CCCLXXXI.—*The Velocity of Saponification of Mono- and Di-substituted Chloro- and Methoxy-derivatives of Ethyl Benzoate.*

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THE influence of a single substituent in the benzene nucleus upon the velocities of such reactions as the saponification of esters and of amides, the esterification of acids, and the hydrolysis of substituted benzyl chlorides has been determined, in many cases, by reference to the actual velocity coefficient for a wide variety of substituents. These results show that a substituent may cause (*a*) a very considerable change in the reactivity and (*b*) a certain order of reactivity related to the position it occupies in the nucleus.

In the saponification of amides *p*-nitrobenzamide alone has a higher reactivity than benzamide, and other substituents cause comparatively small changes in the velocity coefficient (Remsen, *Amer. Chem. J.*, 1899, **21**, 340). The esterification of substituted benzoic acids in the presence of a catalyst proceeds much less readily than with benzoic acid itself (Meyer, *Z. physikal. Chem.*, 1897, **24**, 219), whilst esterification in the absence of a catalyst proceeds most readily with the substituted acids (Michael, *Ber.*, 1909, **42**, 317). The velocity of saponification of an ethyl benzoate substituted by a halogeno- or by a nitro-group is higher than for the simple ester, but methyl and methoxyl groups tend to a lowering of the coefficient, whereas in the hydrolysis of substituted benzyl chlorides the methyl group alone raises the velocity, all other substituents depressing it in comparison with the simple chloride.

A consideration of the effects due to the nature and position of a substituent shows that in the saponification of esters and amides and in the esterification of acids, for the methyl group, the halogens and the hydroxyl and methoxyl groups, the order of reactivity is *m*-> *p*-> *o*- ; whereas for the nitro-group the order is *p*-> *m*-> *o*-.

In the hydrolysis of the benzyl chlorides, the order of reactivity is $p\text{-} > o\text{-} > m\text{-}$ for all groupings except the nitro- and carboxyl groups, where the order is $m\text{-} > o\text{-} > p\text{-}$. The influence of an ortho-substituent in benzyl chloride is small compared with the effect of the same substituent in an ester, and if allowance is made for this decrease in the steric factor it would appear that the two reactions are influenced in opposite ways, although it is the same carbon atom that is involved in the reaction.

Reaction velocities when the nucleus contains a second substituent have been determined only in a few isolated cases; thus, Sirks (*Rec. trav. chim.*, 1908, **27**, 237) determined the esterification coefficients for the dinitrobenzoic acids and Olivier (*ibid.*, 1926, **45**, 296) the velocity of hydrolysis of three dibromobenzyl chlorides.

The ionisation constants of certain disubstituted benzoic acids were determined by Ostwald (*Z. physikal. Chem.*, 1889, **3**, 385), and it was noted that this constant could be calculated approximately if the constants for the mono-substituted and the unsubstituted acids were known. This work was extended by Holleman (*Rec. trav. chim.*, 1901, **20**, 361) to the chloronitro- and bromonitrobenzoic acids, the observed and the calculated values being in reasonable agreement except in the cases of the 2-nitro-3-halogenobenzoic acids. In general, acids substituted in the 2 : 3- and 2 : 6-positions have an abnormally high ionisation constant and show the greatest deviation from the calculated value.

Although there appears to be no proportionality between the ionisation constant of an acid and its coefficient of esterification or the saponification of its esters, yet there is a certain parallelism, and it seemed of interest to determine how far it would be possible to calculate the velocity of saponification of a disubstituted ester from the coefficients for the mono-substituted and for the unsubstituted esters.

The substituents chosen were the methoxyl group and chlorine; the first group has but little effect on the ionisation constant of benzoic acid and might be expected to have a small steric factor, whereas chlorine causes a large increase in the ionisation constant of benzoic acid and the steric effect is large.

The reaction was measured in 95 and 70% alcohol–water mixtures at 30°. The choice of solvent rested upon the following considerations : (1) The reaction could be measured up to 75% change in less than 30 hours even with the most stable esters; (2) the violent disturbance of the velocity coefficient due to traces of water gaining access to absolute alcohol would be eliminated; (3) whatever the nature of the ester, the velocity coefficient is least sensitive to effects due to the solvent in 70% alcohol (J., 1922, **121**, 243).

The results show that in 95% alcohol the order of the velocity coefficients for the methoxybenzoic esters is o-> m-> benzoate> p-, whereas in 70% alcohol the order is m->benzoate> o-> p-. The dimethoxybenzoic esters in 95% alcohol gave the order $2:3 > 2:5 > 3:5 >$ benzoate $> 3:4 > 2:4$, and in 70% alcohol $3:5 > 2:5 > 2:3 >$ benzoate $> 3:4 > 2:4$. The calculated value of the velocity coefficient was determined from an equation of the type :

$$k_{2:4\text{-ester}}/k_{\text{benzoate}} = (k_{2\text{-ester}}/k_{\text{benzoate}}) \times (k_{4\text{-ester}}/k_{\text{benzoate}}).$$

The ratio of the calculated to the observed value of k was $1:1\cdot2$, within an experimental error of 3% on the velocity coefficient. This result is all the more striking when it is considered that in this case even the *relative* order of the velocity coefficients for the mono-substituted esters changes with a change in the composition of the solvent.

In the case of the chloro-esters, the relative order of the velocity coefficients is m-> p-> o-> benzoate, and for the dichloro-esters, $3:5 > 3:4 > 2:5 > 2:4 > 2:3 >$ benzoate, this order being independent of the composition of the solvent. The ratio of the calculated to the observed value of k varied widely.

This difference in behaviour of the dichloro- and the dimethoxy-esters cannot be ascribed solely to steric effects, for if we omit from consideration the 2 : 3-dichlorobenzoic ester (where the steric factor might be supposed to be greatest) the ratio of $k_{\text{obs.}}/k_{\text{calc.}}$ for the other esters still varies over wide limits.

It was thought that this difference in behaviour might possibly be due to the peculiar behaviour of the ortho-substituted chloro-benzoic esters. It has been noted (J., 1922, **121**, 252) that ethyl o-chlorobenzoate on saponification, under apparently identical conditions, gave rise to two values for the velocity coefficient; in the present work, similar results have been obtained. Thus in 95% alcohol k was found to be 0·096 and 0·071, in 70% alcohol 0·162 and 0·116. The ethyl esters of the dichlorobenzoic acids having an ortho-substituent also show this peculiarity, since, in 95% alcohol, the 2 : 3-dichlorobenzoate gave 0·23 and 0·157, and in 70% alcohol 0·44 and 0·34. The lower value of k is in each case about 0·7 times the higher value. This difference in values lies well outside the highest experimental errors; it occurs whether ester, alkali, and solvent are taken from the same or from different samples, and, moreover, one value may be obtained three or four times in succession. It is found, however, that no combination of values will yield an approximately constant value for the ratio $k_{\text{obs.}}/k_{\text{calc.}}$.

Thus it would appear that in those cases in which the presence of

a substituent causes a large increase in the reactivity of an ester, it is impossible to calculate the velocity coefficient of a di-substituted ester from the coefficients for the mono-substituted and unsubstituted esters.

EXPERIMENTAL.

The chlorobenzoic acids were obtained by the usual methods. The 2 : 3- and 2 : 5-dichlorobenzoic acids were obtained by nitration of o-acetotoluidide, separation of the nitroamino-compounds, conversion into the dichlorotoluenes, and oxidation. 3 : 4-Dichlorobenzoic acid was obtained from p-acetotoluidide by a similar series of operations. The 3 : 5-dichlorobenzoic acid was prepared by chlorination of o-acetotoluidide, hydrolysis, deamination, and oxidation of the resulting dichlorotoluene. Acetanilide was converted into 2 : 4-dichloroacetanilide, which was hydrolysed to the amine, and this was converted into the nitrile and thence into 2 : 4-dichlorobenzoic acid.

The three methoxybenzoic acids, and 2 : 4- and 2 : 5-dimethoxybenzoic acids were obtained by the methylation of the corresponding hydroxy-acids, which were Kahlbaum products. The 2 : 3-dimethoxybenzoic acid was prepared by converting o-vanillin into o-veratraldehyde and oxidising this product. The oxidation of eugenol methyl ether yielded 3 : 4-dimethoxybenzoic acid, and the oxidation of orcinol dimethyl ether 3 : 5-dimethoxybenzoic acid.

Certain of the hydroxy-acids could be methylated only with great difficulty and with poor yields; in such cases the best results were obtained by dissolving the acid in methyl sulphate and adding drop by drop a concentrated solution of potassium hydroxide with vigorous stirring.

TABLE I.			TABLE II.		
Ethyl 2 : 4-dichlorobenzoate in 70% alcohol.			Ethyl o-methoxybenzoate in 95% alcohol.		
$a = 0.01314$; $b = 0.00667$.			$a = 0.04625$; $b = 0.03333$.		
t.	x.	k.	t.	x.	k.
30	0.00146	0.66	270	0.01330	0.038
45	0.00199	0.65	390	0.01417	0.037
65	0.00257	0.64	510	0.01660	0.037
85	0.00308	0.64	840	0.02185	0.039
105	0.00354	0.65	960	0.02243	0.037
135	0.00408	0.66	1120	0.02363	0.036
165	0.00447	0.65	1240	0.02480	0.037
205	0.00490	0.64	1360	0.02565	0.037
255	0.00528	0.65	1480	0.02570	0.034
317	0.00568	0.65	1590	0.02627	0.035
	Mean	0.65		Mean	0.037
	Duplicate	0.65		Duplicate	0.035

TABLE III.

Ester.	Solvent, 95% alcohol. Limit k.	k.	Solvent, 70% alcohol. Limit k.	k.
Benzoate	0·0265—0·029	0·028	0·102 —0·108	0·105
o-Methoxy-benzoate	0·0355—0·038	0·0365	0·076 —0·079	0·077
m- ,, ,, ...	0·0350—0·0365	0·035	0·122 —0·129	0·126
p- ,, ,, ...	0·0067—0·0059	0·0063	0·022 —0·024	0·023
o-Chloro- ,, ...	{ 0·094 —0·098 0·069 —0·073	0·096 } 0·071 }	0·111 —0·119 0·158 —0·164	0·116 } 0·162 }
m- ,, ,, ...	0·181 —0·192	0·187	0·73 —0·75	0·74
p- ,, ,, ...	0·112 —0·122	0·116	0·38 —0·42	0·40

TABLE IV.

Ester.	Solvent, 95% alcohol. Limit k.	k.	Solvent, 70% alcohol. Limit k.	k.
2 : 3-Dimethoxy-benzoate	0·057 —0·065	0·061	0·106 —0·115	0·110
2 : 4- ,, ,,	0·0081—0·0088	0·0084	0·0181—0·0200	0·019
2 : 5- ,, ,,	0·055 —0·060	0·057	0·122 —0·130	0·122
3 : 4- ,, ,,	0·0100—0·0107	0·0102	0·037 —0·041	0·038
3 : 5- ,, ,,	0·043 —0·047	0·046	0·172 —0·183	0·175
2 : 3-Dichloro- ,,	0·150 —0·160	0·157	0·33 —0·36	0·34
2 : 4- ,, ,,	0·202 —0·214	0·206	0·64 —0·655	0·65
2 : 5- ,, ,,	0·415 —0·425	0·42	0·99 —1·09	1·04
3 : 4- ,, ,,	0·55 —0·59	0·57	1·90 —2·00	1·95
3 : 5- ,, ,,	1·48 —1·57	1·52	4·05 —4·25	4·20

TABLE V.

Ester.	95% Alcohol. $k_{obs.}$	$k_{calc.}$	$k_{obs.}/k_{calc.}$	70% Alcohol. $k_{obs.}$	$k_{calc.}$	$k_{obs.}/k_{calc.}$
		Ethyl dimethoxybenzoates.				
2 : 3-	0·061	0·046	1·33	0·110	0·093	1·18
2 : 4-	0·0084	0·0082	1·02	0·019	0·017	1·12
2 : 5-	0·057	0·046	1·24	0·122	0·093	1·31
3 : 4-	0·0102	0·0079	1·29	0·038	0·028	1·35
3 : 5-	0·046	0·044	1·05	0·175	0·151	1·16
		Ethyl dichlorobenzoates.				
2 : 3-	0·157	0·474	0·33	0·34	0·817	0·42
2 : 4-	0·206	0·295	0·71	0·65	0·44	1·47
2 : 5-	0·42	0·474	0·89	1·04	0·817	1·27
3 : 4-	0·57	0·775	0·72	1·95	2·82	0·70
3 : 5-	1·52	1·25	1·22	4·20	5·21	0·81

The acids were all recrystallised from water or from aqueous alcohol until a constant melting point was obtained. They were converted into their ethyl esters by the usual method; liquid esters were twice distilled in a vacuum, and the solid esters were crystallised from aqueous alcohol.

The alcohol–water mixtures and the standard solutions of potassium hydroxide, acid, and ester were prepared in the usual manner. The experiments were carried out at $30° \pm 0·05°$. In the tables, time, t, is shown in minutes. " Limit k " represents the extreme values obtained in two determinations, and k the mean value of both determinations.

In calculating the value of k the lower velocity coefficient for ethyl o-chlorobenzoate has been employed.

Summary.

1. The velocities of saponification of six mono-substituted and ten di-substituted benzoic esters have been determined in two ethyl alcohol–water mixtures.

2. It has been shown that both for the chloro- and for the methoxy-esters the m-substituted compounds are the most reactive, except in one case.

3. The values of k found for the dimethoxy-esters bear a definite relation to those of the monomethoxy-esters, whereas in the case of the dichloro-esters this relationship is not observed.

4. It is shown that the relative order of the velocity coefficients for the monomethoxy-esters is altered by a change in the composition of the solvent.