581. *Chemical Constitution and the Dissociation Constants of Monocarboxylic Acids. Part XV.* Steric Effects in Substituted Nitrobenzoic Acids.*

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The dissociation constants of nine disubstituted benzoic acids, two trisubstituted benzoic acids, and three nitrophenols in water at 25° have been determined by the conductivity method; included are two series comprising dinitro- and chloronitro-benzoic acids. The results shed light on the operation of steric effects in the benzoic acid system.

DISSOCIATION constants for dimethylbenzoic acids were published in Part XIII[1] and further constants for disubstituted benzoic acids are provided in the present paper. These acids comprise two series possessing a nitro- or chloro-substituent at the 2-position and a

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* Part XIV, *J.*, 1954, 4102.

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

second nitro-group at positions 3, 4, 5, and 6 in turn. 3 : 4- and 3 : 5-Dinitrobenzo acids have also been included, together with two acids containing a third substituent.

Table 1 sets out the mean thermodynamic dissociation constants (K) of these acids in aqueous solution at 25°. Dissociation constants previously recorded for these acids were (with one exception italicised in Table 1) classical values obtained by older, less reliable techniques; these values are included in Table 1 for completeness. Similarly the dissociation constants of three substituted phenols are contained in Table 2 for comparison.

TABLE 1. *Dissociation constants* (10^3K).

Acid	This paper	Earlier values			M. p.
2 : 3-Dinitrobenzoic	14·1		14·4 [a]		146·5—147°
2 : 4-Dinitrobenzoic	37·6		38·5		182—183
2 : 5-Dinitrobenzoic	23·9		26·4 [a]		179·5—180
2 : 6-Dinitrobenzoic	72·5		81·5		203—204
3 : 4-Dinitrobenzoic	1·52		1·63 [a]		164·5—165
3 : 5-Dinitrobenzoic	1·50	1·63 [a]	1·62 [b]	*1·50* [c]	208—209
2 : 4 : 6-Trinitrobenzoic	222				227—228
4-Methyl-3 : 5-dinitrobenzoic	1·07				160—161
2-Chloro-3-nitrobenzoic	9·51		8·7 [d]		182·5—183
2-Chloro-4-nitrobenzoic	10·9		8·7 [d]		142·0—142·5
2-Chloro-5-nitrobenzoic	6·80		6·5 [b]	6·2 [d]	164—165
2-Chloro-6-nitrobenzoic	45·5				164—164·5
2-Bromo-6-nitrobenzoic	42·4				177—177·5

[a] Sirks, *Rec. Trav. chim.*, 1908, **27**, 207. [b] Bethmann, *Z. phys. Chem.*, 1890, **5**, 385. [c] Kendall, *J.*, 1912, **101**, 1295. Data recalculated by McInnes, *J. Amer. Chem. Soc.*, 1926, **48**, 2068, using a corrected Λ_0. [d] Holleman and de Bruyn, *Rec. Trav. chim.*, 1901, **20**, 208.

TABLE 2. *Dissociation constants* (K).

	This paper	Earlier values	M. p.
2-Nitrophenol	$5·9 \times 10^{-8}$	$4·3 \times 10^{-8}$ to 7×10^{-8} [e–h]	45·0—45·5°
2 : 6-Dinitrophenol	$1·97 \times 10^{-4}$	$1·4 \times 10^{-4}$ [e] $2·7 \times 10^{-4}$ [f]	62·2
2 : 4 : 6-Trinitrophenol	$1·96 \times 10^{-1}$	$2·3 \times 10^{-1}$ [i]	121·4—121·8

[e] Bader, *Z. phys. Chem.*, 1890, **6**, 289. [f] Holleman and Herwig, *Rec. Trav. chim.*, 1902, **21**, 432. [g] Hantzsch, *Ber.*, 1899, **32**, 3066. [h] *Idem, Ber.*, 1907, **40**, 1556. Rothmund and Drucker, *Z. phys. Chem.*, 1903, **46**, 827.

EXPERIMENTAL

Materials.—3 : 4-Dinitrobenzoic acid was prepared from 3 : 4-dinitrotoluene, for which we thank Dr. O. L. Brady, by oxidation with potassium dichromate in 50% sulphuric acid. 2 : 4-Dinitrobenzoic acid was obtained by refluxing 2 : 4-dinitrotoluene with equal volumes of fuming nitric and glacial acids. 2 : 3- and 2 : 6-Dinitrobenzoic acids were made from ethylbenzene and 2 : 4 : 6-trinitrotoluene, respectively, as described by Brady, Day, and Allen.[2]

The four 2-chloromononitrobenzoic acids were provided by Dr. A. A. Goldberg of Ward, Blenkinsop and Co., Ltd., and 2-bromo-6-nitrobenzoic acid by Dr. J. M. Dechary of Coates Chemical Laboratory, Louisiana, whom we thank.

2 : 5- and 3 : 5-Dinitrobenzoic, 4-methyl-3 : 5-dinitrobenzoic, and 2 : 4 : 6-trinitrobenzoic acids and the nitrophenols were purchased.

All acids were recrystallised repeatedly from conductivity water to constant m. p. (determined after drying in desiccators for several weeks), and equivalents were confirmed by alkalimetry.

The water used had specific conductance 0·5—0·8 gemmho.

Conductivity Measurements.—Measurements were made by means of the improved bridge network, and the conductivity cells and other equipment described earlier;[1] solutions were prepared individually by weight at each concentration. The thermodynamic dissociation constants (Table 3) were calculated along the usual lines. A solvent correction was applied in the derivation of K for *o*-nitrophenol.

Many of the acids examined were stronger ($K \gtrsim 10^{-3}$—10^{-1}) than most organic acids (10^{-5}—10^{-3}) hitherto examined in this Series. This entailed a change of procedure; the sodium-salt method of determining Λ_0 (acid) became less convenient and was replaced by Fuoss's extrapolation method[3] in which measurements of equivalent conductivity of the aqueous acid solutions are

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[2] Brady, Day, and Allen, *J.*, 1928. 981.

[3] Fuoss, *J. Amer. Chem. Soc.*, 1935, **57**, 488.

used. In the higher range of acid strengths K is particularly sensitive to the value chosen for Λ_0 and the emergence of a thermodynamic dissociation constant from data covering a moderate range of low concentrations may be taken as justifying both values.

TABLE 3.

10^3C (moles/l.)	Λ (mhos cm.^{2})	10^3K
2 : 3-*Dinitrobenzoic acid* (Λ_0 = 381·9)		
1·880	338·9	14·1
1·537	344·9	14·2
1·133	352·3	13·8
0·9369	356·7	14·1
0·8608	358·3	14·1
2 : 4-*Dinitrobenzoic acid* (Λ_0 = 381·9)		
4·004	343·6	37·2
2·854	351·8	36·8
2·090	358·3	37·8
1·695	361·9	38·5
1·609	362·7	37·8
1·256	365·7	37·7
2 : 5-*Dinitrobenzoic acid* (Λ_0 = 381·9)		
3·909	331·5	24·0
2·729	342·7	24·0
1·132	361·6	23·8
0·9126	364·7	23·4
0·7321	367·6	23·8
0·6176	369·4	23·9
2 : 6-*Dinitrobenzoic acid* (Λ_0 = 381·1)		
2·244	364·4	72·6
1·718	367·5	73·0
1·369	369·3	72·3
1·019	371·8	71·9
3 : 4-*Dinitrobenzoic acid* (Λ_0 = 381·5)		
2·625	202·2	1·51
1·770	228·1	1·52
1·753	228·9	1·53
1·305	247·7	1·53
0·7513	281·4	1·54
0·5455	298·8	1·54
0·4934	303·3	1·52

10^3C (moles/l.)	Λ (mhos cm.^{2})	10^3K
3 : 5-*Dinitrobenzoic acid* (Λ_0 = 383·7)		
4·937	164·6	1·50
3·682	182·4	1·50
2·489	206·6	1·50
2·295	211·6	1·50
1·349	246·2	1·51
1·015	263·6	1·50
0·7228	283·6	1·50
2 : 4 : 6-*Trinitrobenzoic acid* (Λ_0 = 379·6)		
3·065	367·5	224
2·817	368·1	229
2·147	369·8	214
1·617	371·5	214
1·591	371·7	228
4-*Methyl*-3 : 5-*dinitrobenzoic acid* (Λ_0 = 378·2)		
3·275	165·7	1·07
2·356	185·5	1·07
1·337	221·1	1·07
1·174	229·2	1·07
0·8337	250·5	1·07
0·7558	257·2	1·08
0·7071	260·5	1·06
0·5933	270·7	1·06
0·4286	289·2	1·06
2-*Chloro*-3-*nitrobenzoic acid* (Λ_0 = 379·4)		
1·841	323·9	9·43
1·129	340·8	9·58
0·5847	356·7	9·60
0·5531	357·5	9·56
0·5364	357·8	9·42
0·3971	362·6	9·47
2-*Chloro*-4-*nitrobenzoic acid* (Λ_0 = 381·5)		
2·945	311·8	10·9
2·919	312·0	10·9
1·789	331·7	10·9
0·5842	360·7	10·9

10^3C (moles/l.)	Λ (mhos cm.^{2})	10^3K
2-*Chloro*-5-*nitrobenzoic acid* (Λ_0 = 379·1)		
4·079	267·9	6·75
2·942	286·0	6·73
1·729	312·7	6·83
1·492	318·8	6·87
1·018	333·4	6·83
0·5788	349·2	6·72
0·4811	353·6	6·85
2-*Chloro*-6-*nitrobenzoic acid* (Λ_0 = 381·7)		
2·488	357·7	45·9
2·418	357·9	44·2
2·360	358·3	44·1
1·445	365·8	46·4
0·9090	370·6	45·9
0·8198	371·2	46·4
2-*Bromo*-6-*nitrobenzoic acid* (Λ_0 = 382·2)		
3·061	353·2	42·6
2·577	356·6	42·5
1·501	365·3	42·2
1·487	365·4	42·3
0·8459	371·2	42·5
2 : 6-*Dinitrophenol* (Λ_0 = 379·2)		
0·8455	145·6	0·198
0·7859	149·3	0·196
0·7637	151·1	0·197
0·6117	164·0	0·198
0·4211	186·5	0·197
0·4033	189·1	0·197
0·3172	204·6	0·198
0·3051	205·9	0·195
2 : 4 : 6-*Trinitrophenol* (Λ_0 = 385·5)		
4·410	369·0	201
4·024	369·8	199
3·894	370·1	192
2·548	373·9	195
2·358	374·4	195

o-*Nitrophenol* (Λ_0 = 373·0 computed)

10^3C (moles/l.)	Λ (mhos cm.^{2})	10^6K	10^3C (moles/l.)	Λ (mhos cm.^{2})	10^6K
4·237	1·411	5·8	1·905	2·068	5·9
2·601	1·778	5·9	1·693	2·232	6·1
2·365	1·872	6·0			

The values of Λ_0 included in Table 3 exhibit none of the regularities usual in related monocarboxylic acids. This is perhaps connected with the fact that in this series anomalies are introduced by large steric factors which are likely to influence variously and anomalously the solvation characteristics of the different anions.

DISCUSSION

The determination of accurate dissociation constants for polysubstituted benzoic acids serves many useful purposes. Such data are required for the examination of the principle of additivity of structural parameters based on dissociation constants of monosubstituted acids.[4] The series of acids examined in this paper also have an interesting bearing on current theories of the steric interaction of adjacent substituent groups in the benzene ring, and in one case steric inhibition of mesomerism arising at a point remote from the reactive centre (carboxyl) is exhibited.

Dinitrobenzoic Acids.—In a 3 : 4-disubstituted benzoic acid the 3-substituent might inhibit the mesomeric effect of the group in the 4-position;[1] this is not expected when the 4-substituent is methyl but can occur with a substituent such as nitro where the $-M$ effect, to be unimpaired, calls for coplanarity of the group with the benzene ring. A sufficiently bulky 3-substituent interferes with such coplanarity and this can be traced in the similarity in strengths of 3 : 4- and 3 : 5-dinitrobenzoic acids (cf. the appreciable difference in strengths of *m*- and *p*-nitrobenzoic acids, $10^5K = 32{\cdot}1$ and $37{\cdot}6$ respectively,[5] where the $-M$ effect of the nitro-group is fully operative from the 4-position). The mutual steric interference of two adjacent nitro-groups resembles the interference between carboxyl and an adjacent nitro-group, because the steric requirements of carboxyl and nitro-groups are similar. Such steric inhibition of mesomerism cannot occur, however, between two methyl groups, as the strengths of dimethylbenzoic acids show.[1] A similar instance of steric inhibition involving a nitro-group at a point remote from the reactive centre was noted by Wheland, Brownell, and Mayo [6] who point out that 4-nitro-2 : 6 : 1-xylenol is a stronger acid than 4-nitro-3 : 5 : 1-xylenol although this is not to be expected if the formal polar influence of the substituents are normally operative; this is evidence of the steric interference of methyl with nitroxyl, which is reasonable in view of the known obstruction to the coplanarity imposed by methyl in the 2-methyl- and 2 : 6-dimethylbenzoic acids. The ready dinitration of mesitylene has been attributed by Dewar [7] to a similar inhibition of the $-M$ effect of nitro- by methyl groups.

The fact that 2 : 5-dinitrobenzoic acid is considerably stronger than the 2 : 3-isomer is probably due to an additional depression of the $-M$ effect of the 2-nitro-group in the latter. This implies that the normal polar effects of the *ortho*-substituents may make a substantial contribution to the dissociation constant, and that in *o*-nitrobenzoic acid the inhibition of mesomerism, which can be experienced by both substituents, is brought about particularly in carboxyl (which is less strongly conjugated with the benzene ring than nitro) and hence accounts for the unusually high strength. The flanking of the 2-nitro-group by a substituent at the 3-position, however, depresses appreciably the $-M$ effect of nitro-groups (actually both nitro-groups are affected); this is seen in the departure from the additivity principle (expressed in terms of the free energy of ionisation) * which in the case of 2 : 3-dinitrobenzoic acid is relatively large (*viz.* -14%; cf. -6% for the 2 : 5-acid).

Where an additional nitro-group is not in close proximity to groups already present the increment in strength should be normal. Thus no additional steric factor is introduced if a 4-nitro-group is inserted into *o*-nitro- and 2 : 6-dinitro-benzoic acids, and the increase in the strengths of the acids so obtained is as expected.

The dissociation constant for 2 : 6-dinitrobenzoic acid shows that the introduction of a nitro-group into the second *ortho*-position in benzoic acid does not maintain the magnitude of the enhancement caused by the introduction of the first *o*-nitro-group (there is a -25% departure from additivity). It is as though the carboxyl has already experienced such

* The free-energy increment for each individual substituent is derived from the strengths of monosubstituted benzoic acids in water at 25° recorded by Dippy.[5]

[4] (*a*) Shorter and Stubbs, *J.*, 1949, 1180; (*b*) Derick, *J. Amer. Chem. Soc.*, 1911, **33**, 1152; (*c*) Wegscheider, *Montash.*, 1902, **23**, 288; (*d*) Brown, in Braude and Nachod's "Determination of Organic Structures by Physical Methods," Academic Press, New York, 1955, pp. 591—596.

[5] Dippy, *Chem. Rev.*, 1939, **25**, 181.

[6] Wheland, Brownell, and Mayo, *J. Amer. Chem. Soc.*, 1948, **70**, 2492.

[7] Dewar, "Electronic Theory of Organic Chemistry," Oxford Univ. Press, 1949 p. 203.

effective compression that the second nitro-group exerts only a small additional steric obstruction. This is not to say that the $-M$ effect of the second nitro-group is not also inhibited somewhat.

The fall in strength brought about in 3 : 5-dinitrobenzoic acid by the introduction of a 4-methyl group is normal, namely, that predicted by the additivity principle (—1·3% departure). This is a little surprising since some steric interaction leading to inhibition of the mesomeric effects of both nitro-groups might be expected even though this involves relay from the *meta*-position. In addition, a hyperconjugative resonance interaction between vicinal methyl and nitroxyl might have influenced the acid strength.

In certain of the foregoing acids steric interference with the resonance contribution of the nitro-group appears as a reduction of the relative acid strengths, but this feature is not confined to benzoic acids, as the strengths of nitrophenylacetic, β-phenylpropionic, and cinnamic acids reveal [5] (see Table 4).

TABLE 4. *Dissociation constants.*

Substituent	H	*o*-NO₂	*m*-NO₂	*p*-NO₂
Cinnamic acid (10^5K)	3·65	7·07	7·75	8·99
Phenylacetic acid (10^5K)	4·88	9·90	10·8	14·1
β-Phenylpropionic acid (10^5K)	2·19	3·13	—	3·36
Phenylboronic acid ($10^{10}K$)	1·97	5·6	69	98

These data relate to aqueous solution except those for the phenylboronic acids which apply to 25% aqueous ethanol.

Originally an internal hydrogen bond was suggested [8] to explain the fact that in each system the *o*-nitro-acid is the weakest of the three isomers, which were expected to give the order of strengths, *ortho* $\simeq$ *para* > *meta*. Now, a more likely explanation is that the side-chain carrying carboxyl in each of these systems inhibits the $-M$ effect of the *o*-nitro-group by exerting steric obstruction to uniplanarity; this assumes that a mesomeric effect can be relayed through a saturated side-chain, a proposition [9] now generally accepted. Of the isomeric mononitrophenylboronic acids [10] (Table 4) the *o*-nitro-isomer is considerably the weakest, and here again the foregoing explanation could be advanced. Separate and specific explanations have been offered, however, for this observation; one [11] proposes that the oxygen of a nitro-group co-ordinates with the boron atom, and the other [12] regards the interaction of boronic acids with water as one which does not lead to protolysis of the parent acid but to its acquisition of OH^-, a process which is depressed by a bulky *ortho*-substituent (so-called *F*-strain in the anion).

The lack of a large " *ortho*-effect " in substituted phenols has already received much comment. The dissociation constants of 2-nitro-, 2 : 6-dinitro-, and 2 : 4 : 6-trinitro-phenol have now been derived by our conductimetric procedure (Table 2), and the steady increments of strength with progressive introduction of nitro-groups, testify to the absence of appreciable steric factors.

Chloronitrobenzoic Acids.—The acids examined comprise *o*-chlorobenzoic acid substituted in turn at all positions with one nitro-group, and it is seen that the enhancement in strength caused by nitroxyl varies considerably with its position, the departures from additivity being: 3-NO₂, +10%; 4-NO₂, +10%; 5-NO₂, —3%, and 6-NO₂, —13%.

The dissociation constants of 2-chloro-3-nitro- and 2-chloro-5-nitro-benzoic acids differ appreciably and the enhancement shown in the former acid is not easily explained unless it is due to mutual repulsion between the 2- and the 3-substituent leading to more effective steric influence of the spherically symmetrical chlorine atom upon the adjacent carboxyl group.

As in the dinitrobenzoic acid series, occupation of *ortho*-positions by a halogen and a nitro-group leads to an acid strength far short of additivity requirements, as the values

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[8] Dippy and Lewis, *J.*, 1937, 1426.

[9] Dippy, Watson, and Williams, *J.*, 1935, 346.

[10] Bettman, Branch, and Yabroff, *J. Amer. Chem. Soc.*, 1934, **56**, 1865.

[11] Ingold, " Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 750.

[12] McDaniel and Brown, *J. Amer. Chem. Soc.*, 1955, **27**, 3756.

of K for 2-chloro-6-nitro- and 2-bromo-6-nitro-benzoic acids show (deviations of -13% and -16% respectively). Once again, it can be concluded that the second *ortho*-substituent here produces a smaller compression effect upon carboxyl [in contrast with the large steric contribution to the inhibition of resonance made by introducing 6-nitro- or 6-methyl into *o*-toluic acid (10^3K: *o*-toluic, 0·124; 2-methyl-6-nitrobenzoic, 13·4; 2 : 6-dimethylbenzoic acid, 0·568)]. The fact that the bromo-acid is weaker than the chloro-acid in the foregoing cases underlines that bulk is not the only substantial factor determining strength in these *ortho*-acids. The importance of the direct component of the inductive effect must not be overlooked where such a strongly electronegative group as halogen approaches the reactive centre so closely (cf. Brown [13]).

The strength of 2-chloro-4-nitrobenzoic acid is unexpected; the introduction of the 4-nitro-group into 2-chlorobenzoic acid should be normally additive whereas in fact a $+10{\cdot}2\%$ departure from additivity is shown.

It seems reasonable to conclude that the additivity principle cannot in most cases be applied to the strengths of disubstituted benzoic acids $C_6H_3(XY)\cdot CO_2H$ because it embodies the assumption that the carboxyl group is influenced independently by the substituents X and Y. Only in the absence of additional resonance interaction between X and Y, or of additional steric interaction between X and Y or between X or Y and carboxyl, might such an expectation be realised with any degree of certainty. Such factors can have a profound effect upon acid strength and, where they are manifested only in the polysubstituted acid, any prediction based on the dissociation constant data for appropriate monosubstituted acids will be unrealistic. Any conclusions that can be drawn from Shorter and Stubbs's analysis [4a] suffer from the additional disadvantage that the dissociation constants used by them were classical data from the literature, and derived by old, unrefined techniques. Thus, for instance, in acids of a high order of strength the value of $K_{\text{thermodynamic}}$ (true strength) might be as much as twice the value derived for $K_{\text{classical}}$.

As discussed by Ingold [14] and Hammett,[15] the structural changes brought about near the site of proton transfer will affect both the heat change and entropy change of the process, whereas structural changes at a more distant point will affect significantly the heat change only. Again, if the energy of proton transfer is regarded along the lines proposed by Gurney [16] as being made up of a part sensitive to environment and a part insensitive to environment, a short-range disturbance (steric factor), affecting the solvation characteristics of the protolytic system, could render the dissociation constant abnormal by disturbing the proportions of the contributions of the two parts. Thus a wide departure from the additivity principle of the strength of a particular acid might well be regarded as indicating the operation of a steric effect. Further criteria can be taken to be any departure from standard behaviour of the group of related acids under review either when the strengths in different media (of similar chemical character, *e.g.*, hydroxylic solvents) are compared [17] or in respect of the trend of temperature dependence. A very small amount of experimental evidence already exists which may support this approach, but, for the present, scarcity of experimental data prevents the further elucidation of the problem of steric effects in benzoic acids along these lines.

The recent examination of the cumulative effects of substituents on the activation energies of the alkaline hydrolysis of a limited range of substituted ethyl benzoates [18] also shows that the outcome of the joint operation of two groups in the benzoic system is approximately the sum of the individual effects only where steric interaction of groups is negligible (notably in 3 : 5-disubstituted benzoic esters).

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[13] Ref. 4*d*, p. 605.
[14] Ref. 11, p. 727.
[15] Hammett, " Physical Organic Chemistry," McGraw-Hill, New York, 1940, p. 206.
[16] Gurney, " Ionic Processes in Solution," McGraw-Hill, New York, 1953, p. 124.
[17] Dippy, *J.*, 1941, 550; 1944, 411; ref. 15, p. 207.
[18] Jones and Robinson, *J.*, 1955, 2845.