2·64 = 1·66.

DISCUSSION

Influence of Chlorine Substituents in Benzoyl Chloride on Reactivity towards Aniline.—Rate coefficients, *k*, activation energies, *E*, and non-exponential factors, *A*, from the Arrhenius equation are shown in Table 4.

TABLE 4.

Rate coefficients and Arrhenius parameters for reaction of benzoyl chlorides with aniline.

Subst.	10^2k (l. mole^{-1} sec.$^{-1}$) 5°	15°	25°	35°	*E* (cal. mole^{-1})	log *A*
H	3·33	5·07	6·79 [a]	11·8	6910	3·95
o-Cl	15·6	22·0	30·4	42·2	5610	3·60
m-Cl	9·29	14·3	19·7	27·9	6140	3·81
p-Cl	4·91 [b]	7·56	10·7 [c]	15·8	6540 [d]	3·83
2,3-Cl_2	22·2	31·4	42·9	60·5	5630	3·77
2,4-Cl_2	19·7	29·3	41·3	57·7	6070	4·07
2,5-Cl_2	32·9	47·0	66·3	88·7	5630	3·95
2,6-Cl_2	0·110 *	0·153 †	0·0152	—	10,630	3·99
3,4-Cl_2	11·7	16·6	25·3	32·3	5890	3·70
3,5-Cl_2	23·3	32·6	43·7	58·7	5200	3·46

* At 60°. † At 70°.

Values of *k* are accurate within ±2%. Values of *E* are accurate within ±300 cal. mole^{-1}. Values of log *A* are accurate to within ±0·3. Values given by Williams and Hinshelwood [6b] are *a* 6·88; *b* 4·65; *c* 10·4; *d* 7000.

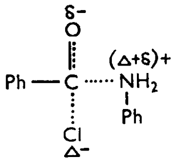

FIG. 1.

Williams and Hinshelwood [6b] showed that electron-attracting substituents in the benzoyl chloride molecule increase the reactivity towards aniline. Withdrawal of electrons from the carbonyl chloride group facilitates the approach of the lone pair of electrons of the amino-group to the carbonyl carbon atom and the attainment of the transition state, which may be represented [8] as in Fig. 1. It is therefore to be expected that *m*- and *p*-chlorobenzoyl chloride will be more reactive than benzoyl chloride. In fact all three monochlorobenzoyl chlorides are more reactive than benzoyl chloride; values of *E* are lower and those of *k* higher for the chloro-substituted compounds. *m*-Chlorobenzoyl chloride is more reactive than the *para*-isomer; in the latter the $-I$ effect of chlorine is in competition with its $+M$ effect. If the effect of a substituent upon reactivity is expressed as log (k/k_0), where k refers to the substituted compound and k_0 to the unsubstituted compound, then the relative effect of *m*-Cl and *p*-Cl upon reactivity is 2·6 (mean value for the four temperatures in Table 4). In the saponification of ethyl benzoates the corresponding value is 1·4, derived from the five temperatures in Table 5. The ratio of the Hammett σ values for *m*-Cl and *p*-Cl is 1·65, this being essentially the relative effect of the substituents on the dissociation of benzoic acid.[17] This striking difference between the effect of chlorine substituents in the benzoylation on the one hand and in ester saponification and acid dissociation on the other may possibly be explained along the following lines. In the transition state for ester hydrolysis the seat of the reaction carries a negative charge, as does the final state in the acid dissociation, the benzoate ion. It may be that under these circumstances the $+M$ mesomeric effect of *p*-Cl has less influence than in the transition state for the benzoylation of aniline, where the seat of the reaction carries no resultant charge. Since the $+M$ effect reduces reactivity in all three reactions under consideration, the relative effect of *m*-Cl and *p*-Cl on reactivity should be lower in ester saponification and acid dissociation than in the benzoylation, as found experimentally.

The relative effect of *m*-Br and *p*-Br in benzoyl chloride calculated from the results of Benkeser *et al.*[7] is 2·01; the ratio of the σ values is 1·68. The behaviour of bromine is thus qualitatively similar to that of chlorine but not so striking. The greater $+M$ effects of certain *para*-substituents in benzoylation than in the dissociation of benzoic acid can also be seen from the *effective* σ values calculated by van Bekkum, Verkade, and Wepster [18] for substituents in the benzoyl chloride molecule.[7] These σ values are: *p*-Cl, +0·172; *p*-Br, +0·202; *p*-Me, −0·231; *p*-OMe, −0·499. The σ values, based on the results of Dippy and his colleagues for the dissociation of substituted benzoic acids,[12] are *p*-Cl, +0·224; *p*-Br, +0·232; *p*-Me, −0·170; *p*-OMe, −0·268. Values in the former set are more negative than corresponding values in the latter, corresponding to a greater $+M$ effect.

The relative effect of *m*-Cl and *p*-Cl on the reactivity of aniline is 1·8, calculated from Stubbs and Hinshelwood's results.[1a] (Electron-attracting substituents in the aniline molecule reduce reactivity.) This value is appreciably smaller than that for substituents in benzoyl chloride. In *p*-chloroaniline the operation of the $+M$ effect of chlorine will enhance reactivity, but the mesomeric effect acts in opposition to the $+M$ effect of the amino-group and may therefore be of less influence than in *p*-chlorobenzoyl chloride. This would lead to a lower value for the relative effect of *m*-Cl and *p*-Cl on the reactivity of aniline than for their relative effect in benzoyl chloride.

o-Chlorobenzoyl chloride is the most reactive of the three isomers. In this behaviour the benzoylation is in marked contrast to the alkaline hydrolysis of ethyl benzoates, where the *o*-chloro-compound is the least reactive of the three isomers; ethyl *o*-chlorobenzoate has the lowest activation energy but the non-exponential factor is much lower than those of the *meta*- and the *para*-isomer (Table 5). *o*-Chlorobenzoyl chloride has the lowest activation energy of the isomers but the non-exponential factors of all three isomers are approximately the same (Table 4). The values of log A for *m*-chloro-, *p*-chloro-, 3,4-dichloro-, and 3,5-dichloro-benzoyl chloride and for benzoyl chloride itself have a mean value of 3·8 ± 0·1. The values for *o*-chloro- and 2,3-, 2,4-, 2,5-, and 2,6-dichloro-benzoyl chloride have a mean value of 3·9 ± 0·2. The absence of an effect of *o*-Cl on log A is particularly striking in the case of 2,6-dichlorobenzoyl chloride; the second *o*-chlorine atom greatly *reduces* the reactivity but this is due entirely to an increase in the activation energy. Stubbs and Hinshelwood [1a] found that there was no effect on log A of *ortho*-substituents in aniline, the groups studied being *o*-Me, 2,6-Me_2, *o*-Cl, and *o*-NO_2. The constancy of log A for a variety of *ortho*-substituents in aniline and for *o*-Cl and 2,6-Cl_2 at least in benzoyl chloride is of interest in connection with the transition state, which is now to be discussed.

The Transition State in the Reaction between Benzoyl Chloride and Aniline.—A representation of the transition state due to Elliott and Mason [8] has been shown above. A model of the transition state can usefully be made from molecular models of the Stuart pattern. The carbon and nitrogen atoms at the reaction centre are represented by a " paraffinic carbon " and a " quaternary nitrogen," respectively. We may distinguish two possible

[17] Jaffé, *Chem. Rev.*, 1953, **53**, 191.

[18] van Bekkum, Verkade, and Wepster, *Rec. Trav. chim.*, 1959, **78**, 815.

extreme configurations for the transition state. In one form, which we shall call the extended configuration, the rings are on opposite sides of the C–N bond linking the two reacting molecules, and in the most symmetrical arrangement the rings lie parallel (Fig. 2a). There is fair freedom of rotation about the ring–COCl bond, but rotation about the ring–NH bond is greatly restricted; when the ring of the aniline is rotated the *ortho*-hydrogen atoms engage with the oxygen and chlorine atoms. In the other form, which we shall call the compact configuration, the rings are on the same side of the C–N bond linking the two reacting molecules. The rings are inclined at an angle to each other (Fig. 2b). There is little freedom of rotation for either ring; slight rotation of either ring causes it to engage with the other.

It seems likely that the withdrawal of the hydrogen and the chloride ions would occur more easily from the compact than from the extended configuration. In the compact configuration, however, the rings are pressed rather close together, since the C–N partial bond is not likely to be more than 2 Å long. The normal closest distance of lateral approach of two aromatic rings,[19] as for example in the formation of charge-transfer complexes,[20] is 3·2—3·5 Å. Thus the compact configuration would involve very considerable interaction of the π-electron systems of the two rings, and this would make it energetically very unfavourable compared with the extended configuration. We therefore conclude that the actual transition state will approximate more closely to the extended than to the compact configuration.

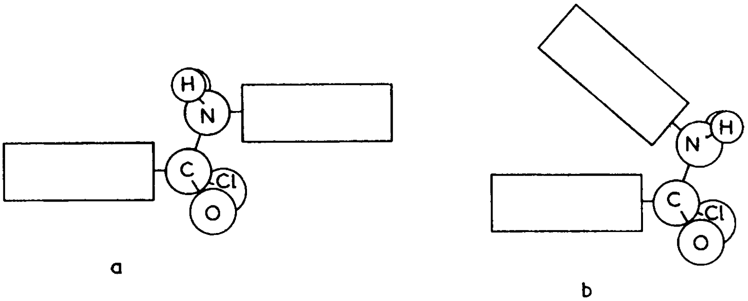

FIG. 2.

Study of the model shows that a chlorine atom, a methyl group, or a nitro-group can be introduced into either *ortho*-position of the aniline in the extended configuration of the transition state without steric strain and without much increase in the restriction of the rotation of the aniline ring, the rotation of which is already greatly restricted. The absence of any effect on log A for *ortho*-substituents in the aniline molecule is thus readily explicable.

We pass now to the effect of introducing an *o*-chlorine atom into the benzoyl chloride molecule. Inspection of the model suggests that this should restrict greatly the rotation of the benzoyl chloride ring in the transition state (as compared with the initial state). If this were really so, however, a fall in log A would result, as in ester hydrolysis. The constancy of the non-exponential term means that the rotation of the ring in the transition state for benzoyl chloride itself must be much more restricted than would at first sight be supposed. We suggest that, in the transition state for benzoyl chloride reacting with aniline, the two rings lie parallel, with little freedom of rotation for either ring. The model shows that in this arrangement an *o*-chlorine atom in the benzoyl chloride molecule can be accommodated adjacent to the oxygen atom without much steric strain or twisting of the ring. There is little decrease in the freedom of rotation, because this is supposed already

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[19] Pauling, "The Nature of the Chemical Bond," Cornell Univ. Press, Ithaca, New York, 1940, 2nd edn., p. 172.

[20] Andrews, *Chem. Rev.*, 1954, **54**, 765.

restricted in the transition state for benzoyl chloride itself. On the other hand an *o*-chlorine atom can only lie adjacent to the bulky reacting chlorine atom with considerable steric strain. When two *o*-chlorine atoms are present the transition state can thus only be achieved with much steric strain or stretching of bonds. We have, therefore, a ready explanation of the observation that, while the first *o*-chlorine atom in benzoyl chloride enhances reactivity, the second reduces it, raising the activation energy by some 5000 cal. mole^{-1}.

The preference of the transition state for the extended configuration with the rings parallel may possibly be due to interaction with the solvent. The transition state is more polar than the initial state of the reactants [1b,8] and will therefore be more highly solvated. Orientation of the benzene molecules around the transition state might well be favoured by parallelism of the benzoyl chloride and aniline rings.

The Relation between the Effects of o-, m-, *and* p-*Chlorine Atoms on Reactivity in the Benzoylation of Aniline.*—For a number of side-chain reactions in the aromatic series it is possible to correlate the effect of a *meta*-substituent on reactivity and the dipole moment associated with the substituent when attached to the aromatic ring, which is a measure of the strength of the electric field produced by the substituent at the seat of the reaction.[21] The correlation is less good in the case of *para*-substituents owing to the intervention of the mesomeric effect. With *ortho*-substituents there is usually little point in attempting such a correlation, since the operation of steric effects will be superimposed on the influence of the electric field of the substituent. Steric effects of *ortho*-substituents seem relatively unimportant in the benzoylation of aniline in benzene, as judged by the constancy of the non-exponential factor, and an attempt to correlate reactivity and the dipole moments of *ortho*-substituents is profitable. Stubbs and Hinshlewood [1a] showed that there was a relation between free energy of activation and dipole moment for *ortho*-substituted anilines. Sufficient *ortho*-substituted benzoyl chlorides have not yet been studied, but an attempt to understand the relative effect of *o*-Cl and *p*-Cl in electrostatic terms is worthwhile.

Jenkins [22] sought to relate the strength of a substituted benzoic acid to the electric field produced by the substituent at the carbon atom to which the carboxyl group is attached. He calculated the electrostatic potentials due to various substituents in the *ortho-*, *meta-*, and *para*-positions, assuming that each substituent could be regarded as having a small dipole, of moment equal to the observed bond moment, located half-way between the carbon atom of the ring and the first substituent atom. The electrostatic potential *in vacuo* at a certain point due to a small dipole whose centre is r cm. away and whose axis is inclined at an angle θ to the line of length r is $\psi = -\mu \cos\theta/r^2$, where μ is the dipole moment. The values of ψ are: *o*-Cl, +0·355; *m*-Cl, +0·158; and *p*-Cl, +0·130.

We now assume that chlorine substituents affect the reactivity of benzoyl chloride through changing the electrostatic potential at the carbon atom to which the COCl group is attached. This is equivalent to the assumption made by Jenkins for benzoic acid, and amounts to regarding the C·COCl system " as a more or less perfect conductor or equipotential surface." The effects of chlorine substituents on reactivity expressed as log (k/k_0) should then be in the ratio of the electrostatic potentials given above. The relative effect of *o*-Cl and *p*-Cl has the mean value 3·8 for the four temperatures in Table 4, compared with a value of 2·73 for the ratio of the electrostatic potentials. It is satisfactory that these quantities agree approximately. One should be cautious in trying to explain the difference between them. The assumption at the beginning of this paragraph may not be strictly valid. Further we have used electrostatic potentials calculated for a vacuum. This does not matter in assessing the relative effect of *o*-Cl and *p*-Cl provided that the effective dielectric constant is the same for both positions, but this could well not be the case. However, it is worth noting that the reactivity ratio is higher than that of the electrostatic potentials and this could mean that the mesomeric effect of the chlorine

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[21] Watson, " Modern Theories of Organic Chemistry," Oxford, 1941, 2nd edn., p. 56.

[22] Jenkins, *J.*, 1939, 640; see also *J.*, 1939, 1137, 1780.

atom is transmitted less effectively from an *ortho*-position than from a *para*-position. The mean relative effect of *m*-Cl and *p*-Cl on the reactivity of benzoyl chloride is 2·6, as noted above, where it was suggested that this indicated a rather powerful operation of the mesomeric effect of *p*-Cl. In this connection it is interesting that the ratio of the electrostatic potentials is much lower, 1·22; this confirms the operation of a powerful mesomeric effect of *p*-Cl reducing reactivity.

We may discuss the effect of chlorine substituents on the reactivity of aniline in the same way, assuming that the electrostatic potential at the carbon atom to which the amino-group is attached governs the reactivity. The relative effect of *o*-Cl and *p*-Cl on reactivity is 3·2 (Stubbs and Hinshelwood's results[1a]). The ratio of the electrostatic potentials is lower, 2·73, but the agreement is better than for the corresponding benzoyl chlorides. As before, it may be that the mesomeric effect of the chlorine atom is transmitted less effectively from an *ortho*- than from a *para*-position. In aniline the mesomeric effect of chlorine as a substituent seems to be of less influence than in benzoyl chloride (see above), and it is thus reasonable that the agreement between reactivity and electrostatic potentials should be better in aniline than in benzoyl chloride. In accordance with this the relative effect of *m*-Cl and *p*-Cl on the reactivity of aniline is 1·8, compared with 1·22 for the ratio of the electrostatic potentials, and 2·6 for the relative effect of *m*-Cl and *p*-Cl on the reactivity of benzoyl chloride.

The Alkaline Hydrolysis of Chloro-substituted Ethyl Benzoates in 84·6% *Ethanol.*—Rate coefficients, *k*, activation energies, *E*, and non-exponential factors, *A*, from the Arrhenius equation are shown in Table 5. No appreciable hydrolysis of ethyl 2,6-dichlorobenzoate could be detected even after some days at the reflux temperature of the solvent.[23]

Earlier work on the influence of a single chloro-substituent on the alkaline hydrolysis of ethyl benzoate showed that log *A* was unaffected by *m*- or *p*-Cl,[15,24] but was appreciably diminished by *o*-Cl.[15] The results in Table 5 show that the same effects are found with the ethyl dichlorobenzoates. The non-exponential factors for ethyl 3,4- and 3,5-dichlorobenzoate are close to those of ethyl *m*- and *p*-chlorobenzoate and of ethyl benzoate, the

TABLE 5.

Rate coefficients and Arrhenius parameters for alkaline hydrolysis of ethyl benzoates in 84·6% ethanol.

	10^3k (l. mole^{-1} sec.$^{-1}$)					E	
Subst.	5°	15°	25°	35°	45°	(cal. mole^{-1})	log A
H	0·082	0·242	0·646	1·82	4·48	17,610[f]	9·75
o-Cl	—	0·568	1·42[a]	3·42	7·98	16,020[g]	8·91
m-Cl	0·641	1·86	4·79[b]	13·1	30·3	16,990[h]	10·16
p-Cl	0·330	1·16	2·80[c]	7·40	17·6	17,250[i]	10·12
2,3-Cl_2	—	2·06	5·07	11·4	24·8	15,070	8·75
2,4-Cl_2	—	2·96	7·29	15·7	32·6	14,500	8·49
2,5-Cl_2	—	5·36	11·0	27·0	59·1	14,720	8·88
3,4-Cl_2	2·34	6·42	15·7[d]	37·2	—	15,620	9·66
3,5-Cl_2	5·59	16·4	36·1[e]	92·9	—	15,690	10·10

Values of *k* are accurate to within ±2%. Values of *E* are accurate to within ±300 cal. mole^{-1}. Values of log *A* are accurate to within ±0·3.

To eliminate the effect of small differences in solvent composition and experimental conditions comparison of values for *k* with data from earlier work is best made in terms of $k/k_0 = r$, the ratio of coefficients for substituted and unsubstituted ethyl benzoates.

[a] $r = 2{\cdot}20$; Evans, Gordon, and Watson (*J.*, 1937, 1430) give $r = 2{\cdot}24$ for 84·8% ethanol. [b] $r = 7{\cdot}42$; Evans, Gordon, and Watson give 7·68; Brynmor Jones and Robinson (*J.*, 1955, 3845) give $r = 7{\cdot}62$ for 84·6% ethanol. [c] $r = 4{\cdot}33$; Brynmor Jones and Robinson give 4·34; Ingold and Nathan (*J.*, 1936, 222) give $r = 4{\cdot}31$ for 85·0% ethanol. [d] $r = 24{\cdot}3$; Brynmor Jones and Robinson give 24·1. [e] $r = 55{\cdot}8$; Brynmor Jones and Robinson give 65·3. [f] Evans, Gordon, and Watson; Ingold and Nathan; and Brynmor Jones and Robinson give 17,700. [g] Evans, Gordon, and Watson give 15,700. [h] Evans, Gordon, and Watson give 16,400. [i] Ingold and Nathan give 16,800.

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[23] See summary and references in Dippy, Evans, Gordon, Lewis, and Watson, *J.*, 1937, 1421.

[24] Ingold and Nathan, *J.*, 1936, 222.

average value of log A for the five compounds being 10·0 ± 0·2. The non-exponential factors for ethyl 2,3-, 2,4-, and 2,5-dichlorobenzoates lie close to that for ethyl *o*-chlorobenzoate. The average value of log A for the four compounds is 8·8 ± 0·1. The lowering of log A by *o*-Cl was formerly ascribed to chelation in the transition state between the carbonyl-oxygen atom of the ester group and the *ortho*-substituent.[15] More recently, following Kadesch,[25] it has been related to the steric effect of the substituent twisting the ester group with respect to the benzene ring, and hindering access of the hydroxyl ion on one side of the ester group.[26]

The value of E for ethyl *o*-chlorobenzoate is *lower* than that of the *para*-isomer by about 1200 cal. mole.$^{-1}$. Earlier values of the activation energies differ by about the same amount, 1100 cal. mole^{-1} (Table 5 footnotes), and Evans, Gordon, and Watson [15] drew attention to this. In the saponification of ethyl benzoates in 56% acetone the activation energies of these compounds are related in the same way.[27] The transfer of the chlorine atom from the *para*- to an *ortho*-position may conceivably change the activation energy through changing various factors, *e.g.*, the transmission of the electron-attracting effect of the chlorine to the reaction centre, the mesomeric interaction of benzene ring and ester side-chain, and the solvation of ester and transition state. It is impossible as yet to assess what part is played by these.

Assessment of the Cumulative Effect of Substituents.—The alkaline hydrolysis of ethyl benzoates. Experimentally measured values of the activation energy are not accurate enough for assessing the cumulative effect of substituents; free energies of activation are therefore used.[1a] The Arrhenius non-exponential factor, however, is unaffected (within the limits of experimental error) by *m*- or *p*-Cl and changes in free energy of activation thus reflect changes in activation energy. For each substituted ethyl benzoate not containing *o*-Cl the quantity $\Delta E'$ (obs.) $= 2{\cdot}303\,\boldsymbol{R}T \log (k/k_0)$ has been evaluated at the various temperatures used for rate measurements; k is the observed rate coefficient for the substituted ethyl benzoate, and k_0 is that for ethyl benzoate itself, derived from the Arrhenius equation with $E = 17{,}610$ cal. mole^{-1}, log $A = 9{\cdot}75$. For *o*-chloro-compounds we evaluate the quantity $\Delta E'$ (obs.) $= -2{\cdot}303\,\boldsymbol{R}T\,[\log (k/k_0) - 0{\cdot}84]$, where 0·84 is the difference between the log A values for ethyl benzoate (9·75) and ethyl *o*-chlorobenzoate (8·91). By this procedure we exclude from consideration the part of the effect of *o*-Cl which changes the non-exponential factor and we deal only with the part which changes the activation energy. Mean values (over the various experimental temperatures) for $\Delta E'$ (obs.) are shown in Table 6. Values of $\Delta E'$ (pred.) for the dichlorobenzoates are calculated from $\Delta E'$ (obs.) values for the monochlorobenzoates by assuming a strictly additive effect.

TABLE 6.

Cumulative effect of chlorine substituents on the alkaline hydrolysis of ethyl benzoate.

Subst.	$\Delta E'$ (obs.)	$\Delta E'$ (pred.)	$\Delta E'$ (obs.) − $\Delta E'$ (pred.)	Departure (%)
2,3-Cl_2	−2320	−2760	+440	−16
2,4-Cl_2	−2510	−2440	−70	+3
2,5-Cl_2	−2840	−2760	−80	+3
3,4-Cl_2	−1860	−2040	+180	−9
3,5-Cl_2	−2380	−2360	−20	+1

$\Delta E'$ (obs.): *o*-Cl, −1580; *m*-Cl, −1180; *p*-Cl, −860.

The reaction of substituted benzoyl chlorides with aniline. The Arrhenius non-exponential factor seems unaffected by chlorine atoms in the *ortho*-, *meta*-, or *para*-position of the benzoyl chloride molecule (see p. 4749). The cumulative effect can thus be assessed in a

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[25] Kadesch, *J. Amer. Chem. Soc.*, 1944, **66**, 1207.

[26] Newman, "Steric Effects in Organic Chemistry," Wiley, New York, 1956, p. 216.

[27] Tommila, *Ann. Acad. Sci. Fennicae*, 1941, **57**, *A*, No. 13.

way analogous to that used for the alkaline hydrolysis of *m*- and *p*-chloro-substituted benzoates. Mean values of $\Delta E'$ (obs.) and $\Delta E'$ (pred.) over the four experimental temperatures are shown in Table 7 (2,6-dichlorobenzoyl chloride being omitted as the cumulative effect of its substituents has been discussed on p. 4751).

TABLE 7.

Cumulative effect of chlorine substituents in benzoyl chloride on the reaction with aniline.

Subst.	$\Delta E'$ (obs.)	$\Delta E'$ (pred.)	$\Delta E'$ (obs.) − $\Delta E'$ (pred.)	Departure (%)
2,3-Cl_2	−1050	−1420	+370	−26
2,4-Cl_2	−1010	−1060	+50	−4·5
2,5-Cl_2	−1280	−1420	+140	−10
3,4-Cl_2	−690	−800	+110	−14
3,5-Cl_2	−1060	−1160	+100	−8·5

$\Delta E'$ (obs.): *o*-Cl, −840; *m*-Cl, −580; *p*-Cl, −220.

TABLE 8.

Cumulative effect of chlorine substituents on the dissociation of benzoic acid.

Subst.	ΔpK_a (obs.)	ΔpK_a (pred.)	ΔpK_a (obs.) − $-\Delta pK_a$ (pred.)	Departure (%)
2,3-Cl_2	−1·63 [b]	−1·65	+0·02	−1·2
2,4-Cl_2	−1·54 [b, f,]	−1·50	−0·04	+2·7
2,5-Cl_2	−1·66 [b, f]	−1·65	−0·01	+0·6
2,6-Cl_2	−2·56 [a, f, g]	−2·54	−0·02	+0·8
3,4-Cl_2	−0·57 [d]	−0·61	+0·04	−6·5
3,5-Cl_2	−0·78 [c]	−0·76	−0·02	+2·6

ΔpK_a (obs.): *o*-Cl, −1·27; *m*-Cl, −0·38; *p*-Cl, −0·23.[e]

At 0·01M. [b] At 0·001M. [c] At 0·0005M. [d] Ref. 13 (the acid was too insoluble for potentiometric study). [e] Ref. 12. [f] Ref. 5: 2,4-Cl_2, −1·53; 2,5-Cl_2, −1·74; 2,6-Cl_2, −2·62. [g] Ref. 13: 2,4-Cl_2, −1·45; 2,6-Cl_2, −2·39.

The ionisation of benzoic acids. The cumulative effect will be assessed in terms of ΔpK_a (Table 8). Values of ΔpK_a (obs.) from the present work and from earlier work are shown, together with values for ΔpK_a (pred.), calculated from Dippy's results.[12]

Cumulative Effect of Chlorine Substituents in the Three Systems.—The alkaline hydrolysis of ethyl benzoates. The rate coefficients were reproducible within about 2% and it follows that little significance should be attached to departures from additivity of less than about 50 cal. Ethyl 3,5-dichlorobenzoate (Table 6) must be regarded as showing strict additivity. This confirms Brynmor Jones and Robinson's earlier result [2a] and is in accord with the general behaviour of 3,5-compounds; *e.g.*, Brynmor Jones and Watkinson [2c] found strict additivity in the alkaline hydrolysis of ethyl 3,5-dichlorocinnamate. Substituent interaction is at a minimum with this arrangement. The departures from additivity in ethyl 2,4- and 2,5-dichlorobenzoate are possibly just significant, but in comparison with the total substituent effect they do not seem important, amounting to not more than about 3%. Thus in spite of the effect of *o*-Cl on the non-exponential factor, the substituents contribute additively to $\Delta E'$. The departure in the case of ethyl 3,4-dichlorobenzoate is more significant, +180 cal. (−9%), in agreement with Brynmor Jones and Robinson's [2a] earlier result. Brynmor Jones and Watkinson [2c] found a −7% departure in the alkaline hydrolysis of ethyl 3,4-dichlorocinnamate. It seems likely that these departures are due to electrostatic interaction between the C–Cl dipoles, reducing the effect of each upon the activation energy. The observed dipole moment of *o*-dichlorobenzene is 2·33D, compared with a value of 2·70 computed vectorially from that of chlorobenzene, and this was attributed by Smallwood and Herzfeld [28] to electrostatic interaction. Departures from additivity in $\Delta E'$ and in

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[28] Smallwood and Herzfeld, *J. Amer. Chem. Soc.*, 1930, **52**, 1919.

dipole moment are of similar magnitude relative to the total substituent effect in each case. The most serious departure occurs in ethyl 2,3-dichlorobenzoate: +440 cal. or −16%; or compared with ethyl 2,5-dichlorobenzoate, +520 cal. or −19%. This large departure from strict additivity is probably due to electrostatic interaction between the C–Cl dipoles, as in the 3,4-compound, combined with an effect arising from three substituents adjacent on the ring. In the discussion of the ionisation of benzoic acids (below) it will be seen that there is a well-established effect in which a 3-substituent presses against a 2-substituent and increases the steric interaction of the latter with the 1-side-chain. It appears likely that an effect of this kind is responsible for some of the departure from additivity in the alkaline hydrolysis of ethyl 2,3-dichlorobenzoate, possibly through a small and experimentally undetectable decrease in the Arrhenius non-exponential factor. The minute reactivity of ethyl 2,6-dichlorobenzoate corresponds to a gross departure from additivity, readily explicable in terms of the chlorine atoms' twisting the side chain and hindering access of the hydroxyl-ion on both sides of the ester group.

The reaction of substituted benzoyl chlorides with aniline. The percentage departures from strict additivity are considerably greater than in ester hydrolysis (Table 7), and with the exception of 2,4-dichlorobenzoyl chloride all the compounds show departures considerably in excess of 50 cal., a reasonable allowance for experimental error. The departure from additivity in 3,5-dichlorobenzoyl chloride is rather unexpected, but there are some cases recorded of departures from strict additivity of substituent effects in 3,5-compounds; *e.g.*, Dippy, Hughes, and Bray[5] find a −32% departure from additivity in the ionisation of 3,5-dihydroxybenzoic acid, which they cannot explain. The poor additivity shown by the dichlorobenzoyl chlorides may possibly be connected with the enhanced rôle of the $+M$ effect of chlorine in the reaction with aniline as compared with the alkaline ester hydrolysis (p. 4749). The breakdown in additivity for $\Delta E'$ may, of course, lie in non-additivity in the changes in activation energy or in the occurrence of small, experimentally undetectable variations in log A. Insofar as the additivity is best with 2,4-dichlorobenzoyl chloride, the unexpected departures in the other compounds seem to be connected with *m*-Cl. While it is probable that this effect is genuine, a spurious effect of this nature would arise from the use of an erroneous $\Delta E'$ (obs.) value for *m*-chlorobenzoyl chloride in the calculation of the values of $\Delta E'$ (pred.). A value for *m*-chlorobenzoyl chloride of −530 cal., instead of −580, would reduce the departure in the 3,5-compound to 0%, in the 2,5-compound to −6·5%, and in the 3,4-compound to −8% (cf. departure in alkaline hydrolysis of ethyl 3,4-dichlorobenzoate). This would imply that the observed rate coefficients for *m*-chlorobenzoyl chloride are some 10% higher than the true values, presumably owing to traces of fast-reacting impurity. Scrutiny of the detailed kinetic results does not, however, reveal any suspicious feature, such as a trend in the rate coefficient over the course of the reaction.

The −14% departure from additivity in 3,4-dichlorobenzoyl chloride suggests that electrostatic interaction between the C–Cl dipoles is responsible for about the same departure as in ester hydrolysis. The departure in the 2,3-compound is about −16% compared with the 2,5-compound, and this is similar to that observed in the hydrolysis of the corresponding esters. The low reactivity of 2,6-dichlorobenzoyl chloride (p. 4749) corresponds to a gross departure from an additive effect of substituents, that is, however, not so serious as in the case of the alkaline hydrolysis of ethyl 2,6-dichlorobenzoate. This is readily explicable in terms of the different transition states and the different ways in which the *o*-chlorine atoms act in the two reactions.

The ionisation of benzoic acids. The substituent effects show good additivity in all six dichlorobenzoic acids (Table 8). Departures of less than 0·04 pK unit are not significant, so none of the departures recorded is more than barely significant, and in all cases the percentage departure is small.

The agreement between observed and predicted values is excellent for the 3,5-acid. In the case of the 2,5-acid the agreement with our ΔpK_a (obs.) is good, but there is a +5%

departure if ΔpK_a (obs.) based on the result of Dippy *et al.*[5] is taken. For the 2,4-acid all the available values of ΔpK_a (obs.) are in reasonable agreement with ΔpK_a (pred.), although the small departure changes sign as between our value and Dippy's on the one hand and Davis and Hetzer's [13] on the other. Thus, on the whole, there is no indication of any serious departures from strict additivity for the 3,5-, 2,5-, and 2,4-acid, and their behaviour is similar to that of the corresponding esters in alkaline hydrolysis.

The most striking feature of Table 8 is the apparent strict additivity shown by the 3,4-, 2,3-, and 2,6-acid. Davis and Hetzer [13] refer to the additivity of substituent effects shown by 3,4-dichlorobenzoic acid. It is difficult, however, to be certain of the exact situation since the total substituent effect is small, and a percentage departure similar to that observed in the alkaline hydrolysis of ethyl 3,4-dichlorobenzoate would correspond to a barely significant departure in terms of pK_a units. The situation is much clearer in the case of 2,3-dichlorobenzoic acid where the total substituent effect is large, and the additivity is certainly much better than that shown in the alkaline hydrolysis of ethyl 2,3-dichlorobenzoate. Thus the effects associated with electrostatic interaction of the C–Cl dipoles and with the three substituents adjacent on the ring are not immediately apparent in the dissociation of benzoic acid. A tentative explanation for this may be advanced. The high ΔpK_a value of *o*- compared with that of *p*-chlorobenzoic acid is due largely to the steric effect of the *o*-chlorine atom, which stabilizes the ion relative to the undissociated acid by twisting the side-chain out of the plane of the ring in both the ion and the acid, thus inhibiting mesomerism involving the interaction of ring and side-chain.[29] The total effect of the substituents in 2,3-dichlorobenzoic acid is thus only partly polar in nature, and departures from additivity due to electrostatic interaction will tend to be obscured. Further, electrostatic interaction of the substituents may be in competition with another factor tending to increase their effect. Dippy *et al.*[30] have shown that 2,3-dimethylbenzoic acid is much stronger than predicted; ΔpK_a (obs.) is $-0{\cdot}37$ compared with a ΔpK_a (pred.) value of $-0{\cdot}24$. Peltier has shown [31] that several 3-substituted *o*-toluic acids are stronger than the isomeric 5-substituted *o*-toluic acids. Dippy *et al.* have suggested that in 2,3-dimethylbenzoic acid the 3-methyl group presses against the 2-methyl group and thereby increases the steric inhibition of mesomerism of the carboxyl group which is probably responsible for the strengthening effect of an *o*-methyl group. This suggestion is in agreement with Peltier's observation that the discrepancy between the 3- and the 5-substituted acid increases with the bulk of the substituent. It seems probable that such an effect will operate in 2,3-dichlorobenzoic acid but will be in competition with electrostatic interaction tending to reduce the strength of the acid. In the result the two effects appear almost to cancel out, so that 2,3-dichlorobenzoic acid shows good additivity of substituent effects.

In 2,6-dichlorobenzoic acid there is good additivity of substituent effects, as judged both by our value of ΔpK_a (obs.) and by Dippy's value. The additivity is not so good if Davis and Hetzer's value is considered, and these authors suggested that the first *o*-Cl is more effective than the second in enhancing the strength of benzoic acid. In any case the percentage departure from strict additivity is clearly much smaller than for many 2,6-disubstituted benzoic acids, as may be seen from the results of Dippy and his colleagues,[5] Peltier's results,[32] and the data summarised by Shorter and Stubbs.[3] If the effect of *o*-Cl on the strength of benzoic acid is due to a combination of steric and polar factors (see above), then it appears that such factors are additive for two *o*-chlorine atoms. It is surprising that the effect of two *o*-chlorine atoms in twisting the side-chain out of the plane of the ring should be strictly additive as measured by ΔpK_a. (In Shorter and Stubbs's Table [3] 2,4,6-tribromobenzoic acid, however, also shows an additive effect of substituents.)

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[29] Newman, ref. 26, p. 429.
[30] Dippy, Hughes, and Laxton, *J.*, 1954, 1470.
[31] Peltier, *Compt. rend.*, 1955, **241**, 57.
[32] Peltier, *Compt. rend.*, 1955, **241**, 1467.

This situation is in sharp contrast to that prevailing in the alkaline hydrolysis of ethyl 2,6-dichlorobenzoate and in the reaction of 2,6-dichlorobenzoyl chloride with aniline.

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