

systems. (This rhombohedral phase probably has the formula M_9O_{16} , as suggested by the possible values in Table V.) A $MO_{1.81}$ phase occurs in the terbium and cerium oxygen systems, and a $MO_{1.83}$ phase is found in the terbium and praseodymium systems. The latter phases are not isostructural. The $TbO_{1.83}$ phase has a rhombohedral cell and the $PrO_{1.83}$ has a face-centered-cubic unit cell. Whether or not there are miscibility gaps between the various phases or homogeneous ranges of composition depends primarily upon the temperature and the oxygen pressure.

A notable omission is a stable M_4O_7 phase in any of the three systems. This phase frequently has been reported for the terbium and cerium systems, but the studies reported and summarized have not given any evidence of special significance for such a stable solid phase. An important group of mixed oxides of formula M_4O_7 recently have been described and named for the mineral Pyrochlore.^{16,17}

Many studies have been made during the last decade¹⁸⁻²⁰ on mixed oxide phases of fluorite type with oxygen vacancies. It is not at present clear how the truly binary oxides discussed above compare with the pseudo binary mixed oxides. It will be important to know if the mixed oxides reported as solid solutions of the fluorite type are really that or if, when properly annealed, they show a tendency toward ordering of oxygen vacancies as demonstrated in the true binary oxide phases reported here. In this respect, it will be necessary to carry out the studies at temperatures where cation mobility is appreciable. Cation mobility is not required in the truly binary systems since electron movement will accomplish the same effect.

(16) R. S. Roth, *J. Research Natl. Bur. Standards*, **56**, 17 (1956), Res. Paper No. 2643.

(17) A. J. E. Welch, private communication.

(18) J. D. McCullough, *J. Am. Chem. Soc.*, **72**, 1386-1390 (1950).

(19) J. D. McCullough and T. D. Britton, *ibid.*, **74**, 5225 (1952).

(20) G. Brauer and H. Gradinger, *Z. anorg. u. allgem. Chem.*, **276**, 209 (1954).

In all these systems, anion mobility is very high at the temperatures at which the experiments were carried out but cation mobility very low.

It seems apparent that there are many ways of ordering vacancies in these materials and simple analogy will not be enough to be sure in any particular case. In some cases, the vacancies are reported as randomly arranged.²¹⁻²³ In these, it would be particularly important to study the electrical properties of the solids.

It has been suggested²⁴ that the oxygen deficiency in structures such as these may result from the formation of surfaces of discontinuity by a shear mechanism. In this way, the oxygen loss would be accommodated without the appearance of vacancies, as such, in the lattice. Structures of this type already have been solved, for example, in the $(Mo, W)_nO_{2n-1}$,²⁵ Ti_nO_{2n-1} ²⁶ and $TiVO_x$ ²⁷ systems. An alternative suggestion for the structure of bixbyite recently has been suggested²⁸ in which the oxygen lattice is changed to give a rather more octohedral arrangement around the metal atoms without the vacancies previously proposed.

This large set of anion defect structures related to the fluorite structure is at once one of the simplest and yet most beautifully intricate systems. A detailed elaboration of them would go far in advancing an understanding of the relationship between ordered intermediate phases and non-stoichiometry in chemical compounds.

(21) E. Zintl and U. Croatto, *Z. anorg. Chem.*, **292**, 79 (1939).

(22) U. Croatto and M. Bruno, "Proc. 11th Intern. Cong. Pure & Appl. Chem.," Vol. I, 69 (1947).

(23) J. S. Anderson, D. N. Eddington, L. E. J. Roberts and E. Wait, *J. Chem. Soc.*, 3324 (1954).

(24) A. D. Wadsley, *J. and Proc. Roy. Soc. of N.S.W.*, **XCII**, 25 (1958).

(25) C. Hagy and A. Magneli, *Revs. of Pure Appl. Chem.*, **4**, 235 (1954).

(26) S. Andersson, *Acta Chem. Scan.*, in press.

(27) A. D. Wadsley, *Acta Cryst.*, in press.

(28) H. Dachs, *Z. Krist.*, **107**, 370 (1956).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NOTRE DAME, NOTRE DAME, INDIANA]

Chelate Stabilities of Certain Oxine-type Compounds. II. 4-Hydroxybenzothiazoles¹

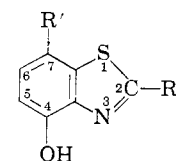
BY T. J. LANE, C.S.C., AND A. SAM

RECEIVED NOVEMBER 5, 1960

The acid dissociation constants of 4-hydroxybenzothiazole, 2-amino-4-hydroxybenzothiazole, 2-methylamino-4-hydroxybenzothiazole and 2-amino-4-hydroxy-7-methylbenzothiazole were determined in 50% v./v. *p*-dioxane at 25° and the chelate stability constants of the ligands with Cu(II), Pb(II), Ni(II), Co(II), Zn(II) and Cd(II) were obtained by Calvin-Bjerrum potentiometric titration technique. The results were compared with those previously reported for 8-hydroxyquinoline, 4-hydroxybenzimidazole and 4-hydroxybenzoxazole. The stability constants of the 4-hydroxybenzothiazole chelates are lower than those of the corresponding 8-hydroxyquinolines. This is explained by larger nitrogen-oxygen distance and by unfavorable electron orientation on the donor nitrogen atom. The stability values are higher than those of 4-hydroxybenzimidazoles and 4-hydroxybenzoxazoles and this is attributed to the influence of the larger sulfur atom in the 1-position.

In the previous paper² the chelate stabilities of 4-hydroxybenzimidazoles and of 4-hydroxybenzoxazoles with divalent ions have been reported. In the present paper are presented and discussed the values obtained for the metal chelates of the 4-hydroxybenzothiazoles, represented by the

formula



R = H, NH₂, NHCH₃
R' = H, CH₃.

(1) Presented at the 138th Meeting of the American Chemical Society, New York, N. Y., 1960.

(2) T. J. Lane, A. Sam and A. J. Kandathil, *J. Am. Chem. Soc.*, **82** 4462 (1960).

Experimental

Materials.—4-Hydroxybenzothiazole was prepared by the method of Erlenmeyer, *et al.*³ The compound was recrystallized from aqueous ethanol several times, m.p. 145–146°.

Anal. Calcd. for C₇H₅NOS: C, 55.60; H, 3.34; N, 9.27; S, 21.20. Found: C, 55.90; H, 3.44; N, 9.22; S, 21.25.

2-Amino-4-hydroxybenzothiazole was obtained by the method of Erlenmeyer and Ueberwasser.⁴ The compound was recrystallized from water several times, m.p. 185–186°.

Anal. Calcd. for C₇H₆N₂OS: C, 50.58; H, 3.64; N, 16.86; S, 19.29. Found: C, 50.64; H, 3.60; N, 16.72; S, 19.46.

2-Amino-4-hydroxy-7-methylbenzothiazole.—2-Methoxy-5-methylaniline was converted to 2-methoxy-5-methylphenylthiourea by a method similar to that of Tuda, *et al.*⁵ This product was recrystallized from 50% water-alcohol several times, m.p. 128–129°.

A chloroform solution of the thiourea was converted by bromine to 2-amino-4-methoxy-7-methylbenzothiazole according to the method of Erlenmeyer and Ueberwasser.⁴ The compound was recrystallized from 50% water-alcohol, m.p. 172–173°.

The 2-amino-4-methoxy-7-methylbenzothiazole was hydrolyzed with 48% HBr. When the resulting solution was neutralized with sodium hydrogen carbonate, 2-amino-4-hydroxy-7-methylbenzothiazole precipitated. The product was recrystallized from 30% alcohol, m.p. 182–183°.

Anal. Calcd. for C₈H₈N₂OS: C, 53.31; H, 4.48; N, 15.54; S, 17.79. Found: C, 53.06; H, 4.46; N, 15.50; S, 17.81.

2-Methylamino-4-hydroxybenzothiazole.—Equimolar amounts of 2-amino-4-methoxybenzothiazole and formic acid (85–90%) were refluxed in toluene for 3 hr. After distilling off the toluene, 2-formylamino-4-methoxybenzothiazole separated. The product was recrystallized from alcohol m.p. 264–265°.

N-Formyl amines can be reduced with lithium aluminum hydride to the N-methyl compounds, as indicated by Gaylord.⁶ Accordingly, 2 g. of 2-formylamino-4-methoxybenzothiazole was placed in the thimble of a Soxhlet extractor, attached to a round bottom flask containing lithium aluminum hydride (3 g.) dissolved in anhydrous tetrahydrofuran (100 ml.). Extraction of 2-formylamino-4-methoxybenzothiazole by tetrahydrofuran was continued for 48 hr. to complete the reduction and then the reaction mixture was cooled in an ice-bath. Enough water was added, dropwise, to destroy the excess lithium aluminum hydride. After evaporation under reduced pressure the residue was treated with 10% NaOH solution to dissolve inorganic material. The organic material remaining was then extracted with hot benzene. The benzene extract was concentrated to give a crystalline product which was hydrolyzed with 48% HBr. On neutralizing with sodium hydrogen carbonate, 2-methylamino-4-hydroxybenzothiazole was obtained. The product was recrystallized from 50% water-alcohol several times, m.p. 169–170°.

Anal. Calcd. for C₈H₈N₂OS: C, 53.31; H, 4.48; N, 15.54; S, 17.79. Found: C, 53.36; H, 4.70; N, 15.50; S, 17.95.

2-Amino-4-hydroxy-7-methylbenzothiazole and 2-methylamino-4-hydroxybenzothiazole apparently have not been reported in the literature.

Apparatus, Procedure and Calculations.—The stability constants were determined at 25° by the Bjerrum method⁷ of potentiometric titration in 50% v./v. dioxane-water. The titration apparatus and procedure have been described previously.⁸ Titrations were carried out using ligand to metal ratios of 16:1 and 8:1 and in one case, 4:1.

(3) H. Erlenmeyer, H. Ueberwasser and H. M. Weber, *Helv. Chim. Acta*, **21**, 709 (1938).

(4) H. Erlenmeyer and H. Ueberwasser, *ibid.*, **25**, 515 (1942).

(5) K. Tuda, S. Sakamoto, H. Matsuda and T. Kanno, *J. Pharm. Soc. Japan*, **60**, 462 (1940).

(6) N. G. Gaylord, "Reduction with Complex Metal Hydrides," Interscience Publishers, Inc., New York, N. Y., 1956, p. 551.

(7) J. Bjerrum, "Metal-Ammine Formation in Aqueous Solution," P. Haase and Son, Copenhagen, 1941.

(8) H. Freiser, R. G. Charles and W. D. Johnston, *J. Am. Chem. Soc.*, **74**, 1383 (1952).

Stability values were calculated by the method described by Freiser, *et al.*⁸ Since the pH value at which a metal ion begins to hydrolyze sets an approximate upper limit for the calculation of formation constants, the \bar{n} values in the metal hydrolysis regions were obtained by extrapolation from lower values.

Results

Acid dissociation constants of the various benzothiazolium ions are given in Table I. The pK values represent the negative logarithms of the dissociation constants obtained from the equations

$$K_{NH} = \frac{[RH][H^+]}{[RH_2^+]} \text{ and } K_{OH} = \frac{[R^-][H^+]}{[RH]}$$

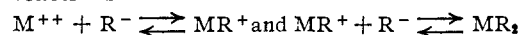
where $[RH_2^+]$, $[RH]$, $[R^-]$ and $[H^+]$ represent the concentrations of the protonated ligand, the free ligand, the phenolate ion and the free proton, respectively.

TABLE I

SUMMARY OF THE ACID DISSOCIATION CONSTANTS FOR THE LIGANDS

	pK_{NH}	pK_{OH}
4-Hydroxybenzothiazole	1.80	10.78
2-Amino-4-hydroxybenzothiazole	3.82	11.74
2-Methylamino-4-hydroxybenzothiazole	3.75	11.66
2-Amino-4-hydroxy-7-methylbenzothiazole	3.71	11.86

A summary of the formation constants of the ligands with various metal ions appears in Table II. The stepwise formation constants of the chelation reactions



may be expressed as

$$K_1 = \frac{[MR^+]}{[M^{++}][R^-]} \text{ and } K_2 = \frac{[MR_2]}{[MR^+][R^-]}$$

where M^{++} and R^- refer to the metal ion concentration and the chelate anion concentration, respectively, while MR^+ and MR_2 refer to various aggregates of the two.

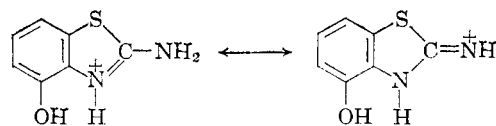
It should be pointed out that the numerical values obtained by the above equations are not thermodynamic constants since activity coefficients of the various species have not been taken into consideration. However, these values are reported for purposes of comparison and discussion.

Values obtained for 4-hydroxybenzothiazole and its chelates are in agreement with those previously reported⁹ and are included for the discussion.

Discussion

Acid Dissociation Constants.—The pK_{NH} of 4-hydroxybenzothiazole (<2) is lower than that of 8-hydroxyquinoline and of 4-hydroxybenzimidazole. This decrease in value can be attributed to the electronegativity of the sulfur atom in the 1-position tending to decrease the electron cloud on the nitrogen atom.

The large increase in the pK_{NH} of the 2-amino derivatives compared to that of 4-hydroxybenzothiazole (higher by about 2 log units, Table I) can be explained by the base strengthening resonance of the protonated species



(9) P. K. Feng and Q. Fernando, *ibid.*, **82**, 2115 (1960).

TABLE II
SUMMARY OF THE METAL CHELATE FORMATION CONSTANTS
FOR THE LIGANDS

	Ligand: Metal 8:1			Ligand: Metal 16:1		
	Log K_1	Log K_2	2 Log K_{av}	Log K_1	Log K_2	$\frac{2}{\text{Log } K_{av}}$
4-Hydroxybenzothiazole						
Cu(II)	9.0	8.0	17.1	8.7	7.5	16.6
Pb(II)	7.7	5.0	12.5	7.2	5.5	12.4
Zn(II)	6.7	6.6	(5.8)	12.5
Ni(II)	7.3	..	13.5	7.3	6.0	13.4
Co(II)	7.1	6.9	(5.9)	12.8
Cd(II)	6.9	..	12.3	6.7	(5.4)	12.1
2-Amino-4-hydroxybenzothiazole						
Ligand: Metal 4:1						
Cu(II)	..	9.8	21.1	11.8	(10.3)	21.7
Pb(II)	9.0	6.3	15.1	9.2	6.5	15.2
Zn(II)	8.0	7.6	15.7	8.2	7.8	16.0
Ni(II)	8.0	6.7	14.9	8.2	7.2	15.4
Co(II)	7.6	6.6	14.3	7.7	6.7	14.4
Cd(II)	7.9	6.1	14.2	7.8	6.8	14.4
2-Methylamino-4-hydroxybenzothiazole						
Ligand: Metal 16:1						
Cu(II)	10.9	..	21.3	10.8	(10.4)	21.1
Pb(II)	9.8	(9.0)	17.8
Zn(II)	8.3	7.9	16.2
Ni(II)	8.3	7.4	15.7
2-Amino-4-hydroxy-7-methylbenzothiazole						
Cu(II)	11.5	10.5	21.7	11.3	(10.2)	21.5
Pb(II)	9.5	6.9	16.4	9.5	..	16.5
Zn(II)	8.5	..	(16.4)	8.4	7.8	16.2
Ni(II)	8.6	7.6	16.2	8.5	7.3	16.1
Co(II)	8.2	7.1	15.2	8.0	7.1	15.1
Cd(II)	8.2	7.0	15.1	8.2	7.1	15.3

This effect would preclude protonation of the 2-amino nitrogen atom. Results from a study of pyridine¹⁰ and 2-aminopyridine¹¹ show that only the pyridine nitrogen of these compounds is protonated and that the basicity of the 2-aminopyridine is higher by about 1.6 log units.

The pK_{NH} values of the 2-amino derivatives indicate that the inductive effect of the methyl group is negligible in comparison with the contribution of the resonance structures.

The pK_{OH} value of 4-hydroxybenzothiazole, like that of 4-hydroxybenzimidazole and 4-hydroxybenzoxazole, is lower than that of 8-hydroxyquinoline, indicating weaker hydrogen bonding in these compounds than in 8-hydroxyquinoline. In the 2-amino derivatives the pK_{OH} values are higher

(10) R. K. Murmann and F. Basolo, *J. Am. Chem. Soc.*, **77**, 3484 (1955).

(11) H. B. Jonassen and C. C. Rolland, Report to the Office of Naval Research, Project No. Nnr. 685.

probably from the inductive effect of the substituents.

Chelate Formation Constants.—The stability values for the metal chelates of the 4-hydroxybenzothiazoles are much lower than those of the corresponding chelates of 8-hydroxyquinoline. This appreciable decrease in the stability values could be explained by the larger nitrogen–oxygen distance and by the more unfavorable electron orientation on the donor nitrogen atom, as discussed previously.² The absence of any appreciable degree of intramolecular hydrogen bonding in 4-hydroxybenzothiazole, as shown by infrared investigation,¹² suggests that the distance between the donor atoms is too large for hydrogen bonding and for strong chelation.

The stability values (2 log K_{av}) for the Cu(II) chelates of 4-hydroxybenzothiazole (Table II), 4-hydroxybenzimidazole and 4-hydroxybenzoxazole² are 17.1, 14.8 and 12.3, respectively. The other metal ions studied show this same trend of decreasing stability. Although the pK_{NH} of 4-hydroxybenzimidazole² is 4.92, while that of 4-hydroxybenzothiazole is less than 2, the chelates of the latter ligand are more stable. These results are explained by the differences in the size of the atoms, $O < N < S$. With an increase in the size of the atom in the 1-position, the nitrogen atom in the 3-position would be closer to the chelating oxygen, resulting in smaller O–N distance and thus reducing the strain in the metal chelate ring. A larger atom like sulfur could also cause the donor electrons on the nitrogen atom to be orientated more favorably for chelation.²

The values obtained for the formation constants of the metal chelates of 2-amino-4-hydroxybenzothiazole, 2-methylamino-4-hydroxybenzothiazole and 7-methyl-2-amino-4-hydroxybenzothiazole (Table II) are higher than those obtained for the corresponding metal chelates of 4-hydroxybenzothiazole. This increase in stability is expected in view of the higher basicity of the unsaturated nitrogen atom in these ligands. These values are lower than those of 8-hydroxyquinoline chelates for the reasons indicated above in the discussion of 4-hydroxybenzothiazole.

Acknowledgments.—The authors gratefully acknowledge financial aid from the Radiation Laboratory of the University of Notre Dame, supported in part under the U. S. Atomic Energy Commission Contract AT(11-1)-38 and from a research grant A-2763 from the Department of Health, Education and Welfare, Public Health Service.

(12) S. Mizushima, private communication.