necessary to invoke this same assumption.[18] A definitive answer to this question must, of course, await a detailed structural determination of one of these complexes.

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(18) Reference 5 and papers cited therein.

Acknowledgment.—This investigation was supported in part by PHS Research Grant GM-08394 from the Division of General Medical Studies, Public Health Service, and in part by the National Science Foundation through its Undergraduate Research Participation Program.

CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY AND
ORGANIC CHEMISTRY OF THE UNIVERSITY OF SYDNEY, SYDNEY, AUSTRALIA

Sexadentate Chelate Compounds. XI

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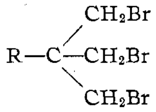
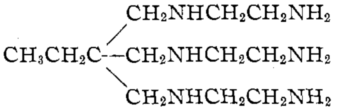
The base 5-ethyl-5-(δ-amino-β-azabutyl)-1,9-diamino-3,7-diazanonane has been synthesized and shown to be capable of functioning as a sexadentate chelating agent. Some sexadentate chelate compounds containing it have been prepared and stability constants of certain of its complexes determined. Its ability to function sometimes as a quadridentate chelating agent enables it to be used in the synthesis of certain multi-nucleate ammines whose cations carry high positive charges.

Heating together of 1-bromo-2,2-bis-(bromomethyl)-butane (I; R = C_2H_5) and ethylenediamine in large excess under reflux for some considerable time yields a mixture of bases from which 5-ethyl-5-(δ-amino-β-azabutyl)-1,9-diamino-3,7-diazanonane (II) can be isolated in reasonable yield. Similar type reactions between poly-bromo compounds and ethylenediamine have been extensively studied previously by van Alphen and co-workers.[2] Hexamines homologous to II should similarly be accessible from available 1,1,1-trimethylolalkanes.


$R{-}C(CH_2Br)_3$

I


$CH_3CH_2C(CH_2NHCH_2CH_2NH_2)_3$

II

Models show that it is readily possible for the molecules of the base II so to arrange themselves spatially that all six nitrogen atoms can be simultaneously presented and bonded to a six-coördinate metal atom of suitable size from the apices of a circumscribing octahedron in one or the other of two enantiomorphous arrangements (Fig. 1). Thus, II should be capable of functioning as a sexadentate chelating agent of Type 9 of the classification previously suggested by one of us.[3] Sexadentates with this donor atom pattern have been previously described.[4] The only recorded saturated aliphatic hexamine previously demonstrated to be capable of functioning as a sexadentate chelating agent would appear to be the base "penten," (III) which is of Type 4[3] and which was prepared and studied by Schwarzenbach and co-workers.[5] The base II resembles III in that both bases present six aliphatic nitrogen donor atoms to a metal atom when coördinating as sexadentate chelating agents. However, in II three of these are primary and three secondary amino, while in III four are primary and two tertiary amino nitrogen atoms.

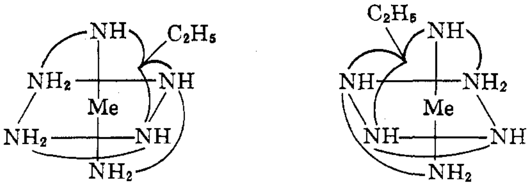
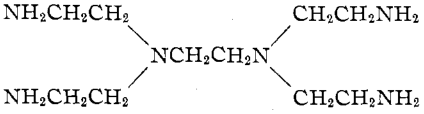


Figure 1.


$(NH_2CH_2CH_2)_2NCH_2CH_2N(CH_2CH_2NH_2)_2$

III

II coördinates readily with nickel(II) salts and a pink crystalline iodide, $Ni(C_{12}H_{32}N_6)I_2$, can be isolated whose magnetic moment (3.1 B.M. at 20°) is consistent with its formulation as a sexadentate chelate compound. II also appears to coördinate as a simple sexadentate with cobalt(III) salts since the gold-colored diamagnetic salt $Co(C_{12}H_{32}N_6)Cl_3 \cdot H_2O$ was isolated from the brown solution obtained when sodium triscarbonatocobaltate-(III)-3-water[6] was stirred into a warm acid solution of II. Attempts to resolve this salt into its diastereoisomers have not so far succeeded.

On the other hand, from a solution of II and cobalt-(II) chloride in dilute hydrochloric acid that had been

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(1) Commonwealth Research Scholar, University of Sydney.

(2) J. van Alphen, *Rec. trav. chim.*, **55**, 412, 669, 835 (1936); **56**, 343, 529, 1007 (1937); **57**, 265 (1938).

(3) F. Lions, *Record Chem. Progr.*, **22**, 73 (1961).

(4) *Cf., e.g.*, F. P. Dwyer, N. S. Gill, E. C. Gyarfas, and F. Lions, *J. Am. Chem. Soc.*, **79**, 1269 (1957).

(5) G. Schwarzenbach and P. Moser, *Helv. Chim. Acta*, **36**, 581 (1953), and subsequent papers.

(6) H. F. Bauer and W. C. Drinkard, *J. Am. Chem. Soc.*, **82**, 5031 (1960).

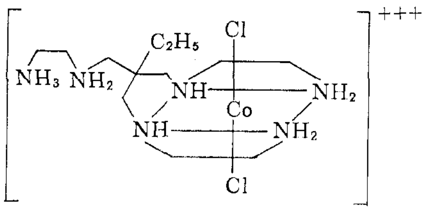


Figure 2.

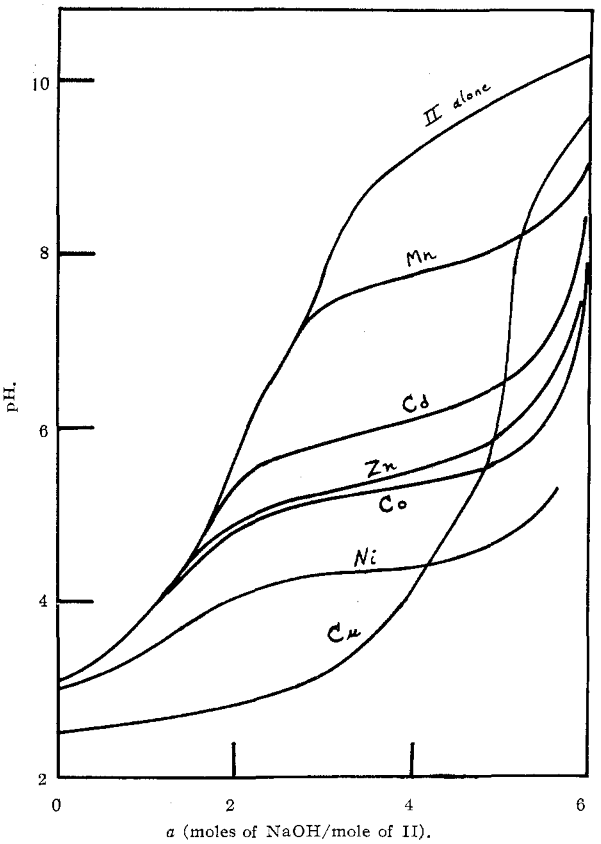
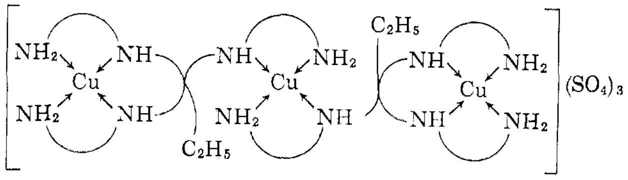


Fig. 3.—Titration of amine (II) (10^{-3} *M*) in the presence of perchloric acid (6×10^{-3} *M*), alone or in the presence of metal ions (10^{-3} *M*); a = moles of NaOH/mole of amine.

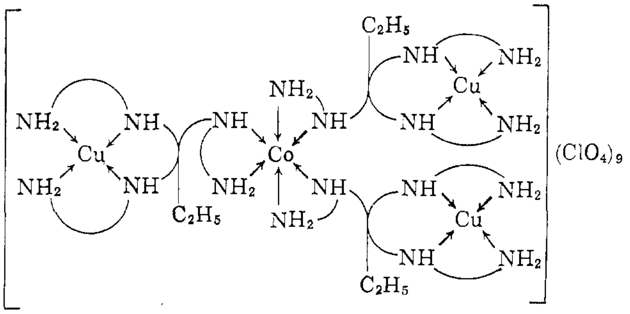
aerated for 20 hr. it was possible to isolate an extremely hygroscopic dark green solid. Its color and properties suggest that it should be formulated as a *trans*-dichlorotetraminecobalt(III) salt, in each of the cations of which one of the ethylenediamine residues of the base II moiety remains uncoördinated while the other four nitrogens orientate themselves in a square planar arrangement about the cobalt atom (Fig. 2).

Interaction of II (1 mole) and copper(II) chloride (1 mole) in ethanol gave a very hygroscopic purple salt (IV) in which it would again appear that only four of the six nitrogen atoms of the II moiety function as strong donors to copper. The other two (in one of the ethylenediamine residues) remain uncoördinated, or at most weakly coördinated. Support for this view is forthcoming in the observation that coördination of *three* moles of copper(II) sulfate with every *two* moles of II in aqueous methanol solution yields the stable blue salt V from which the corresponding hexaiodide and hexaperchlorate can be readily isolated. The molar conductivity of this latter salt clearly indicates that the complex cation carries six positive charges. Formula V shows it as a *trans* isomer about the central copper atom. It could equally well be *cis*.



V

Further evidence on this availability of the unused ethylenediamine residue in the complex cations of IV is to be found in the fact that interaction of the corresponding perchlorate in dilute perchloric acid solution with sodium triscarbonatocobaltate(III)–3-water led to formation of the salt VI, $\mathrm{Co[Cu_3(C_{36}H_{96}N_{18})](ClO_4)_9}$.



VI

The cations of this complex salt, obtained analytically pure, contain one cobalt(III) atom and three copper(II) atoms and carry nine positive charges. The molar conductivity (1080 mhos cm.^{2}) adequately supports this formulation.

Stability Constants.—In determining stability constants in dilute aqueous solution for systems where the formation of protonated complexes cannot be ignored, we have followed the method of Schwarzenbach and Moser[5] and carried out titrations upon the ligand alone and in the presence of one and of ten molar proportions of each metal ion. In Fig. 3 some results are presented in the form of alkali titration curves of the fully protonated amine, $\mathrm{H_6A^{6+}}$.

The titration curve in the absence of metal differs markedly from that of penten (III), the only other hexamine which appears to have been examined in this way. Whereas penten was found to bind a maximum of four hydrogen ions in dilute solution, it is evident from Fig. 3 that all six nitrogen atoms of II have measurable basic properties. Hence, six more or less closely overlapping equilibria exist, governed by the equation

$$\sum_{j=0}^{6} (g - j)\,[\mathrm{H}^+]^j \bar{K}^{\mathrm{H}}_{\mathrm{H}_j\mathrm{A}} = 0 \qquad (1)$$

where g is the average number of H^+ attached to A at any point in the titration

$$K^{\mathrm{H}}_{\mathrm{H}_j\mathrm{A}} = \frac{[\mathrm{H}_j\mathrm{A}]}{[\mathrm{H}^+][\mathrm{H}_{j-1}\mathrm{A}]}$$

and

$$\bar{K}^{\mathrm{H}}_{\mathrm{H}_j\mathrm{A}} = K^{\mathrm{H}}_{\mathrm{HA}}\, K^{\mathrm{H}}_{\mathrm{H}_2\mathrm{A}} \ldots .\; K^{\mathrm{H}}_{\mathrm{H}_j\mathrm{A}}$$

TABLE I

PROTON ASSOCIATION CONSTANTS log $K^{H}_{H_jA}$

	j					
	1	2	3	4	5	6
Amine II	10.39	9.56	8.79	6.54	4.25	1.5
penten	10.20	9.70	9.14	8.56	...	...

The computing involved in a complete solution of (1) would be formidable, but the distinct inflections at $a = 2$ and $a = 3$ (Fig. 3) suggest the possibility, as a first approximation, of subdividing the curve and treating it in several isolated dibasic or tribasic portions. This was done and the results were progressively refined by changing the points of subdivision of the curve and using neighboring equilibrium constants to compute small corrections. The six stoichiometric proton association constants shown in Table I were derived in this way, without any attempt to apply activity corrections. As a final check, the g *vs.* pH curve was calculated from eq. 1 and Table I and was shown to coincide throughout its course with the observed curve.

From a knowledge of these proton association constants and from an analysis, according to the method of Schwarzenbach and Moser,[5] of the two types of metal titration curves, the constants

$$K^{M}_{MA} = [MA]/[M][A]$$
$$K^{M}_{MHA} = [MHA]/[M][HA]$$
$$K^{H}_{MHA} = [MHA]/[H][MA]$$

were calculated and are recorded in Table II.

TABLE II

EQUILIBRIUM CONSTANTS OF COMPLEXES

	log K^{M}_{MA}		log K^{M}_{MHA}		log K^{H}_{MHA}	
	II	penten	II	penten	II	penten
Mn	8.2	9.4	5.1	..	7.3	...
Co	17.3	15.8	12.3	12.5	5.3	7.0
Ni	21.5	19.3	15.1	15.9	4.0	6.8
Cu	22.7	22.4	21.3	20.4	9.0	8.2
Zn	16.4	16.2	12.1	14.2	6.1	8.2
Cd	14.4	16.2	10.1	12.4	6.1	6.5

Equilibration was almost instantaneous except for nickel, where it took more than 2 hr. In practice, the nickel curves were obtained by measurement of individual points after 24 hr. equilibration. Only for copper did the simple titration method fail, due to virtually complete complex formation, and here we used the EDTA competition method.[5] In the dilute aqueous solutions used in this part of the work, constant stability quotients resulted from the assumption that the copper complexes were mononuclear, and no evidence was found for such complexes as V, which had been prepared from methanol solution.

In Tables I and II we have reproduced for comparison the corresponding constants for penten measured at 20°.[5] Because of the difference in experimental temperatures, small apparent disparities between the two amines must be ignored, but there is a number of more marked differences which seem worthy of comment. The first of these is concerned with the grouping of the proton association constants. It is well known that, other things being equal, primary, secondary, and tertiary aliphatic nitrogen atoms differ little in basicity.[7] In a polyamine the basicity depends rather on the degree of electrostatic repulsion encountered from neighboring groups. Penten has four widely separated and strongly basic nitrogen atoms, and two others, each under the influence of two neighboring positive charges, whose basic properties in dilute solution are imperceptible. On the other hand, while II has only three strongly basic terminal nitrogen atoms, all three remaining nitrogens can bind protons, since each has only one close neighbor that is positively charged.

Somewhat similar considerations apply to protonated metal complexes, particularly those of copper, whose common tendency toward four- or five-coördination is illustrated in the formation of stable complexes, $CuHA^{3+}$ and CuH_2A^{4+}, and strong inflections in the equivalent titration curve. The high log K^{H}_{CuHA} recorded here is within 1.4 units of log K^{H}_{HA}, a difference small enough to be attributed entirely to electrostatic repulsion and not at all to a tendency of the last nitrogen to coördinate. The fifth nitrogen atom of II, being separated by a three-carbon chain from the nearest strongly coördinated nitrogen atom, is also more basic (log $K^{H}_{CuH_2A} = 4.9$) than in the penten complex (log $K^{H}_{CuH_2A} = 3.6$), where only two carbon atoms are interposed. This enhanced basic character of the fifth and sixth nitrogen atoms evidently is associated with the wider freedom of movement we have already mentioned. It seems very probable that in dilute solution II behaves toward copper as a strong quadridentate with perhaps some weaker coördination as a quinquedentate, but that the sixth nitrogen atom is not coördinated.

All the other metals examined also form protonated complexes, but these are now less stable than the corresponding penten complexes. They are found in the lower regions of the pH titration curves, and the low values of K^{H}_{MHA} indicate that in every case II readily assumes the full sexadentate function. Thus it appears that the greater flexibility of II in contrast to penten can operate in two ways: with a five-coördinate atom like copper it permits greater separation between the metal ion and the last protons, thus increasing K^{H}_{MHA}; with a six-coördinate atom it permits more nearly strainless coördination of the last nitrogen atom, with a consequent fall in K^{H}_{MHA}.

The relationships between the stability constants appear to be more complex. The elimination of strain through the flexibility of II should produce a favorable enthalpy effect, but the unfavorable entropy change when a flexible molecule is coördinated should not be overlooked. The relative numbers of primary, secondary, and tertiary amino groups in the two ligands also may have a bearing on the problem. It seems to call for more information, possibly derived over a range of temperature, from other types of sexadentate amines.

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(7) R. A. Robinson and R. H. Stokes, "Electrolyte Solutions," Butterworths Scientific Publications, London, 1959, p. 525.

Experimental

a. **Preparative.** **5-Ethyl-5-(δ-amino-β-azabutyl)-1,9-diamino-3,7-diazanonane** (II).—A solution of 1-bromo-2,2-bis-(bromomethyl)-butane[8] (65 g.) in anhydrous ethylenediamine (450 g.) was heated under reflux for 30 hr. out of contact with atmospheric moisture and carbon dioxide. Excess ethylenediamine then was distilled off, a solution of sodium hydroxide (60 g.) in water (100 ml.) was added to the viscous brown residue, and this then was extracted three times with pyridine (1 l.). The combined, filtered extracts were concentrated under vacuum and the residual viscous oil distilled under high vacuum. The yellow oil boiling at 120–164° (0.004 mm.) was collected and refractionated, the pure hexamine being finally obtained as a yellow, viscous very hygroscopic oil, b.p. 170–172° (0.05 mm.), n^{22}_{D} 1.5081.

Anal. Calcd. for $C_{12}H_{32}N_6$: C, 55.4; H, 12.3. Found: C, 55.1; H, 12.0.

The hexakis-(phenylthiourea) derivative was a pale yellow powder (from ethanol), m.p. 143–144°.

Anal. Calcd. for $C_{54}H_{62}N_{12}S_6$: C, 60.6; H, 5.8; N, 15.7. Found: C, 60.3; H, 6.2; N, 15.4.

5-Ethyl-5-(δ-amino-β-azabutyl)-1,9-diamino-3,7-diazanonane-nickel(II) Iodide.—A methanolic solution of sodium iodide in excess was added to the reddish purple solution obtained by mixing solutions of nickel(II) chloride–6-water (0.94 g.) in methanol (20 ml.) and II (1.02 g.) in methanol (10 ml.). Pink needles separated. They were collected and recrystallized from water and obtained as fine pink needles which did not melt below 350°; the conductivity was 232 mhos cm.^{2} at 23°.

Anal. Calcd. for $C_{12}H_{32}N_6NiI_2$: C, 25.2; H, 5.6; N, 14.7; Ni, 10.3. Found: C, 25.4; H, 5.8; N, 14.3; Ni, 10.2.

5-Ethyl-5-(δ-amino-β-azabutyl)-1,9-diamino-3,7-diazanonane-cobalt(III) Chloride–1-Water.—Sodium triscarbonatocobaltate (III)–3-water (1.8 g.) was added with gentle warming to a solution of II (1.3 g.) in hydrochloric acid (10 ml. of 3 *N*). A vigorous evolution of carbon dioxide occurred. The brown solution was concentrated and acetone added. The golden yellow precipitate was recrystallized from methanol. It formed diamagnetic golden plates, m.p. 312° dec. The visible spectrum shows a broad absorption band at 465 mμ (ε 113). The conductivity was found to be 387 mhos cm.^{2} at 20°.

Anal. Calcd. for $Co[C_{12}H_{32}N_6]Cl_3H_2O$: C, 32.6; H, 7.7; N, 19.0; Co, 13.3. Found: C, 32.4; H, 7.5; N, 18.7; Co, 12.7.

Attempts were made to effect resolution of this salt into its enantiomorphs by such methods as conversion to the chloro-*d*-tartrate and recrystallization from solvents such as dimethylformamide and water–acetone mixtures or conversion to the *d*-antimonyltartrate followed by fractional crystallization, but no evidence of resolution was obtained.

5-Ethyl-5-(δ-amino-β-azabutyl)-1,9-diamino-3,7-diazanonane-copper(II) Chloride.—Solutions of copper(II) chloride–2-water (0.78 g.) in ethanol (20 ml.) and II (1.2 g.) in ethanol (10 ml.) were mixed. The resultant deep purple solution was concentrated and diluted with dry acetone. The purple powder which precipitated was collected, washed with dry acetone and ether, and then quickly dried *in vacuo*. It was recrystallized from a dry methanol–acetone mixture and obtained as a very hygroscopic purple powder, m.p. 196°. Its visible absorption spectrum shows a broad band at 527 mμ (ε 65).

Anal. Calcd. for $Cu(C_{12}H_{32}N_6)Cl_2$: C, 36.5; H, 8.1; Cu, 16.0. Found: C, 36.3; H, 8.1; Cu, 15.6.

Bis-[5-ethyl-5-(δ-amino-β-azabutyl)-1,9-diamino-3,7-diazanonane]-tricopper(II) Iodide.—A solution of copper(II) sulfate–5-water (1.465 g.; 3 moles) in methanol (30 ml.) was mixed with a solution of II (1.017 g.; 2 moles) in methanol (10 ml.). To the resulting deep blue solution after heating on the steam bath for 30 min. and filtering was added a concentrated methanolic sodium iodide solution. A fine insoluble steel-blue powder was precipitated. It was collected, washed thoroughly with water and ethanol, and dried *in vacuo*. It melted at 219°.

Anal. Calcd. for $Cu_3(C_{24}H_{64}N_{12})I_6$: C, 19.6; H, 4.4; N, 11.4; Cu, 13.0. Found: C, 19.7; H, 4.7; N, 11.0; Cu, 12.8.

Bis-[5-ethyl-5-(δ-amino-β-azabutyl)-1,9-diamino-3,7-diazanonane]-tricopper(II) perchlorate was prepared in an exactly similar way. Analysis by combustion methods was not possible because of its tendency to explode when heated above its melting point of 276°. Copper was determined.

Anal. Calcd. for $Cu_3(C_{24}H_{64}N_{12})(ClO_4)_6$: Cu, 14.6; Found: Cu, 14.8.

Its conductivity at 23° was 661 mhos cm.^{2}.

Tris-[5-ethyl-5-(δ-amino-β-azabutyl)-1,9-diamino-3,7-diazanonanecopper(II)]-cobalt(III) Perchlorate (VI).—A solution of II (0.78 g.) in water (10 ml.) was added to a solution obtained by dissolving copper(II) oxide (0.238 g.) in 72% perchloric acid (0.828 g.) and water (10 ml.). Powdered sodium triscarbonatocobaltate(III)–3-water (0.362 g.) then was stirred into the deep purple solution. The resultant permanganate-colored solution obtained after the evolution of carbon dioxide was carefully filtered free from some brown undissolved solid and allowed to crystallize slowly in a desiccator over concentrated sulfuric acid. The reddish purple crystals which separated were collected and dried at 100°.

Anal. Calcd. for $Co[Cu_3(C_{36}H_{96}N_{18})](ClO_4)_9$: C, 22.5; H, 5.0; N, 13.1; Cu, 9.3. Found: C, 22.7; H, 5.6; N, 13.1; Cu, 9.9.

b. **Titrations.**—Metal perchlorates were prepared from Analar chemicals by standard methods and recrystallized from hot water. Solutions in boiled water, stored under purified nitrogen, were standardized by electrodeposition or by complexometric titration.

Stability constants were derived from pH titrations of dilute perchloric acid solutions of the amine (10^{-3} *M*) in the presence and absence of metal ions. Titrations were carried out in a closed cell partially immersed in a thermostat bath at 25 ± 0.05°. The contents of the cell were stirred and protected from the atmosphere by a stream of purified nitrogen while carbonate-free sodium hydroxide was delivered beneath the surface of the solution from a fine capillary tube connected to a Metrohm piston buret. The ionic strength was maintained at 0.1 by appropriate additions of sodium perchlorate solution.

pH measurements were made with a Radiometer 4 pH meter with saturated calomel and glass electrodes standardized against 0.05 *M* potassium hydrogen phthalate (pH 4.005) or 0.01 *M* sodium borate (pH 9.177).[9]

Acknowledgments.—The authors acknowledge their indebtedness to Miss B. Stevenson, M.Sc., for the organic microanalyses recorded in this paper. A. T. P. gratefully acknowledges the receipt of a Commonwealth Research Scholarship which has enabled him to take part in the work.

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[8] J. M. Derfer, K. W. Greenlee, and C. E. Boord, *J. Am. Chem. Soc.*, **67**, 1863 (1945).

[9] V. E. Bower and R. G. Bates, *J. Res. Natl. Bur. Std.*, **59**, 261 (1957).