39. *The Relationship between the Proton Dissociation Constants of Salicylaldehydes and the Stability Constants of their Complex Ions.*

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The proton acid dissociation constants of certain salicylaldehydes and the stability constants of their complexes with copper(II) in 50% dioxan–water have been measured. These and other results confirm that these quantities do not obey a simple linear relation. Complex-formation of these aldehydes with other metal ions, particularly magnesium(II) and calcium(II), has also been studied.

ALTHOUGH several authors [1-3] have indicated that a linear relation should exist between the logarithms of the stability constants, log K, of a series of 1 : 1 complex ions, ML, derived from a series of similar ligands, L, and a particular metal, M, and the logarithms (pκ) of the acid dissociation constants, of the ligands, Jones, Poole, Tomkinson, and Williams [4] have more recently suggested that the general form [3]

$$\log K = a\ p\kappa + b,\qquad (1)$$

where a and b are constants, is an over-simplification, and that the relation between log K and pκ is more complex. Jones *et al.*[4] based these conclusions upon their comparisons

[1] Schwarzenbach, Anderegg, Schneider, and Senn, *Helv. Chim. Acta*, 1955, **38**, 1147.
[2] Martell and Calvin, " The Chemistry of the Metal Chelates," Prentice-Hall, New York, 1953, p. 76.
[3] Bjerrum, *Chem. Rev.*, 1950, **46**, 381.
[4] Jones, Poole, Tomkinson, and Williams, *J.*, 1958, 2001.

of the proton acid dissociation constants of certain derivatives of salicylaldehyde and of 8-hydroxyquinoline with the stability constants of the ligands derived from these acids and several cations, *e.g.*, nickel(II), zinc(II), and copper(II). By plotting pκ against log K_1 for the 8-hydroxyquinolines and a particular cation, M, it was shown that no straight line could be drawn through the points, and that for the salicylaldehydes a significant scatter of the points about the best straight line, $a = 0.68$, was obtained in the case of copper(II). These authors pointed out that the σ-electron-donor or -acceptor properties

TABLE 1.

Acid dissociation constants and stability constants of cupric complexes of derivatives of salicylaldehyde in 50% dioxan–water.

Substance	pκ	log K_1	log K_2
None	9·35 [9·5]	6·6(2) [7·05]	5·4(4) [5·63]
3-Chloro-	7·72	5·6(1)	3·8(6)
4-Chloro-	9·42	6·8(5)	5·5(9)
5-Chloro-	8·47	5·7(3)	4·6(6)
6-Chloro-	8·99	6·3(9)	5·1(8)
5-Bromo-	8·43	5·8(2)	5·0(6)
5-Methyl-	[9·70]	[7·15]	[5·71]
3-Methoxy-	[9·10]	[7·17]	[5·45]
4-Methoxy-	[9·3]	[7·5]	
5-Methoxy-	[9·65]	[6·76]	
3-Nitro-	[6·0]	[4·15]	
4-Nitro-	7·33 [7·4]	4·8(6) [4·9]	3·7(0)
5-Nitro-	5·96 [5·85]	4·2(1) [4·16]	3·7(1) [3·60]
3,5-Dichloro-	6·54	4·6(1)	3·0(3)
3,5-Dibromo-	6·54	4·6(7)	3·6(5)
3,5-Di-iodo-	6·89	5·0(2)	3·9(1)
3,5-Dinitro-	2·05	2·1(5)	1·7(4)

of the substituent in the ligand exert a similar effect on the stabilities of the metal ion in the complex and of the proton, but that these stabilities will be affected differently by the π-electron-donor or -acceptor properties of the substituent. Slopes, a, of the plots of log K_1 against pκ may therefore be less than or greater than unity depending on the π-electron-donor or -acceptor properties of the cation. Moreover, for substituents such as chloro- which have π-donor but σ-acceptor properties, it was suggested that the general linear relation for substituents not of this kind would not be obeyed, and that this would also be the case for ligands related as *ortho-*, *meta-*, and *para-*isomers, for which the balance of the electronic interactions between the substituent and the acidic centre differ. Instances in which this linear relation had been found [5] to be obeyed were considered to be fortuitous and to depend upon a particular choice of ligand substituents.

Jones *et al.*[4] used either a 50% or 75% dioxan–water medium for the measurements of log K and pκ, although most of the results for the salicylaldehydes were for the latter medium, and these were used to demonstrate the deviations from the straight-line relation between log K_1 and pκ.

During studies of the bactericidal properties of certain phenolic systems, the proton acid dissociation constants of a number of substituted salicylaldehydes and the stability constants of their complexes with copper(II) have been obtained by using the potentiometric-titration technique and the method of calculation described by Irving and Rossotti.[5] In the present studies, 50% dioxan–water has been used exclusively as solvent, but the general experimental conditions for obtaining log K_1 and pκ were identical with those used by Jones *et al.*[4] It is therefore of interest to find whether the results for this particular range of salicylaldehydes, in the more aqueous medium, support and extend the earlier results of Jones *et al.*[4]

The available results for salicylaldehyde and sixteen of its derivatives are contained in Table 1. Results obtained by Jones *et al.*[4] are recorded in square brackets.

[5] Irving and Rossotti, *J.*, 1953, 3397; 1954, 2904, 2910.

The acid dissociation constants are practical constants, considered to be accurate to ± 0.02 unit. For the values of log K_1 and log K_2, the second decimal figures in parentheses are probably not significant. The results for 4- and 5-nitrosalicylaldehyde agree closely with those obtained by Jones *et al.*,[4] although in the case of salicylaldehyde the present values of pκ, log K_1, and log K_2 are significantly lower. In the Figure, both sets of results for salicylaldehyde have been plotted.

In agreement with the conclusions reached by Jones *et al.*,[4] using the results obtained with a 75% dioxan–water medium, the plot (see Figure) of pκ against log K_1 for the salicyl-aldehydes listed in Table 1 shows that, although the linear relation given by equation (1) is very approximately obeyed, with *a* equal to about 0.73 and *b* = 0, there is a significant

The relation between the acid dissocia-tion constants of salicylaldehydes and the stability constants of the cupric salicylaldehyde complexes.

A, Salicylaldehyde. Also the following derivatives: B, 3-chloro-; C, 4-chloro-; D, 5-chloro-; E, 6-chloro-; F, 5-bromo-; G, 5-methyl-; H, 3-me-thoxy-; I, 4-methoxy-; J, 5-methoxy-; K, 3-nitro-; L, 4-nitro-; M, 5-nitro-; N, 3,5-dichloro-; O, 3,5-dibromo-; P, 3,5-di-iodo-; Q, 3,5-dinitro-.
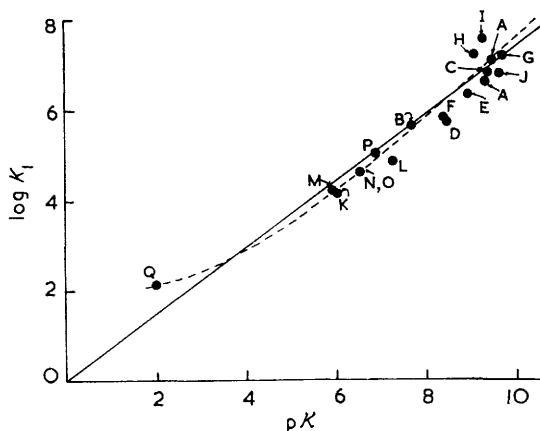
scatter of the points about this straight line. The points fit better with the broken curve drawn.

Calvin and Wilson [6] also observed a roughly linear relation between pκ and log K for a range of salicylaldehydes. Their experimental conditions were different from those used in the present work, but the slope of the best line was 0.7. These authors noted that 4-nitro- and 4-methoxy-salicylaldehyde did not behave as expected, and Jones *et al.*[4] drew attention to the fact that 4-chloro- and 3-methoxy-salicylaldehyde give abnormally stable complexes. These observations led Jones *et al.*[4] to conclude that the 4-substituents give a relation in which *a* and *b* differ from those for the best straight line for the 5-substituents, because π-electron interactions between the 4-substituent and the phenolic oxygen will be smaller. The line for the 5-substituted salicylaldehydes will therefore have the smaller slope, *a*.

For the results in Table 1, the best straight line for the 5-substituents has a slope (0.71 $\pm$ 0.05) similar to that of the best straight line for the whole series. The constant *b* would be -0.25 for *a* = 0.71. Only three points in the Figure are for 4-substituents (C, I, and L), but the best straight line through these has a slope of 1.12 $\pm$ 0.1. This greater slope (*b* = -3.1 for *a* = 1.12) substantiates the views expressed by Jones *et al.*,[4] and as they observe, explains the curvature of the line which gives the best fit for the range of salicylaldehydes with substituents in various positions.

The 3-substituted salicylaldehydes are of interest because of the *ortho*-disposition of the substituent and the hydroxyl group. If steric and/or other factors which may operate in solutions of *ortho*-substituted systems interfere with π-electron interactions between the 3-substituent and the phenolic oxygen atom, then, on reasoning as above for the

[6] Calvin and Wilson, *J. Amer. Chem. Soc.*, 1945, **67**, 2003.

4-substituted compounds, the best line for the 3-substituted salicylaldehydes may have a slope intermediate between that for the 4- and the 5-substituted analogues. The number of points for the 3-substituted salicylaldehydes is again limited to three (B, H, and K), but the best line has a slope $a = 0.96$ ($b = -1.8$). The limits of error for this slope are estimated as ± 0.04. The slope is therefore greater than that for the 5-substituted salicylaldehydes, and possibly only just lower than that for the 4-substituted systems. This suggests that there is a considerable interference with π-electron interactions in the *ortho*-substituted salicylaldehydes.

Next, for the 3,5-disubstituted salicylaldehydes, the four points (N, O, P, and Q) approximate to a straight line with $a = 0.57 \pm 0.04$ ($b = 0.9$ when $a = 0.57$). This slope is lower than for the 5-substituents, implying a greater combined π-electron interaction between the 3,5-substituents and the phenolic oxygen atom, but, in general agreement with what has been said above, suggesting that the π-electron interactions from a 3-substituent are less than from a 5-substituent.

TABLE 2.

The stability constants of metal complexes of derivatives of salicylaldehyde in
50% dioxan–water.

Subst.	Ca(II)	Mg(II) log K_1	Ni(II) log K_1	Subst.	Ca(II)	Mg(II) log K_1	Ni(II) log K_1
None	—	2·(5)	4·5(3)	4-Nitro-	—	—	*
3-Chloro-	—	—	3·8(4)	5-Nitro-	—	—	*
4-Chloro-	—	3·(1)	*	3,5-Dichloro-	—	—	3·0(9)
5-Chloro-	—	—	*	3,5-Dibromo-	—	—	*
6-Chloro-	—	2·(7)	4·5(4)	3,5-Di-iodo-	—	—	*
5-Bromo-	—	2·(0)	*	5-Chloro-4-methyl	—	—	4·1(7)
				5-Chloro-4,6-dimethyl ...	—	—	4·1(7)

— No detectable chelation. * Not studied. Decimal figures in parentheses are of doubtful significance (see Experimental section).

It should be noted that the sets of points for each of the various positions of substitution only roughly approximate to straight lines, for, as pointed out by Jones *et al.*,[4] substituents exerting opposed π- and σ-electronic interactions, *e.g.*, halogen and methoxyl, would be expected to give deviations from the best straight line for substituents with π- and σ-donor (*e.g.*, methyl) or π- and σ-acceptor (*e.g.*, nitro) properties.

For a series of salicylaldehydes substituted variously in the 3-, 4-, 5-, and 3,5-positions, there may therefore be four *approximate* straight-line relations between log K_1 and pκ, each with a different slope, a. The range of values of pκ and log K_1 for a series of salicyl-aldehydes such as that in Table 1 would therefore be expected to give a poor approximation to *one* straight line, and might fit better with some curve which represents the mean path of several straight lines of different gradient.

The complex-formation by the salicylaldehydes prepared for the present work with other metals was also surveyed, again with the 50% dioxan–water medium. The results are summarised in Table 2, which includes 5-chloro-4-methyl- (p$\kappa = 8.90$) and 5-chloro-4,6-dimethyl-salicylaldehyde (p$\kappa = 9.51$). The copper complexes of these two derivatives and the iron(III) and zinc(II) complexes of all the salicylaldehydes studied are precipitated early in the titrations, and log K values could not be obtained.

The limited ranges of log K_1 values for the magnesium(II) and nickel(II) complexes have been plotted against the pκ values for the acids. In each case there are significant deviations from a single straight-line relationship, but the best lines have slopes of 0·47 and 0·89, respectively, for the nickel(II) and the magnesium(II) complexes, although for the latter the gradient of the line must be regarded as very approximate because of the probable large error involved in obtaining the log K values.

EXPERIMENTAL

Materials.—Salicylaldehyde, b. p. 90—91°/18 mm., and 5-chlorosalicylaldehyde, m. p. 98·5—99°, were commercial samples purified respectively by distillation under reduced pressure in an atmosphere of nitrogen, and by steam-distillation and crystallisation from aqueous ethanol. 3,5-Dichloro- and 5-chloro-4,6-dimethyl-salicylaldehyde were gifts.

3-Chloro- and 4-chloro-salicylaldehyde, m. p. 54·5° and 52°, respectively, were prepared by the Reimer–Tiemann reaction, the procedures of Hodgson and Jenkinson [7] being used. The aldehydes were first isolated as their bisulphite compounds.

2-Chloro-6-nitrobenzaldehyde was obtained [8] from 2-chloro-6-nitrotoluene, and by standard procedures the nitro-compound was reduced [9] and the amine converted [10] into 6-*chlorosalicylaldehyde*, m. p. 54° (from aqueous ethanol) (Found: C, 53·7; H, 3·2. $C_7H_5ClO_2$ requires C, 53·8; H, 3·2%).

5-Bromosalicylaldehyde, m. p. 105°, was obtained by bromination of salicylaldehyde in acetic acid.

3,5-Dibromosalicylaldehyde, m. p. 85°, was prepared according to Wentworth and Brady's directions.[11]

Salicylaldehyde was 3,5-di-iodinated by the method of Henry and Sharp,[12] and the product, m. p. 107°, crystallised from methanol. Attempts to monoiodinate salicylaldehyde by iodine monochloride [13] gave the di-iodo-derivative. Attempted preparation of 5-iodosalicylaldehyde from 5-aminosalicylaldehyde was not successful.

4-Nitrosalicylaldehyde, m. p. 134°, was prepared from 2-acetoxy-4-nitrotoluene as described by Goldberg and Walker.[14]

5-Nitrosalicylaldehyde, m. p. 126°, was obtained by the Sommelet reaction.[15]

3,5-Dinitrosalicylaldehyde, m. p. 59°, was prepared by dinitration of salicylaldehyde.[16]

5-Chloro-4-methylsalicylaldehyde, m. p. 68°, was obtained by the Reimer–Tiemann reaction as described by Duff.[17]

Methods.—The standard procedure described by Irving and Rossotti [5] was adopted for the measurement of the acid dissociation constants of the salicylaldehydes and the stability constants of the metal complexes. The test solution (50% v/v dioxan–water) was 0·02M, 0·3M, 0·003M, and 0·006M with respect to perchloric acid, sodium perchlorate, metal salt, and salicylaldehyde, respectively. Commercial dioxan was purified by Hess and Frahm's method [18] and the metal salts were " AnalaR " samples of $CuSO_4,5H_2O$, $NiSO_4,7H_2O$, $ZnSO_4,7H_2O$, $MgSO_4,7H_2O$, $NH_4Fe(SO_4)_2,12H_2O$, and $Ca(NO_3)_2$ (anhydrous). Before the potentiometric titrations were carried out the salicylaldehydes were further purified by steam-distillation, and crystallised from aqueous ethanol (ion-depleted water). An Electronic Instruments, Limited, direct-reading pH-meter, model No. 23A, was used to follow the changes in pH during the titrations. Irving and Rossotti [5] used a stream of nitrogen to agitate the reactants, but a glass stirrer was preferred in the present work, and the nitrogen, saturated with the vapour of 50% dioxan–water, was passed over the surface of the solution, which was kept at 20° ± 0·1°. For each metal and a particular salicylaldehyde, the three titrations were repeated on the following day, and the titration curves were averaged to give the values used to calculate the stability constants by the method described by Irving and Rossotti.[5]

In certain cases it was necessary to extrapolate the formation curve to the line $\bar{n} = 1$. This was done by making a series of experimental extensions of the curves, and the values of log K_1 were calculated for the whole length of each curve ($d = 0·1$—$0·9$). The extension curve which gave the smallest deviation of log K_1, over the whole range of values of d, was accepted.

[7] Hodgson and Jenkinson, *J.*, 1927, 1740; 1929, 469.
[8] Clarke, *J.*, 1957, 3807.
[9] Smith and Opie, *Org. Synth.*, 1948, **28**, 11.
[10] Misslin, *Helv. Chim. Acta*, 1920, **3**, 626.
[11] Wentworth and Brady, *J.*, 1920, **117**, 1040.
[12] Henry and Sharp, *J.*, 1922, **121**, 1055.
[13] Jones and Richardson, *J.*, 1954, 713.
[14] Goldberg and Walker, *J.*, 1954, 2540.
[15] Angyal, Morris, Tetas, and Wilson, *J.*, 1950, 2141.
[16] Lovett and Roberts, *J.*, 1928, 1975.
[17] Duff, *J.*, 1941, 547.
[18] Hess and Frahm, *Ber.*, 1938, **71**, 2627.

In all cases, the formation curve had to be mirrored about the line $\bar{n} = 1$ in order to obtain the second stability constant from the expression $\log K_2 = 2\mathrm{pL}_{n-1} - \log K_1$.

In relation to the accuracy of the stability constants, the inherent inaccuracies involved in the extrapolation and mirroring procedures seem more important than any irreproducibility of the titration curves. For this reason, only the first decimal figures for the stability constants of the copper and the nickel complexes are considered to be reliable. For the magnesium complexes, the necessary very lengthy extrapolations of the formation curves to $n = 1$ cast doubt on even the first decimal figures for the stability constants.