461. *Chemical Constitution and the Dissociation Constants of Mono-carboxylic Acids. Part XVII.* ortho-Effects in Substituted Salicylic Acids.*

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The dissociation constants of nine substituted salicylic acids have been determined together with those of 3-hydroxy-2-naphthoic acid and its methyl ether. The dissociation constants of salicylic acid and its *meta*- and *para*-isomers have also been measured for the first time by a modern conducto-metric procedure. The evidence suggests that in the 6-substituted salicylic acids the measured strength is an outcome of competing *ortho*-effects; it appears that the secondary steric effect, imposed by the 6-nitro-substituent, suppresses the internal hydrogen bond involving the carboxyl and hydroxyl groups.

THE strength of salicylic acid (in water at 25°) is anomalously high compared with the strengths of the isomeric *m*- and *p*-hydroxybenzoic acids and with those of its methyl and phenyl ethers (as shown by the values of K/K_u, where K_u is the dissociation constant of benzoic acid, in Table 1 [1]—all obtained in this Series).

TABLE 1. *Values of K/K_u for $X \cdot C_6H_4 \cdot CO_2H$.*

X = *o*-OH, 16·1; *m*-OH 1·32; *p*-OH, 0·471
X = *o*-OMe, 1·28; *m*-OMe 1·30; *p*-OMe, 0·539
X = *o*-OPh, 4·74; *m*-OPh 1·79; *p*-OPh, 0·479

To account for the extraordinary dissociation constant of salicylic acid, Branch and Yabroff [2] suggested that an internal hydrogen bond is formed between the carboxyl and hydroxyl groups which stabilises the anion much more than the undissociated acid, so disturbing the equilibrium in favour of dissociation. Additional hydrogen bonding is possible in 2 : 6-dihydroxybenzoic acid, and hence the further large increase in strength ($K/K_u = 830$). More recently, Ingold [3] has suggested that the acid-strengthening influence is due to the introduction of a positive charge into the carboxyl group as a result of the hydrogen bonding which arises partly from electrostatic attraction of the adjacent groups and partly through covalent interaction of these substituents.

The dissociation constants of 3-hydroxy-2-naphthoic acid and its methyl ether (Table 2) again show a remarkably high relative strength for the hydroxy-acid. In fact the situation encountered in the benzene system is reproduced; this is best shown by the results for the relative strengths (K/K_u) where K_u is the strength of the parent acid in each case, *viz.*: salicylic, 16·1; *o*-methoxybenzoic, 1·28; 3-hydroxy-2-naphthoic, 28·4; 3-methoxy-2-naphthoic 2·23.

The nitrosalicylic acids examined display a particularly interesting series of strengths. The most striking fact is that 6-nitrosalicylic (CO_2H is at position 1) is weaker than *o*-nitro-benzoic acid ($10^3 K = 6·71$), which implies that the specific hydrogen bond operating in salicylic acid (and in its anion in particular) is absent from it. This can be understood on assumption that the $O \cdots H-O$ bridge in the anion (I) requires coplanarity with the benzene ring for its creation.

The nitro-group is like carboxyl in that both groups have $-I$, $-M$ polar characteristics and similar steric requirements. However, the nitro-group is doubtless the more strongly conjugated with the benzene ring (see Part XV), and hence when the two substituents are adjacent their conflicting bulks twist the carboxyl rather than the nitro-group out of the plane of the ring, with the resultant enhancement of strength exhibited by *o*-nitrobenzoic

* Part XVI, *J.*, 1957, 265.
[1] Dippy, *Chem. Rev.*, 1939, **25**, 151.
[2] Branch and Yabroff, *J. Amer. Chem. Soc.*, 1934, **56**, 2568.
[3] Ingold, " Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 749.

acid. It follows, then, that when a substantial group such as nitro is introduced into the 6-position of benzoic acid it will so alter the steric conformation of the carboxyl group that a hydrogen-bridge is no longer formed when hydroxyl enters the 2-position. The hydroxyl group which, being small, exercises very little bulk obstruction, will then have the net effect of depressing acid strength through the normal internal electromeric displacements $(+M)$, in much the same way as it does in p-hydroxybenzoic acid $(10^5 K = 2.9$; cf. benzoic acid $10^5 K = 6.27)$.

The near identity of the strengths of 4-nitro- and 6-nitro-salicylic acids is quite fortuitous; the 4-nitro-acid is an orthodox salicylic acid into which introduction of a

TABLE 2. *Dissociation constants* $(10^3 K)$.

Acid	This paper	Earlier values	M. p.	Acid	This paper	Earlier values	M. p.
3-Nitrosalicylic	13·4	15·7 [a, b]	146·5—147°	5-Chlorosalicylic	2·35	1·97 [d]	165°
4-Nitrosalicylic	5·88	—	235—236	6-Chlorosalicylic	2·36	—	171·3—172·3
5-Nitrosalicylic	7·57	8·00 [b]	232—233	5-Bromosalicylic	2·44	—	170—171
		8·90 [c]		6-Methylsalicylic	0·478	0·295,[e]	171·3—171·8
6-Nitrosalicylic	5·81	—	166—167			1·06 [f]	
3 : 5-Dinitrosalicylic	201	—	172—172·5	3-Hydroxy-2-naphthoic	1·96	—	224
				3-Methoxy-2-naphthoic	0·15	—	134—135

[a] Ostwald, *Z. phys. Chem.*, 1887, **1**, 61; 1889, **3**, 260. [b] Magnanini, *Gazzetta*, 1891, **21**, 215. [c] Ostwald, *Z. phys. Chem.*, 1889, **3**, 241, 260. [d] Coppadoro, *Gazzetta*, 1902, **32**, 542. [e] Peltier, *Compt. rend.*, 1955, **241**, 1467 (in 1% aqueous alcohol solution). [f] Stohmann and Langbein, *J. prakt. Chem.*, 1894, **50**, 389.

TABLE 3. *Dissociation constants* $(10^5 K)$.

Acid	This paper	Earlier values	M. p.
o-Hydroxybenzoic (salicylic)	101	105,[a] 107 [b]	159—159·5°
m-Hydroxybenzoic	8·27	8·3,[a] 8·71 [b]	197—198
p-Hydroxybenzoic	2·95	2·9,[a] 3·31 [b]	217

[a] Ref. 2. [b] Kuhn and Wassermann, *Helv. Chim. Acta*, 1928, **11**, 31.

4-nitro-group simply produces its expected acid-strengthening effect, giving only about 2% deviation from the additivity principle discussed in Part XV.[4]

The fact that 3-nitro- and 5-nitro-salicylic acids are stronger than 4-nitrosalicylic acid is a special feature of this series. A nitro-group at the *para*-position with respect to carboxyl in an aromatic acid normally enhances the strength more than when it occupies the *meta*-position (cf. K/K_u for *m*-nitro- and *p*-nitro-benzoic acids, 5·12 and 5·90 respectively). This is due to the ready operation of the $-M$ effect when the nitro-group is in effective
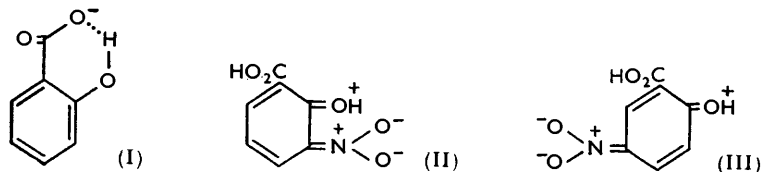
conjugation. The converse of this feature in the salicylic series can be attributed to the increased polarity of the bond between hydrogen and oxygen in the hydroxyl group brought about by the resonance interaction of hydroxyl with the nitro-group at the *ortho*- or *para*-position with regard to it, as illustrated in the structures (II) and (III) (a possibility denied to the 4-nitrosalicylic acid system). This means that the hydroxyl group can more readily participate in the hydrogen bridge, particularly of the anion, in the cases of the 3- and the 5-nitro-acids [a trend which bestows additional stabilisation on the anion, leading to a larger K (21% and 8% in excess of additivity)] than in that of the 4-nitro-acid (0·3% departure from additivity). The further enhancement of strength shown by 3 : 5-dinitrosalicylic acid, although very great (i.e., +33% departure from additivity), lends emphasis to this interpretation. Any tendency to hydrogen bonding between the

[4] Dippy, Hughes, and Laxton, *J.*, 1956, 2995.

hydroxyl and the nitro-group in 3-nitrosalicylic acid is apparently of secondary significance. It is noteworthy that 3- and 5-nitrosalicylic acids are the only disubstituted benzoic acids treated by us so far which show a large *positive* deviation from additivity, a fact which indicates that a special kind of anomaly operates here.

The strengths of 6-methyl- and 6-chloro-salicylic acids have also been determined. The strength is much less enhanced in each case than expected on the additivity principle as the following departures show : 6-methylsalicylic, -41% ; 6-chlorosalicylic, -36% ; cf. 6-nitrosalicylic, -39%. Clearly the two substituents at the *ortho*-positions are again unable to exert the influences possible when present independently in benzoic acid; their simultaneous presence seems to inhibit formation of the hydrogen bridge.

Several potentiometric determinations of the approximate strengths of monosubstituted *o*-methylbenzoic acids were made recently by Peltier [5] (in water containing 1% of ethanol) who records pK 3·07, 3·53, and 3·98 respectively for salicylic, 6-methylsalicylic, and *o*-toluic acids. This sequence is consistent with our findings. Peltier observes that this order signifies an important modification of the hydrogen bond in 6-methylsalicylic acid.

It is noteworthy that the strengths of 5-chloro- and 5-bromo-salicylic acids are almost the same and approximately that of 6-chlorosalicylic acid; probably the hydrogen-bridge is strengthened in the 5-halogeno-salicylic acids by the inductive influence of halogen $(-I)$ situated in the *para*-position to the hydroxyl group, thereby enhancing the dissociation constant.

The strengths of the monohydroxy-benzoic acids (Table 3) have now been determined by a modern conductometric procedure and the values of K obtained confirm the lower values of the many to be found in the literature.

EXPERIMENTAL

Materials.—6-Chlorosalicylic acid. 2-Chloro-6-nitrotoluene (5 g.) when refluxed with aqueous alkaline permanganate for 5 hr. gave 2-chloro-6-nitrobenzoic acid (3·5 g.) which upon reduction (ferrous sulphate and aqueous ammonia) yielded 2-amino-6-chlorobenzoic acid (2·3 g.). When diazotised, gently warmed, and set aside, this (4·4 g.) gave 6-chlorosalicylic acid, m. p. 164° (Cohn [6] records m. p. 166°).

6-Methylsalicylic acid was similarly prepared [7] from 2-methyl-6-nitrobenzoic acid (obtained by Gabriel and Thieme's method).[8]

4-Nitro- and 6-nitro-salicylic acids were kindly supplied by Dr. A. A. Goldberg of Ward, Blenkinsop and Co., Ltd., and 3-methoxy-2-naphthoic acid by Dr. K. Kerridge whom we thank. The remaining acids were purchased.

Acids were recrystallised from conductivity water, except for 3-hydroxy- and 3-methoxy-2-naphthoic acids which were recrystallised from aqueous acetone and benzene–light petroleum (b. p. 60—80°) respectively. Final specimens were dried in desiccators for two weeks and equivalents confirmed by alkalimetry.

TABLE 4.

o-Hydroxybenzoic acid (salicylic acid)			m-Hydroxybenzoic acid			p-Hydroxybenzoic acid		
10^3c	Λ	10^5K	10^3c	Λ	10^5K	10^3c	Λ	10^5K
			2·561	61·23	8·29	4·187	30·24	2·92$_5$
4·634	145·5	101	2·129	66·29	8·23	2·997	35·47	2·93
4·293	149·8	101	1·790	71·77	8·28	2·307	40·18	2·94$_5$
1·595	210·1	102	1·488	77·71	8·24	1·843	44·67	2·95
1·149	232·2	102	1·374	80·65	8·29	1·455	49·89	2·95$_5$
0·7973	255·2	102	1·114	88·33	8·29	0·8775	62·83	2·95$_5$
0·4057	294·7	100	0·8458	98·87	8·22	0·7530	67·31	2·95$_5$
	$\Lambda_0 = 385·2$		0·6071	114·0	8·33	0·2909	101·3	2·92$_5$
			0·2916	151·0	8·26		$\Lambda_0 = 372·2$	
				$\Lambda_0 = 367·1$				

[5] Peltier, *Compt. rend.*, 1955, 58.
[6] Cohn, *Mitt. Technol. Gewerb.-Mus. Wien*, **11**, 178; *Chem. Zentr.*, 1901, II, 925.
[7] Asahina and Kondo, *J. Pharm. Soc. Japan*, 1922, Nr. 482, S. 3.
[8] Gabriel and Thieme, *Ber.*, 1919, **52**, 1079.

The specific conductance of the water employed was 0·5—0·8 gemmho.

Conductivity Measurements.—Methods and equipment previously described were used.[9] Λ_0 was evaluated by the extrapolation methods of Fuoss [10] and Ives *et al.*[11] Results are given in Tables 4 and 5 (concn. in moles l.$^{-1}$; Λ in mho cm.^{2}).

TABLE 5.

2-Hydroxy-3-nitrobenzoic acid (3-nitrosalicylic acid)

10^3c	Λ	10^3K
4·299	309·1	13·3
2·729	330·4	13·6
1·035	359·6	13·0
1·649	347·5	13·4
0·9745	361·3	13·5
0·5023	372·8	13·7

$\Lambda_0 = 388·6$

2-Hydroxy-4-nitrobenzoic acid (4-nitrosalicylic acid)

10^3c	Λ	10^3K
2·444	295·9	5·95
1·304	325·4	5·85
1·225	328·9	5·93
1·052	334·6	5·81
0·9168	339·6	5·82
0·7571	346·0	5·83

$\Lambda_0 = 387·5$

2-Hydroxy-5-nitrobenzoic acid (5-nitrosalicylic acid)

10^3c	Λ	10^3K
3·643	287·2	7·52
3·214	294·0	7·47
2·457	308·5	7·55
2·204	314·5	7·65
1·525	330·1	7·53
1·075	343·5	7·62
0·8160	351·8	7·63

$\Lambda_0 = 388·2$

2-Hydroxy-6-nitrobenzoic acid (6-nitrosalicylic acid)

10^3c	Λ	10^3K
3·239	277·0	5·91
2·274	295·9	5·84
1·625	311·6	5·73
1·055	331·1	5·85
0·7769	341·2	5·78
0·3551	355·0	5·75

$\Lambda_0 = 383·9$

2-Hydroxy-3 : 5-dinitrobenzoic acid (3 : 5-dinitrosalicylic acid)

10^3c	Λ	10^3K
5·304	366·0	188
3·247	371·6	195
2·199	374·6	203
2·137	374·9	202
1·852	375·6	204
1·613	376·5	212

$\Lambda_0 = 385·0$

5-Chloro-2-hydroxybenzoic acid (5-chlorosalicylic acid)

10^3c	Λ	10^3K
1·369	272·4	2·34
1·216	279·4	2·34
1·033	289·4	2·37
0·8781	297·9	2·35$_5$
0·7552	305·8	2·36$_5$
0·5976	316·7	2·35
0·5872	317·5	2·35
0·5181	323·1	2·36
0·4819	326·2	2·36
0·2972	343·0	2·31$_5$

$\Lambda_0 = 383·6$

2-Chloro-6-hydroxybenzoic acid (6-chlorosalicylic acid)

10^3c	Λ	10^3K
1·069	286·9	2·37$_5$
0·7503	305·2	2·36
0·6156	314·5	2·35
0·5867	316·5	2·34
0·5754	317·9	2·34
0·4475	329·1	2·41
0·4443	327·9	2·32
0·2882	344·2	2·41

$\Lambda_0 = 382·6$

5-Bromo-2-hydroxybenzoic acid (5-bromosalicylic acid)

10^3c	Λ	10^3K
1·349	274·6	2·42$_5$
1·164	283·4	2·44
0·6974	310·7	2·46$_5$
0·6589	312·8	2·43$_5$
0·5515	319·8	2·38
0·4938	325·5	2·44
0·4318	331·0	2·45$_5$
0·2210	351·6	2·42

$\Lambda_0 = 382·4$

3-Hydroxy-2-naphthoic acid

10^3c	Λ	10^3K
0·7873	285·5	1·94$_5$
0·7103	291·3	1·96
0·5666	303·0	1·99
0·5194	306·3	1·95$_5$
0·3334	324·8	1·98
0·2948	329·7	(2·01$_5$)
0·2525	334·6	2·00
0·2037	339·0	(1·88$_5$)
0·1437	348·0	1·92$_5$

$\Lambda_0 = 373·3$

3-Methoxy-2-naphthoic acid *

10^3c	Λ	10^3K
0·06529	291·6	0·178
0·05475	292·3	0·151
0·03877	303·1	0·132

Λ_0 (assumed) = 375

2-Hydroxy-6-methylbenzoic acid (6-methylsalicylic acid)

10^3c	Λ	10^3K
1·189	174·5	0·475
1·167	175·5	0·473
0·9182	189·7	0·470
0·8523	195·2	0·478
0·7903	200·0	0·478
0·5463	224·0	0·483
0·4139	241·3	0·482
0·2565	269·6	0·479
0·1796	288·4	0·471
0·1145	309·8	0·467

$\Lambda_0 = 373·2$

* The values of dissociation constant of this acid were derived from the classical Ostwald expression, and are very approximate in consequence of the extremely sparing solubility of this acid in water.

[9] Dippy, Hughes, and Laxton, *J.*, 1954, 1470.
[10] Fuoss, *J. Amer. Chem. Soc.*, 1935, **57**, 488.
[11] Ives, *J.*, 1933, 731; Ives and Sames, *J.*, 1943, 511.