# 10. *Thermodynamic Dissociation Constants of Hydroxy- and Alkoxy-benzoic Acids.*

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The thermodynamic dissociation constants of *o*-, *m*-, and *p*-hydroxybenzoic acids, and of their methyl, ethyl, *n*-propyl, and *iso*propyl ethers have been measured in aqueous solution at 20° by an electrometric method. The results are discussed in terms of the various influences known to be operative in benzene derivatives.

DETAILED studies of the polar influence of alkoxy-groups on the reactivity of organic compounds have been made (Kindler, *Annalen*, 1926, **450**, 1; 1928, **454**, 278; Robinson and Smith, J., 1926, 392; Robinson, Clarke, and Smith, J., 1927, 2647; Blakey, McCombie, and Scarborough, J., 1926, 2963; Bradfield and Brynmor Jones, J., 1928, 1006, *et seq.*; *Trans. Faraday Soc.*, 1941, **37**, 726; Brynmor Jones, J., 1943, 430), but there is on record no parallel series of measurements, using modern methods, of their influence on the dissociation constants of acids and bases. In the aliphatic series the only available data are due to Palomaa (*Chem. Zentr.*, 1912, **2**, 596), who measured the effects of alkoxy-groups on the dissociation constants of saturated aliphatic acids by the conductivity method. His values, expressed as p$K$ ($= -\log_{10}K$), for the alkoxyacetic acids at 25° are given below. For comparison the accurate value for acetic acid (Harned and Ehlers, *J. Amer. Chem. Soc.*, 1932, **54**, 1350) is also included.

*Dissociation constants of alkoxyacetic acids* ($CH_2R{\cdot}CO_2H$).

| R = | H. | HO. | MeO. | EtO. | Pr$^{\alpha}$O. | Pr$^{\beta}$O. | Bu$^{\alpha}$O. | Bu$^{\beta}$O. |
|---|---|---|---|---|---|---|---|---|
| p$K$ ........... | 4·756 | 3·82 | 3·53 | 3·60 | 3·65 | 3·69 | 3·66 | 3·67 |

In the aromatic series measurements are almost wholly confined to the hydroxy- and methoxy-acids; recent available data (references cited by Dippy, *Chem. Rev.*, 1939, **25**, 206—208) expressed as p$K$ are summarised in the following table; Tait's value for *m*-ethoxybenzoic acid (J., 1943, 423) is also included: it is identical with that found in the present work. These measurements relate to aqueous solutions except those for the boric acids, which were made in 25% alcohol.

| R = | H. | OH. | | | OMe. | | | OEt. | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | *o*-. | *m*-. | *p*-. | *o*-. | *m*-. | *p*-. | *o*-. | *m*-. | *p*-. |
| $C_6H_4R{\cdot}CO_2H$ ................. | $4{\cdot}20_3$ | — | — | — | $4{\cdot}09_3$ | $4{\cdot}08_8$ | 4·47 | — | 4·17 | — |
| | 4·18 | 2·98 | 4·08 | 4·54 | 4·09 | 4·05 | 4·44 | — | — | — |
| $C_6H_4R{\cdot}CH{:}CH{\cdot}CO_2H$ ...... | 4·44 | 4·61 | 4·40 | — | 4·46 | 4·38 | 4·54 | — | — | — |
| $C_6H_4R{\cdot}B(OH)_2$ ............... | 4·71 | — | — | — | — | — | — | 5·04 | 4·52 | 6·17 |
| $C_6H_4R{\cdot}CH_2{\cdot}CO_2H$ ........... | 4·66 | — | — | — | 4·80 | 4·65 | 4·69 | — | — | — |

Thermodynamic dissociation constants have now been determined in aqueous solution at 20° for the three isomeric monohydroxybenzoic acids and for thirteen alkoxybenzoic acids.

## EXPERIMENTAL.

*Materials.*—Pure crystalline specimens of the *m*- and *p*-alkoxybenzoic acids were available from earlier studies of their rates of chlorination (J., 1928, 1006; 1935, 1874; 1939, 420; 1943, 430), and these were recrystallised from benzene immediately before use and thoroughly dried.

*o*-Methoxybenzoic acid was obtained by alkaline hydrolysis of the methyl ester, prepared, but not isolated, from methyl salicylate, sodium methoxide, and methyl iodide; crystallised from glacial acetic acid and from benzene, it melted at 101° (Cohen and Dudley, J., 1910, **97**, 1737, give m. p. 99—101°). The other *o*-alkoxybenzoic acids were obtained from the purified ethyl esters by hydrolysis, the esters being prepared from ethyl salicylate, sodium ethoxide, and the appropriate alkyl iodide. They were hydrolysed by heating under reflux with an excess of alcoholic sodium hydroxide for 45 minutes; and after removal of the alcohol the ice-cold alkaline solutions were acidified with 4N-sulphuric acid, the alkoxybenzoic acids separating as colourless oils. *o*-*n*-Propoxybenzoic acid, from ethyl *o*-*n*-propoxybenzoate (b. p. 147°/12 mm.), quickly solidified, and after two crystallisations from ethyl alcohol melted at 40° (Found: C, 66·7; H, 6·5. Calc.: C, 66·7; H, 6·7%); Cohen and Dudley (*loc. cit.*) record that the m. p. is low but give no definite value; Price, Salsbury, and Fredericksen (*J. Amer. Chem. Soc.*, 1942, **64**, 1691) record b. p. 205—207°. From the earlier work of Cohen and Dudley (who record m. p. 19—20°) *o*-ethoxybenzoic acid was known to be a liquid at room temperature, and special care was therefore taken in its purification. Ethyl *o*-ethoxybenzoate (b. p. 136°/10 mm.) was hydrolysed as above, and the acid liberated by the addition of 4N-sulphuric acid was extracted with ether. The extract was shaken repeatedly with an aqueous solution of sodium hydrogen carbonate, and the *o*-ethoxybenzoic acid liberated from the aqueous layer by the addition of more sulphuric acid was extracted with ether, washed, and dried. After removal of solvent it distilled as a colourless oil (b. p. 153—155°/0·2 mm.). It was further purified by freezing. *o*-*iso*Propoxybenzoic acid, similarly prepared from ethyl *o*-*iso*propoxybenzoate (b. p. 147°/13 mm.), distilled as a colourless liquid (b.p. 182°/18 mm.).

The benzoic acid was a commercially pure sample thrice crystallised from water.

*Method.*—Thermodynamic dissociation constants at 20° were determined by potentiometric titration, a glass electrode being used. The method was based on one previously described (J., 1940, 855); but for the present work the pH scale was standardised by experiments on benzoic acid, the p*K* of which at 20° was taken to be 4·23—a value derived by interpolation from the accurate data of Rule and La Mer (*J. Amer. Chem. Soc.*, 1938, **60**, 1981). Dippy and Williams's conductivity measurements (J., 1934, 1888) would lead to a slightly lower value of p*K*.

*Results.*—These, expressed as p*K*, are given in the following table. Each value is based on at least four separate determinations. The accuracy, an estimate of which is shown for each acid, was limited mainly by the slight solubility, which prevented measurements on the higher members of the *m*- and *p*-series, and was the more troublesome in the latter. *p*-Ethoxybenzoic acid had a particularly low solubility (probably less than 0·0003M), which may be related to its high m. p. (cf. J., 1939, 420).

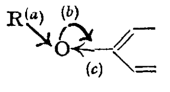
*Thermodynamic dissociation constants of alkoxybenzoic acids*, $C_6H_4R{\cdot}CO_2H$, at 20°.

| R. | | *o*- | | *m*-. | | *p*-. | |
|---|---|---|---|---|---|---|---|
| H | 4·23 | | | | | | |
| HO | | 3·07 | ± 0·02 | 4·19 | ± 0·02 | 4·62 | ± 0·03 |
| MeO | | 4·08 | 0·03 | 4·11 | 0·03 | 4·52 | 0·03 |
| EtO | | 4·21 | 0·03 | 4·17 | 0·04 | 4·80 | 0·10 |
| $Pr^{\alpha}O$ | | 4·24 | 0·03 | 4·20 | 0·05 | 4·78 | 0·10 |
| $Pr^{\beta}O$ | | 4·24 | 0·04 | 4·15 | 0·05 | 4·68 | 0·10 |
| $Bu^{\alpha}O$ | | — | | 4·25 | 0·05 | — | |

By continuing the titration, the values of $pK_2$, corresponding to the secondary (phenolic) dissociation constants ($K_2$), of *m*- and *p*-hydroxybenzoic acid were found to be respectively 9·94 ± 0·03 and 9·39 ± 0·03. This constant of salicylic acid is too small to be easily measurable in water.

*Discussion.*—Although hydroxyl and alkoxyl groups linked to saturated carbon atoms or to the *m*-carbon atom of the benzene ring exhibit an attraction for electrons (— *I* effect), an opposing mesomeric (+ *M*) effect (and in reactions an electromeric effect also) operates when the group is in the *p*-position of compounds such as benzoic or cinnamic acid. As a result, all *m*-substituted benzoic acids are stronger, and all *p*-substituted acids weaker, than the parent acid (cf. table). If these two effects were the only ones operating, then salicylic acid and all the *o*-alkoxybenzoic acids should also be weaker than benzoic acid. Instead, salicylic acid and *o*-methoxy- and *o*-ethoxy-benzoic acid are stronger, and the *o*-propoxybenzoic acids only a little weaker, than benzoic acid. The high dissociation constant of salicylic acid is generally attributed to chelation between the hydroxyl and the carboxyl group, a process which will occur more readily when the latter group is ionised and which will therefore stabilise the anion at the expense of the undissociated acid molecule (cf. Branch and Yabroff, *J. Amer. Chem. Soc.*, 1934, **56**, 2568). This explanation finds support in the further increase in strength which accompanies the introduction of a second hydroxyl, as in 2 : 6-dihydroxybenzoic acid, in which hydrogen bonds can be formed by both oxygen atoms of the carboxyl group (Baker, *Nature*, 1936, **137**, 236), and by the marked fall in strength which occurs when chelation is prevented by alkylation of the hydroxyl group in salicylic acid. The dissociation constants ($K \times 10^5$) fall in the following order; 2 : 6-$(OH)_2$ 5000, *o*-OH 85·1, *o*-OMe 8·32, *o*-OEt 6·17, *o*-$OPr^{\alpha}$ 5·75, *o*-$OPr^{\beta}$ 5·75.

The strengths of the *o*-alkoxybenzoic acids, however, are still higher than would be expected at first sight. To account for this in methoxybenzoic acid, Watson ("Modern Theories of Organic Chemistry," 2nd edn., p. 248) has suggested that the electron-attracting inductive effect (*c*) of methoxyl operating at close range more than balances the mesomeric effect (*b*) which is responsible for the low dissociation constant of anisic acid. If this be so, then the subsequent gradual fall in strengths in the order MeO > EtO > $Pr^{\alpha}O$ = $Pr^{\beta}O$ can be accounted for by the normal increase in the inductive effect (*a*) of alkyl groups assisting the mesomeric effect (*b*) of alkoxyl to overcome its inductive effect (*c*).



Certain features of the dissociation constants of the *m*- and *p*-alkoxybenzoic acids call for comment (i) The increase in strength, found by earlier workers and confirmed now, which accompanies the replacement of hydroxyl hydrogen by methyl. This behaviour, also shown by the aliphatic acids (see table p. 19), is contrary to expectation in that alkyl groups are normally regarded as electron repelling (cf Dippy and Page, J., 1938, 358; Dippy, *ibid.*, p. 1324; Evans, Gordon, and Watson, *ibid.*, p. 1441, and references cited therein). The general tendency of hydroxyl and alkoxyl groups to strengthen an acid is to be attributed to the electron-attracting (inductive) power of the oxygen atom. It should be observed, however that the $\overset{+}{\mathrm{H}}$–$\overset{-}{\mathrm{O}}$ dipole (as distinct from the dipole associated with the $\overset{-}{\mathrm{O}}$–$\overset{+}{\mathrm{C}}$ bond) is so directed that it has a resolved part which opposes the inductive effect and so tends to weaken the acid. The same influence is exerted by the Me–O dipole; but, in that this dipole is weaker (about 1·1 D.) than that of H–O (about 1·5 D.) it will weaken the acid to a less extent. In other words, when the hydrogen atom is replaced by alkyl, the negative ionic character of the oxygen atom is diminished, with a consequent increase in its inductive effect In this way the enhanced strengths of the methoxy-acids in both aromatic and aliphatic series may perhaps be explained. Applying a suggestion of Ingold (*Chem. Rev.*, 1934, **15**, 238), Dippy (*loc. cit.*) accounts for the phenomenon by postulating that in methoxyl the methyl group, contrary to its normal habit, attracts electrons. This suggestion is in a sense covered by that given above: in that the moment of MeO is less than that of HO, methyl may be regarded as attracting electrons more than does hydrogen; more precisely, it responds to the electron attraction of the oxygen to a relatively smaller extent.

(ii) It is not so easy to understand the unexpected rise in strength resulting from a branching of the hydrocarbon chain: in both the *m*- and the *p*-series the *iso*propoxy- is stronger than the *n*-propoxy-benzoic acid.

(iii) Finally, when log *K* for these acids is plotted against the logarithm of the specific velocity of chlorination, an approximately linear relationship is shown (cf. Hammett, *Chem. Rev.*, 1935, **17**, 125; Bradfield and B. Jones, *loc. cit.*). The range of dissociation constants here is, however, too restricted to justify fuller discussion.

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