67. The Stabilities of Metal Complexes of Some α-Hydroxy-α-pyridylmethanesulphonic Acids.

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The acid dissociation constants of α-hydroxy-α-2-, -3-, and -4-pyridyl-methanesulphonic acid and α-hydroxy-α-(6-methyl-2-pyridyl)methanesul-phonic acid, and of 2-2′-pyridylethanesulphonic acid are reported, and follow an expected pattern on comparison with analogous derivatives of 8-hydroxy-quinoline. The stability constants of their complexes with bivalent cobalt, nickel, copper, and zinc ions at 25° and $\mu = 0\cdot1M$ (sodium perchlorate) lie in the order Cu > Ni > Zn > Co, except for α-hydroxy-α-(6-methyl-2-pyridyl)-methanesulphonic acid for which log $K_{ZnL} >$ log K_{NiL}.

THE powerful complexing action of 8-hydroxyquinoline and related compounds has been carefully investigated in both water [1] and in mixed solvents.[2] However, little information is available on the stability of complexes of analogous ligands in which the hydroxyl group is attached to an alkyl carbon atom rather than directly to an aromatic ring. We

[1] Albert, *Biochem. J.*, 1953, **54**, 646.
[2] Irving and Rossotti, *J.*, 1954, 2910.

have now investigated the complexing action of two such ligands, α-hydroxy-α-2-pyridyl-methanesulphonic acid (I) R = H and its 6-methyl derivative (II). To study further the

(I: R = H)
(II: R = Me)
(III)
(IV)
(V)
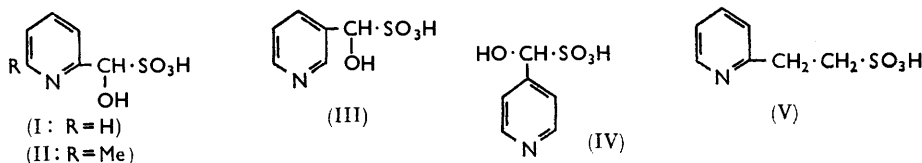
effect of the position of substitution in the heterocyclic ring we have investigated the 3- and 4-substituted isomers (III) and (IV), and to study the effect of the hydroxyl group we have investigated the complexing action of 2-2'-pyridylethanesulphonic acid (V). Measurements were made by potentiometric titration at 25° in an aqueous medium at constant ionic strength 0·1M (sodium perchlorate), under an atmosphere of oxygen-free nitrogen.

EXPERIMENTAL

Materials.—Reagents used were commercially available and were recrystallised before use. Solutions of metal ions were prepared from " AnalaR " salts, and of perchloric acid from the " AnalaR " reagent. Carbonate-free M-sodium hydroxide was prepared by the method of Davies and Nancollas.[3]

Titration Procedures.—Proton and metal stability constants were calculated from results obtained by titrating solutions (total volume 70 ml.) of the ligand in the presence and in the absence of metal ions, and of a little perchloric acid, with 1·01M-sodium hydroxide. A constant ionic strength of 0·1M-sodium perchlorate was employed, and concentration levels were as follows: $C_L = 0·007142$M, $C_M = 0·003571$M, $C_{HClO_4} = 0·0063$M. The titration cell and contents were maintained at 25° by immersion in a thermostat-bath, and alkali was added from a calibrated 0·50-ml. " Agla " micrometer syringe. An inert atmosphere of pre-saturated oxygen-free nitrogen was maintained. Measurements of pH were made using an Ingold glass–calomel electrode system, and a Pye " Dynacap " pH-meter.

Calculation of Stability Constants.—The degrees of formation of the ligand–proton complexes, $\bar{n}_H$, were calculated by Irving and Rossotti's method.[4] These values were plotted against the corresponding values of pH, and the acid dissociation constants thus obtained are summarised in Table 1. Values for the sulphonic acid dissociation were not determined, being appreciably less than the pH at which titration was normally started.

The degrees of formation $\bar{n}$, of the ligand–metal complexes, and of the free ligand exponent, pL, were calculated by Irving and Rossotti's method.[4] The stability constants were then calculated from the formation curves of $\bar{n}$ against pL by the correction-term method.[5] In

TABLE 1.

Acid dissociation constants of hydroxypyridylmethanesulphonic acids at 25°.

	Ligand	(I)	(II)	(III)	(IV)	(V)
pK_1	H$_2$L$^\pm$	4·05	4·83	4·60	4·95	5·14 *
pK_2	HL$^-$	9·70	9·88	9·53	10·05	

* Corresponds to HL$^\pm$.

certain cases (see Table 2) precipitation occurred before $\bar{n} = 2$, but never before $\bar{n} = 1·4$. Computation of stability constants was therefore not seriously hindered. The detailed values of $\bar{n}$ and pL are given in Table 2.

With ligand (IV), only very weak complexes were formed, and precipitation occurred by $\bar{n} = 0·2$. No significant complex formation was apparent for ligand (V). The values of the stability constants computed from these results are given in Table 3.

[3] Davies and Nancollas, *Nature*, 1950, **165**, 237.
[4] Irving and Rossotti, *J.*, 1954, 2904.
[5] Irving and Rossotti, *J.*, 1953, 3397.

TABLE 2.

Formation curves for hydroxypyridylmethanesulphonic acids

Ligand (I)

Copper complexes

$\bar{n}$	0·017	0·120	0·273	0·657	1·026	1·283	1·496	1·644	1·740	1·835
pL	11·981	11·005	9·997	9·177	8·485	7·923	7·491	7·110	6·801	6·185

Nickel complexes

$\bar{n}$	0·035	0·094	0·225	0·371	0·604	0·834	1·074	1·302	1·672 (ppt.)
pL	6·900	6·382	5·903	5·437	5·001	4·584	4·189	3·930	3·712

Cobalt complexes

$\bar{n}$	0·034	0·075	0·155	0·259	0·503	0·773	1·031	1·279	1·508 (ppt.)
pL	6·904	6·378	5·886	5·408	4·974	4·561	4·170	3·815	3·410

Zinc complexes

$\bar{n}$	0·037	0·156	0·319	0·604	0·955	1·326	1·538 (ppt.)
pL	6·371	5·886	5·423	5·003	4·631	4·327	4·102

Ligand (II)

Copper complexes

$\bar{n}$	0·042	0·125	0·467	0·788	0·956	1·079	1·210	1·362	1·496	1·624
pL	9·885	8·946	8·025	7·200	6·695	6·386	5·940	5·526	5·127	4·808

Nickel complexes

$\bar{n}$	0·054	0·080	0·109	0·309	0·531	0·831	1·202	1·410 (ppt.)
pL	6·067	5·553	5·054	4·602	4·166	3·777	3·298	2·920

Cobalt complexes

$\bar{n}$	0·041	0·199	0·390	0·698	1·052	1·428 (ppt.)
pL	5·630	5·075	4·623	4·219	3·868	3·524

Zinc complexes

$\bar{n}$	0·029	0·071	0·165	0·349	0·637	0·899	1·147	1·419 (ppt.)
pL	7·257	6·071	5·571	5·112	4·696	4·351	4·001	3·650

Ligand (III)

Copper complexes

$\bar{n}$	0·006	0·148	0·340	0·700	1·154	1·524	1·683
pL	10·288	9·343	8·454	7·717	7·195	6·852	6·493

Nickel complexes

$\bar{n}$	0·106	0·272	0·624	1·062	1·430	1·727	1·829
pL	9·333	8·437	7·693	7·150	6·772	6·047	5·600

Cobalt complexes

$\bar{n}$	0·010	0·085	0·234	0·543	1·062	1·438	1·657
pL	10·289	9·328	8·427	7·668	7·150	6·779	6·250

Zinc complexes

$\bar{n}$	0·063	0·193	0·516	1·025	1·397	1·602 (ppt.)
pL	9·323	8·417	7·660	7·134	6·752	6·394

TABLE 3.

Ligand–metal stability constants for hydroxypyridylmethanesulphonic acids.

Ligand	(I)	(II)	(III)	Ligand	(I)	(II)	(III)
Copper complexes				*Cobalt complexes*			
log K_{ML}	9·43	7·75	7·81	log K_{ML}	4·92	4·25	7·54
log K_{ML_2}	7·57	5·32	6·98	log K_{ML_2}	3·53	3·58	6·97
log β_2	17·00	13·07	14·79	log β_2	8·45	7·83	14·51
Nickel complexes				*Zinc complexes*			
log K_{ML}	5·13	4·27	7·67	log K_{ML}	5·08	4·79	7·58
log K_{ML_2}	3·55	2·84	6·72	log K_{ML_2}	4·21	3·59	6·71
log β_2	8·68	7·11	14·39	log β_2	9·29	8·38	14·29

RESULTS AND DISCUSSION

The presence of 1 : 1 and 1 : 2 complexes was established for all four metal ions with ligands (I)—(III). Complex formation certainly occurred with ligand (IV), but heavy precipitation precluded calculation of stability constants. The titration curves for ligand (V) in presence and absence of metal ions were practically superimposable almost to the points of hydroxide precipitation.

A deep violet-blue colour was particularly apparent in the titration of ligand (I) with cupric ions, and we have since obtained pure solid complexes from this system. Details of these results will be reported elsewhere.

We assign the values of pK_1 to the dissociation of a pyridinium proton, and the values of pK_2 to the dissociation of a hydroxyl group. The values obtained may be related to those obtained by other workers for the analogous 8-hydroxyquinoline derivatives. We show in Table 4 comparative data for ligand (I), 8-hydroxyquinoline, (VI), and 8-hydroxy-quinoline-5-sulphonic acid (VII).

TABLE 4.

Acid dissociation constants for ligands (I), (VI), and (VII).

Ligand	(I)	(VI)		(VII)	
pK_1	4·05	5·13 *	5·01 †	4·15 *	4·19 ‡
pK_2	9·70	9·89 *	9·90 †	8·74 *	8·48 ‡

* Albert, ref. 1. † Näsänen and Pentlinen, *Acta Chem. Scand.*, 1952, **6**, 837. ‡ Maley and Mellor, *Austral. J. Sci. Res.*, 1949, **2**, A, 579.

The correct correlation is probably between ligands (I) and (VII). The relatively close values of pK_1 are perhaps surprising, but as expected the hydroxyl group in compound (I) is appreciably more basic than when it is a ring substituent as in (VII).

The effect of the methyl group adjacent to the heterocyclic nitrogen in the ligand (II) follows the expected pattern. Thus pK_1 (for the pyridinium dissociation) shifts from 4·05 to 4·83, but pK_2 only from 9·70 to 9·88. This is in agreement with results for 8-hydroxyquinoline and 8-hydroxy-2-methylquinoline, for which pK_1 increases from 4·48 to 5·01, but pK_2 only from 10·80 to 11·01 (data for 50% dioxan).[2] The shift is also noticeable [6] for picolinic acid ($pK_2 = 5·43$) and 6-methylpicolinic acid ($pK_2 = 5·77$).

It is somewhat surprising to find a steady increase in pK_1 for compounds (I), (III), and (IV), since it is more usual to find that substitution β to a heterocyclic nitrogen atom results in a lower value of pK_{NH} than substitution at the α- or γ-position. It should be also noted that our values for the dissociation of a pyridinium proton (4·05—5·15) are significantly different from the value of 2·8 suggested by Irving and da Silva [7] on the basis of their work with *N*-(2-pyridylmethyl)iminodiacetic acid.

The ligand–metal stability constants show a number of expected trends. A comparison of available data for ligands (I), (VI), and (VII) is given in Table 5.

TABLE 5.

Ligand–metal stability constants for reagents (I), (VI), and (VII).

Metal	Ligand	(I)	(VI)		(VII)	
Copper..............................	$\log K_{ML}$	9·43	12·2 *	12·56 †	12·50 *	11·50 ‡
Nickel	$\log K_{ML}$	5·13	9·9 *		10·00 *	
Cobalt	$\log K_{ML}$	4·92	9·1 *		9·20 *	9·25 ‡
Zinc	$\log K_{ML}$	5·08		8·50 †	8·40 *	8·70 ‡

*†‡ See Table 4.

There is an expected decrease in $\log K_{ML}$ (and also in $\log \beta_2$) for all metal ions with ligand (I) compared with ligands (VI) and (VII). The value of $\Delta \log K_{ML}$ varies from 4·87 for nickel to 2·07 for copper. The effect of the methyl group in ligand (II) is to produce a decrease in the values of $\log K_{ML}$ and $\log \beta_2$ compared with the values for ligand (I).

[6] Holmes and Crimmin, *J.*, 1955, 1175.
[7] Irving and da Silva, *J.*, 1963, 945.

TABLE 6.

Values of $\Delta \log K_{ML}$ for pairs of ligands.

Ligand	Copper	Nickel	Cobalt	Zinc
(VI) ....} (VIII) ....}	2·81 *	1·91 *	0·92 †	0·68 *
(I) ....} (II) ....}	1·68	0·86	0·67	0·29

* Irving and Rossotti, ref. 2. † Johnston and Freiser, *J. Amer. Chem. Soc.*, 1952, **74**, 5239.

This again is noticeable in results for 8-hydroxyquinoline (VI) and 8-hydroxy-2-methyl-quinoline (VIII). The comparative data are shown in Table 6. The values for the quinolines are for 50% dioxan, and after allowance for the usual increase in values from aqueous to mixed solvent the results are quite comparable.

A comparison of the ligand–metal stability constants $\log K_{ML}$ for ligands (I)—(III) shows the expected order Cu > Ni > Zn > Co, except for ligand (II) for which $\log K_{ZnL} > \log K_{NiL}$. This is again in agreement with data for 8-hydroxy-2-methyl-quinoline. A much more striking point is the remarkable uniformity of values of $\log K_{ML}$ and $\log \beta_2$ for reagent (III). This is well shown in the Figure, where values of $\log K_{ML}$
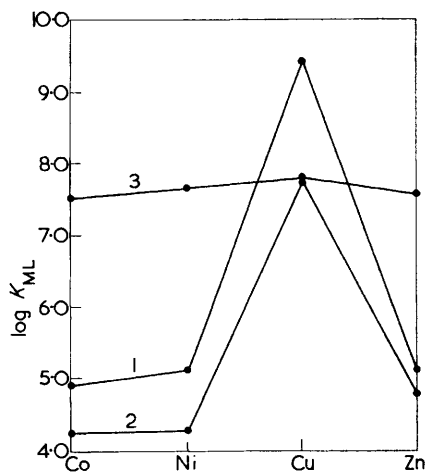
The stability constants of some α-hydroxy-α-pyridylmethanesulphonic acids: (1) 2-Pyridyl. (2) 6-Methyl-2-pyridyl. (3) 3-Pyridyl.

for the three ligands are plotted. It is apparent that except for the cupric complexes, the six-membered chelate ring present in the complexes of compound (III) is more stable than the five-membered ring in the complexes of compounds (I) and (II). The structure of the ligand seems to be a dominating factor; however, the ratio $\log K_{ML}/\log K_{ML_2}$ is practically constant for this ligand, and as Irving and Pettit have pointed out [8] this may be taken to indicate that structural factors involved in the formation of the first ring do not significantly influence the attachment of the second.

Because of the powerful ligand effect with reagent (III) the plot of $\log K_{ML}$ against $\log K_{ML^1}$ for pairs of ligands only approaches linearity in the case where L = (I) and L^1 = (II). The slope of the best straight line is ~1·2. It is also apparent that there is no direct relation between $\log K_{ML}$ and $\log K_{HL}$ for the various ligands; this largely arises from the stability of the chelates of ligand (III). Calculations of $pK' = pK_2 - \log K_{ML}$ and $pK'' = pK_2 - \log K_{ML_2}$ (following Irving and Pettit [8]) reinforce the view that the absence of such a relation is largely steric in origin.

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[8] Irving and Pettit, *J.*, 1963, 1546.