26. *The Cumulative Effect of Substituents in an Aromatic Nucleus on Reactions of the Side-chain. Part II.*[1] *The Effect of Chlorine as Substituent on the Reaction of Benzoic Acids with Diazodiphenylmethane.*

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Rate coefficients have been measured for the reaction at 30° of diazodiphenylmethane in ethanol with benzoic acid, three monochlorobenzoic acids, and six dichlorobenzoic acids. Departures from additivity of substituent effects are appreciable for all dichlorobenzoic acids except the 2,6-compound, but there are no special effects associated with the 3,4- or 2,3-arrangements. The results are discussed with reference to related systems. The strict additivity of substituent effects shown by 2,6-dichlorobenzoic acid in various processes is in contrast to the behaviour of 2,6-dimethylbenzoic acid; it is suggested that the secondary steric effect is of much greater importance for *o*-Me than for *o*-Hal.

In Part I[1] the cumulative effect of chlorine as a nuclear substituent was studied for the reaction of benzoyl chlorides with aniline, the alkaline hydrolysis of ethyl benzoates, and the ionisation of benzoic acids. The 3,5-, 2,4-, and 2,5-dichloro-compounds showed strict additivity of substituent effects in ester hydrolysis and acid dissociation, whereas appreciable departures from additivity were observed in the reactions of benzoyl chlorides with aniline. Departures from additivity in the reactions of 2,3- and 3,4-dichloro-compounds were attributed to proximity effects. Only for the ionisation of the acid did the 2,6-dichloro-compound show strict additivity; the other systems showed great departures. The present work extends this study to the reactions of substituted benzoic acids with

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[1] Part I, Mather and Shorter, *J.*, 1961, 4744.

diazodiphenylmethane to give diphenylmethyl benzoates. Esterification by this reagent has been much studied in recent years.[2] This paper presents results for the reaction of diazodiphenylmethane with benzoic acid, the three monochlorobenzoic acids, and all six dichlorobenzoic acids in ethanol at 30°.

EXPERIMENTAL

Materials.—Commercial benzoic and monochlorobenzoic acid were recrystallised from glacial acetic acid, aqueous ethanol, and light petroleum (b. p. 60—80°). The dichlorobenzoic acids were those prepared by Dr. J. G. Mather; [1] these were again recrystallised from light petroleum (b. p. 60—80°). The purity of the acids was examined by vapour-phase chromatography of the methyl esters (prepared by adding diazomethane in ether to an ethereal solution of the acid). In all cases the acids were found to be of purity not less than 99·2%. Further, in every case the equivalent weight determined by titration with alkali was found to be well within 1% of the calculated value.

Diazodiphenylmethane was prepared by Smith and Howard's method.[3] Ethanol was purified either by Lund and Bjerrum's method [4a] or by that of Adickes.[4b] The water content of the ethanol was determined by the Karl Fischer titration [5] and was always found to be less than 0·02% w/w. The ethanol was stored under dry nitrogen.

Measurement of Rate Coefficients.—These were determined spectrophotometrically as described previously,[6] a Unicam S.P. 600 spectrophotometer being used. In most cases a ten-fold excess of acid was used and the reaction was studied as a first-order process. In the case of 2,6-dichlorobenzoic acid, owing to the speed of the reaction, it was necessary to use comparable concentrations of the reactants and study the reaction as a second-order process. The equation used to calculate the rate coefficient for this acid was:

$$k_2{}^a = \frac{2{\cdot}303}{at(1-R)} \log \frac{(a - R\,.\,x)}{(a - x)},$$

where a is the initial concentration of diazodiphenylmethane and of 2,6-dichlorobenzoic acid (mole l.^{-1}), x is the concentration of diazodiphenylmethane that has reacted after time t (min.), and R and $k_2{}^a$ are defined below.

Cumulative effect of chlorine substituents in benzoic acid on the reaction with diazodiphenylmethane.

Subst.	$k_2{}^a$	R	k_t	$\Delta E'$ (obs.)	$\Delta E'$ (pred.)	$\Delta\Delta E'$	Departure ‡ (%)
H	0·992 *	0·591	0·586 †	—	—	—	—
o-Cl	4·96	0·616	3·06 †	−1000	—	—	—
m-Cl	2·42	0·600	1·45 †	−550	—	—	—
p-Cl	1·80	0·596	1·07 †	−360	—	—	—
2,3-Cl_2	10·05	0·632	6·35	−1440	−1550	+110	−7·0
2,4-Cl_2	7·67	0·624	4·79	−1270	−1360	+90	−6·6
2,5-Cl_2	9·57	0·631	6·04	−1410	−1550	+140	−9·0
2,6-Cl_2	26·0	0·638	16·6 †	−2010	−2000	−10	+0·5
3,4-Cl_2	3·88	0·597	2·32	−830	−910	+80	−8·8
3,5-Cl_2	5·14	0·596	3·06	−1000	−1100	+100	−9·1

$k_2{}^a$ and k_t are in l. mole^{-1} min.^{-1}.

* Roberts, McElhill, and Armstrong (*J. Amer. Chem. Soc.*, 1949, **71**, 2923) give 1·04; Benkeser, de Boer, Robinson, and Sauve (*J. Amer. Chem. Soc.*, 1956, **78**, 682) give 1·07; Hine and Bailey (*J. Amer. Chem. Soc.*, 1959, **81**, 2075) give 1·00; Chapman, Shorter, and Utley (*J.*, 1962, 1824) give 1·08.

† Chapman, Shorter, and Utley give: H, 0·666; *o*-Cl, 3·31; *m*-Cl, 1·46; *p*-Cl, 1·12; 2,6-Cl_2, 17·7.

‡ The additivity pattern is essentially the same if $k_2{}^a$ is used instead of k_t in assessing the cumulative effect.

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[2] Roberts, Watanabe, and McMahon, *J. Amer. Chem. Soc.*, 1951, **73**, 760, and references therein; Hancock and Westmoreland, *ibid.*, 1958, **80**, 545, and references therein.

[3] Smith and Howard, *Org. Synth.*, **24**, 53.

[4] (*a*) Lund and Bjerrum, *Ber.*, 1931, **64**, 210, (*b*) Vogel, " Practical Organic Chemistry," Longmans, London, 1956, 3rd edn., p. 168.

[5] Seaman, McComies, and Allen, *Analyt. Chem.*, 1949, **21**, 511.

[6] Chapman, Shorter, and Utley, *J.*, 1962, 1824.

Diazodiphenylmethane reacts with ethanol in the presence of acid, as well as with the acid itself.[7] The ratio (R) of the amount of diazodiphenylmethane consumed in the reaction with each substituted benzoic acid to the total amount consumed was determined as described previously.[6] The true second-order rate coefficient (k_t) for the reaction of each benzoic acid with diazodiphenylmethane is given by $k_t = k_1{}^aR/[\text{acid}] = k_2{}^aR$, where $k_1{}^a$ is the observed apparent first-order rate-coefficient, and $k_2{}^a$ is the second-order rate-coefficient uncorrected for the competing reaction.

DISCUSSION

Rate coefficients are listed in the Table. The values of $k_2{}^a$ for benzoic acid obtained by different authors vary from 0·99 to 1·08. The reaction rate is very sensitive to traces of water in the ethanol[7] and observed rate coefficients are not those proper to 100% ethanol unless the solvent is very thoroughly dried. The values of k_t for the monochlorobenzoic acids and for 2,6-dichlorobenzoic acid are about 5% lower than those obtained by Chapman, Shorter, and Utley;[6] that for benzoic acid is 12% lower, and it should be noted that the value of $k_2{}^a$ recorded by Chapman, Shorter, and Utley marks the upper limit of the range of values observed by different authors. The rate coefficients obtained by Chapman, Shorter, and Utley should, however, be reliable for purposes of internal comparison since they refer to constant solvent conditions.

The cumulative effect of substituents is assessed in terms of free energy of activation.[1] For each substituted benzoic acid the quantity $\Delta E'(\text{obs.}) = -2{\cdot}303\boldsymbol{R}T\log(k_t/k_0)$ has been evaluated, where k_t and k_0 are true rate coefficients for substituted benzoic acid and for benzoic acid itself respectively (Table). Values of $\Delta E'$(pred.) for the dichlorobenzoic acids are calculated from $\Delta E'$(obs.) for the monochlorobenzoic acids by assuming a strictly additive effect. The rate coefficients were reproducible to within about 2% and it follows that little significance should be attached to departures from additivity assessed in terms of $\Delta E'$, of less than about 50 cal. mole^{-1}.

Except for 2,6-dichlorobenzoic acid all the compounds show significant departures from strict additivity. A general breakdown in additivity was shown previously to characterise the reaction of chloro-substituted benzoyl chlorides with aniline. [The overall additivity pattern is greatly influenced by the value for $\Delta E'$(obs.) used for the *meta*-chloro-compound, and the corresponding value of k_t was very carefully determined.] A feature common to the benzoylation and to the reaction under discussion is the use of a non-aqueous reaction medium: ethanol for the diazodiphenylmethane reaction and benzene for the benzoylation reaction (cf. water for the ionisation of dichlorobenzoic acids, and 84·6% ethanol for the alkaline hydrolysis[7] of the dichlorobenzoates). The importance of the solvent in this respect is suggested also by some results of Davis and Hetzer on the reaction of benzoic acids with diphenylguanidine in benzene:[8] departures from additivity shown by 3,4- and 2,4-dichlorobenzoic acid were —10·3% and —6·5%, respectively, compared with —6·5% and +2·7% for the ionisation of the acids in water.[1] A non-aqueous medium might well accentuate departures from additivity due to electrostatic interaction of substituent dipoles[1] and render such interaction detectable even for 3,5-, 2,4-, and 2,5-arrangements, for which it is not apparent in aqueous media.

The additivity pattern for the dichlorobenzoic acids reacting with diazodiphenylmethane differs from that observed in the benzoylation in that there are no special effects associated with the 3,4-, 2,3-, and 2,6-arrangements of substituents. This behaviour is similar to that observed for the ionisation of the acids in water.[1] Insofar as the departure from additivity for 2,6-dichlorobenzoic acid reacting with diazodiphenylmethane is appreciably smaller than for the other compounds, there is an indication that a second *o*-Cl has a slightly greater effect than the first, so as to counteract the general breakdown in additivity discernible in the other compounds. An insensitivity to proximity effects seems to characterise the reactions of the benzoic acids we have studied, as compared with

[7] Roberts, Watanabe, and McMahon, *J. Amer. Chem. Soc.*, 1951, **73**, 760.

[8] Davis and Hetzer, *J. Res. Nat. Bur. Stand.*, 1958, **60**, 569.

the benzoylation and alkaline ester hydrolysis.[1] Davis and Hetzer's results [8] with 3,4- and 2,6-dichlorobenzoic acid for the reaction with diphenylguanidine in benzene show a similar absence of proximity effects. Comparison of their results for 2,4- and 3,4-dichlorobenzoic acid shows that any effect peculiar to the 3,4-arrangement is very small. For 2,6-dichlorobenzoic acid $\Delta\log K''$(obs.) is $+2{\cdot}08$ (K'' is the equilibrium constant for reaction with diphenylguanidine); $\Delta\log K''$(pred.) is $+1{\cdot}64$ (Davis and Hetzer,[8] Table 6), so at first sight there is a large departure from additivity. However, a comparison of log K'' values with pK_a values for the corresponding phenols in water suggests that undissociated *o*-chlorobenzoic acid is stabilised in benzene by internal hydrogen-bonding. In the absence of this, $\Delta\log K''$ for *o*-Cl would be somewhat higher; Davis and Hetzer's Fig. 3 indicates a value of about 1·34, compared with 0·82 actually observed. Since only one *o*-Cl can engage in hydrogen-bonding in 2,6-dichlorobenzoic acid, $\Delta\log K''$ is more properly predicted by adding to 0·82 the value of 1·34 for the effect of a second *o*-Cl not involved in hydrogen bonding. The value of $\Delta\log K''$(pred.) is then $+2{\cdot}16$, in good agreement with $\Delta\log K''$(obs.).

It is difficult to be certain of the exact situation for 3,4-dichlorobenzoic acid since the total substituent effect is small.[1] The situation is much clearer for 2,3-dichlorobenzoic acid. For the ionisation of this acid it was previously pointed out [1] that the total effect of the substituents is only in part polar and so departures from additivity due to electrostatic interaction will tend to be masked. It was also suggested that the effect of such interaction might be counteracted by the 3-Cl pressing against the 2-Cl, thereby increasing steric inhibition of the mesomerism involving carboxyl group and the ring. The good additivity in the ionisation of 2,6-dichlorobenzoic acid was found surprising in view of the supposed importance of the secondary steric effect of *o*-Cl. We shall now re-examine the cumulative effect for the 2,3- and the 2,6-acid in the light of other information.

The influence of *o*-halogeno- and *o*-alkyl substituents on the ionisation of benzoic acid in water is usually attributed mainly to a secondary steric effect.[9] Such an effect would not be expected to be additive for two *ortho*-substituents. The situation should be analogous to the placing of bulky groups adjacent to a nitro-group, the effect of which can be observed in the activating properties of the nitro-group for aromatic nucleophilic substitution, *e.g.*, one adjacent methyl group produces a comparatively small effect, since the nitro-group can bend away from it, but the deactivating effect of two adjacent methyl groups is tremendous.[10] Now for the effect of two *o*-methyl groups in benzoic acid the situation does indeed turn out to be analogous. While ΔpK_a for one *o*-Me in the dissociation [11] in water is $-0{\cdot}29$, for two *o*-methyl groups it is $-0{\cdot}95$. ΔpK_a for *o*-t-butylbenzoic acid [11] is $-0{\cdot}66$. A model suggests that steric inhibition of mesomerism should be virtually complete in this acid. Chapman, Shorter, and Utley [6] suggested that there is steric inhibition of solvation in the *o*-t-butylbenzoate ion; but for this, ΔpK_a would be about $-0{\cdot}9$ (read from their Fig. 4). The closeness of this value to that for 2,6-dimethylbenzoic acid suggests that in the latter also there is almost complete steric inhibition of mesomerism. (A more detailed attempt to correlate the strengths of these two acids would require consideration of polar effects, of possible steric inhibition of solvation in the 2,6-dimethylbenzoate ion, and of the possible occurrence of a general strengthening effect associated with *ortho*-substitution; see below.[6]) In the reaction of these acids with diazodiphenylmethane in ethanol the situation is similar. $\Delta\log k_2{}^a$ for *o*-Me is [12] $-0{\cdot}05$, whereas for 2,6-dimethylbenzoic acid it is [13] $+0{\cdot}54$; the value for *o*-t-butylbenzoic acid [6] is $+0{\cdot}42$.*

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* R for 2,6-dimethylbenzoic acid is not known, but should not be seriously different from that for benzoic acid and for *o*-toluic acid. Hence the use of $k_2{}^a$ rather than k_t in assessing cumulative behaviour is justified.

[9] Newman, " Steric Effects in Organic Chemistry," Wiley, New York, 1956, p. 429.

[10] Chapman, Chaudhury, and Shorter, *J.*, 1962, 1975 and references therein.

[11] Dippy, Hughes, and Laxton, *J.*, 1954, 1470.

[12] Roberts and Yancey, *J. Amer. Chem. Soc.*, 1951, **73**, 1011.

[13] Roberts and Regan, *J. Amer. Chem. Soc.*, 1954, **76**, 939.

In this case the secondary steric effect of one *o*-Me is not able to outweigh its inductive effect. For *o*-toluic acid and 2,6-dimethylbenzoic acid in Davis and Hetzer's system [8] the secondary steric effect appears to be even smaller; $\Delta \log K''$ values are —0·32 and —0·02, respectively. Davis and Hetzer conclude that the secondary steric effect of one *o*-Me is minute, but that of two is considerable. They point out that solvation of the carboxyl group will influence its effective size and hence the extent of steric interaction with the *o*-methyl group.

The good additivity of substituent effects shown by 2,6-dichlorobenzoic acid in the various reactions means that very little of the influence of *o*-Cl on reactivity is due to the secondary steric effect, even when two such substituents are present. Chapman, Shorter, and Utley [6] have suggested that in the reaction with diazodiphenylmethane the influence of *o*-Cl is due mainly to a large polar effect. McDaniel and Brown [14] have suggested that in the ionisation of *o*-chlorobenzoic acid in water, about —0·74 of the ΔpK_a of —1·26 is due to the polar effect; the remainder, —0·52, has usually been attributed to the secondary steric effect. Chapman, Shorter, and Utley [6] have suggested, however, that there is some common factor strengthening by about 0·4 unit all *o*-halogeno- and *o*-alkyl-benzoic acids. Most of the acid strengthening influence of *o*-Cl can therefore be explained without postulating a secondary steric effect. Indeed, if the existence of the general strengthening factor is accepted, the secondary steric effect of a single *o*-Me on the ionisation of benzoic acid is fairly small; it is only with two methyl groups that it becomes great.

2,4,6-Tribromobenzoic acid appears to show good additivity of substituent effects in ionisation,[15] which suggests that *o*-Br exerts little secondary steric effect in the system. Further evidence for the small importance of secondary steric effects of *o*-Hal in benzoic acid dissociation is provided by Peltier's results for 2-methyl-6-halogenobenzoic acids in 1% ethanol.[16] Departures from additivity in pK_a units (and %) are: 2-Me-6-Cl, —0·02 (+1·5%); 2-Me-6-Br, +0·09 (—5·5%); 2-Me-6-I, +0·03 (—2·0%). Thus even *o*-I is unable to fulfil the role of a second *o*-Me in producing a large secondary steric effect. The 3-halogeno-2-methylbenzoic acids show substantial departures from additivity in 1% ethanol,[17] as does 2,3-dimethylbenzoic acid in water: [11] 2-Me-3-Cl, —0·17 (+27%); 2-Me-3-Br, —0·22 (+33%); 2-Me-3-I, —0·36 (+58%); 2,3-Me_2, —0·13 (+54%). This is presumably due to a buttressing effect of the 3-Hal or 3-Me on the secondary steric effect of the 2-Me.[11] The departures from additivity in the 2-halogeno-3-methyl acids in 1% ethanol are much smaller: [18] 2-Cl-3-Me, —0·08 (+7%); 2-Br-3-Me, —0·04 (+3%); 2-I-3-Me, —0·07 (+5·5%). Presumably the buttressing effect is less important because the secondary steric effect of *o*-Hal is much less than that of *o*-Me. It now seems likely that the buttressing effect will not operate in 2,3-dichlorobenzoic acid. Hence the absence of any specific effect in the dissociation, or in the reaction with diazodiphenylmethane, of this acid is probably not due to a cancelling of two opposing proximity effects, as previously suggested,[1] but is due to the absence of direct electrostatic interaction between the substituents. The suspected absence of such an effect in 3,4-dichlorobenzoic acid may therefore well be genuine. As yet no explanation can be offered for the absence of the effect in acid dissociation and in reaction with diazodiphenylmethane and its occurrence in ester hydrolysis and in the benzoylation reaction.[1]

The secondary steric effects of *o*-Hal compared with *o*-Me are not therefore what would be expected from van der Waals radii: Cl, 1·80; Br, 1·95; I, 2·15; Me, 2·0 Å. An *ortho*-halogen can apparently accommodate a carboxyl group in a way not possible for an *ortho*-methyl group, and thus avoid twisting the carboxyl group out of the plane of the ring to any great extent. Possibly there is attraction between the halogen atoms and the

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[14] McDaniel and Brown, *J. Amer. Chem. Soc.*, 1955, **77**, 3756.

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

[16] Peltier, *Compt. rend.*, 1955, **241**, 1467; Peltier and Conti, *ibid.*, 1957, **244**, 2811.

[17] Peltier, *Compt. rend.*, 1955, **241**, 57.

[18] Peltier and Pichevin, *Compt. rend.*, 1957, **243**, 436.

carboxyl-oxygen atoms arising from the overlap of a *p*-orbital (lone-pair orbital) on an oxygen atom with a *d*-orbital on the halogen atom. There is spectroscopic evidence [19] for a physical distinction between a conformation with *o*-Hal disposed towards the carbonyl-oxygen and one with halogen disposed towards hydroxyl-oxygen.

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[19] Brooks, Eglinton, and Morman, *J.*, 1961, 106.