TABLE IV

LIGAND FIELD PARAMETERS[a] OF THE 2,5-DITHIAHEXANE
2,5-DIOXIDE COMPLEXES

Compound	Dq, cm^{-1}	$E(P) - E(F)$, cm^{-1}	β[b]
[Co(DTHO$_2$)$_3$](ClO$_4$)$_2$	900	12,000	0.81
[Ni(DTHO$_2$)$_3$](ClO$_4$)$_2$	860	12,820	0.87
[Fe(DTHO$_2$)$_3$](ClO$_4$)$_2$	1030	...	...

[a] A description of the procedure which was followed in calculating ligand field parameters is given by J. H. Bright, R. S. Drago, D. M. Hart, and S. K. Madan, *Inorg. Chem.*, 4, 18 (1965). [b] The quantity β is defined as the ratio B'/B where B' is the P–F term splitting for the complex and B the value for the gaseous ion with no crystalline field.

hexane 2,5-dioxide is a bidentate ligand, it gives larger Dq values than do other sulfoxides.[28] This may be attributed to chelation. The chelate effect is demonstrated by comparing the Dq values for nickel(II) perchlorate complexes of various monodentate ligands and similar bidentate ligands: pyridine (1010 cm^{-1})[29] *vs.* 2,2-bipyridine (1150 cm^{-1}),[30] pyridine N-oxide (840 cm^{-1})[28] *vs.* 2,2-bipyridine 1,1'-dioxide (857 cm^{-1}),[4] methyl-

(28) D. W. Meek, R. S. Drago, and T. S. Piper, *Inorg. Chem.*, 1, 285 (1962).
(29) W. E. Bull and L. E. Moore, *J. Inorg. Nucl. Chem.*, 27, 1341 (1965).
(30) C. K. Jørgensen, *Acta Chem. Scand.*, 10, 887 (1956).

amine (993 cm^{-1})[31] *vs.* ethylenediamine (1150 cm^{-1}),[32] and N,N-dimethylacetamide (769 cm^{-1})[33] *vs.* N,N,-N'N'-tetramethylmalonamide (860 cm^{-1}).[34] 2,4-Dithiahexane 2,5-dioxide (860 cm^{-1}) may thus be compared with dimethyl sulfoxide (773 cm^{-1})[28] or tetramethylene sulfoxide (775 cm^{-1}).[28] On this basis we conclude that there is chelation. Furthermore, the Dq value for the five-membered ring chelate complex of 2,5-dithiahexane with nickel(II) ion (1060 cm^{-1})[35] is considerably greater than that of the seven-membered chelate of DTHO$_2$ with nickel(II) (860 cm^{-1}). A similar trend has previously been reported[8] for tris(2,2-bipyridine)nickel(II) ion (with five-membered rings, Dq = 1150 cm^{-1}) and tris(2,2-bipyridine 1,1'-dioxide)nickel(II) ion (with seven-membered rings, Dq = 857 cm^{-1}). Therefore, it is quite reasonable to conclude that chelate complexes with seven-membered rings around nickel(II) ion are generally less stable than those with five-membered rings.

(31) R. S. Drago, D. W. Meek, R. Longhi, and M. D. Joesten, *Inorg. Chem.*, 2, 1056 (1963).
(32) C. K. Jørgensen, "Absorption Spectra and Chemical Bonding in Complexes," Addison-Wesley Publishing Co., Inc., Reading, Mass., 1962, p 111.
(33) R. S. Drago, D. W. Meek, M. D. Joesten, and L. LaRoche, *Inorg. Chem.*, 2, 124 (1963).
(34) W. E. Bull and R. G. Ziegler, *ibid.*, 5, 689 (1966).
(35) R. L. Carlin and E. Weissberger, *ibid.*, 3, 611 (1964).

Multidentate Coordination Compounds. Chelating Properties of Aliphatic Amines Containing α-Pyridyl Residues and Other Aromatic Ring Systems as Donor Groups[1-3]

BY DIETER W. GRUENWEDEL[4]

A series of multidentate polyamines containing α-pyridyl residues or other aromatic ring systems as donor groups were synthesized and their affinity for divalent transition metal ions investigated. The substances prepared are 2,6-dimethylenebis-(N-2-picolylamino)pyridine, di(2-picolyl)amine, N,N'-bis(2-picolyl)ethylenediamine, N,N'-bis(4-(5)-imidazolylmethyl)-ethylenediamine, N,N'-bis(o-aminobenzyl)ethylenediamine, and N,N'-bis(o-hydroxybenzyl)ethylenediamine. The proton association constants of the ligands and the stability constants of the Zn(II), Co(II), and Ni(II) chelates were determined by pH titrations at 25° in 0.1 M KCl. The formation constants for Cu(II) with 2,6-dimethylenebis(N-2-picolylamino)pyridine, N,N'-bis(4-(5)-imidazolylmethyl)ethylenediamine, and N,N'-bis(o-hydroxybenzyl)ethylenediamine were determined also.

Introduction

Metal chelates of Schiff bases derived from pyridine-2-aldehyde and other *ortho*-substituted aromatic

(1) This work is described in more detail in the Diplom Thesis (Universitat Tubingen, 1961) and Ph.D. Thesis (Universitat Tubingen, 1963) by Dieter W. Gruenwedel.
(2) Material supplementary to this article has been deposited as Document No. 9786 with the ADI Auxiliary Publications Project, Photoduplication Service, Library of Congress, Washington 25, D. C. A copy may be secured by citing the document number and by remitting $3.75 for photoprints, or $2.00 for 35-mm microfilm. Advance payment is required. Make checks or money orders payable to: Chief, Photoduplication Service, Library of Congress.
(3) The author expresses his appreciation to Dr. G. Weitzel, director of the Physiologisch-chemisches Institut der Universitat Tubingen, for initiation and generous financial support of this work.
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aldehydes and various aliphatic amines have been the subject of intensive research not only because of their interesting stereochemical properties[5] but also because of their usefulness as model systems in the study of enzymatic reactions.[6]

Quite in contrast, the metal complexes of the closely related saturated amine compounds (the latter are easily obtainable by hydrogenation of the aldimines) have received relatively little attention. While some of the relevant work has dealt with the configurational

(5) H. A. Goodwin, "Chelating Agents and Metal Chelates," F. P. Dwyer and D. P. Mellor, Ed., Academic Press, New York and London, 1964, p 143.
(6) W. Langenbeck, G. Reinisch, and K. Schonzart, *Chem. Ber.*, 92, 2040 (1959).

aspects of complex formation[7] only a few investigations were concerned with the determination of complex formation constants and other thermodynamic data.[8,9]

It is to be expected that reduction of the aldimino groups of the Schiff bases will yield ligands which are much more flexible than the parent compounds and which thus can present their donor atoms to a metal atom from either a planar or a nonplanar arrangement. On the other hand, removal of the steric constraints about the $-CH=N-$ groups should not affect their ability to form strong bonds with transition metal ions unless it depends on the presence of conjugated double bonds extending from the aromatic ring systems into the aliphatic carbon chain.

In an attempt to gain more information about the chelating tendencies of such polyamines containing suitably arranged aromatic and aliphatic donor atoms within their molecules, the multifunctional ligands 2,6-dimethylenebis(N-2-picolylamino)pyridine (DMPAP), di(2-picolyl)amine (DPA), N,N'-bis(2-picolyl)ethylenediamine (BPEDA),[10,11] N,N'-bis(4-(5)-imidazolylmethyl)ethylenediamine (BIMEDA), N,N'-bis(o-aminobenzyl)ethylenediamine (ABEDA), and N,N'-bis(o-hydroxybenzyl)ethylenediamine (HYBEDA) were synthesized and the complex formation constants with several divalent transition metal ions determined. The structural formulas for DMPAP, DPA, and BPEDA are given below.

2,6-dimethylenebis(N-2-picolylamino)pyridine (DMPAP)

di(2-picolyl)amine (DPA)

N,N'-bis(2-picolyl)ethylenediamine (BPEDA)
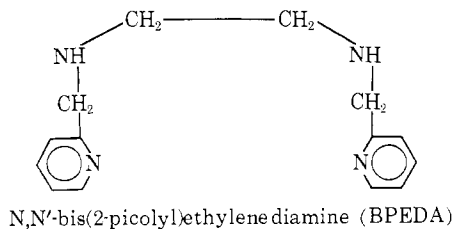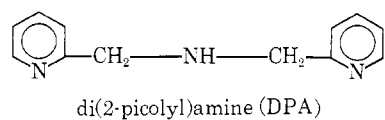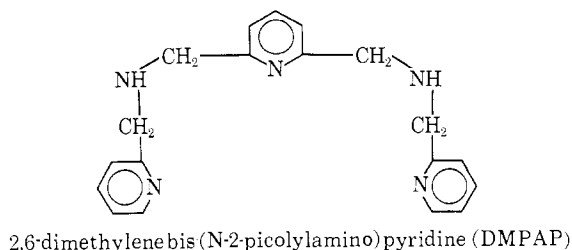
The structural formulas for ABEDA, BIMEDA, and HYBEDA are readily derived from the structure of BPEDA given above by replacing the α-pyridyl groups with o-aminophenyl groups, 4-(5)-imidazolyl groups, and o-hydroxyphenyl groups, respectively.

(7) H. A. Goodwin and F. Lions, *J. Am. Chem. Soc.*, **82**, 5013 (1960).

(8) D. E. Goldberg and W. C. Fernelius, *J. Phys. Chem.*, **63**, 1246 (1959).

(9) E. Hoyer, *Chem. Ber.*, **93**, 2475 (1960).

(10) After completion of this work it was learned that the stability constants of BPEDA also had been determined by R. G. Lacoste (Ph.D. Thesis, Clark University, Worcester, Mass., 1957).

(11) R. G. Lacoste and A. E. Martell, *Inorg. Chem.*, **3**, 881 (1964).

Experimental Section

Preparation of Ligands. 2,6-Dimethylenebis(N-2-picolylamino)pyridine (DMPAP).—2-Picolylamine (11 g, 0.1 mol) and 7 g (0.05 mol) of pyridine-2,6-dialdehyde were dissolved in 70 ml of alcohol, and the mixture was added to 1 g of 10% Pd–C catalyst which had been activated with hydrogen. The mixture was reduced with hydrogen at a pressure slightly above atmospheric with gentle agitation.

The catalyst was filtered off and hydrogen chloride was passed through the filtrate for a sufficient period of time.

The clear filtrate was kept in the cold for several days after which slightly colored crystals could be collected. The crystals were dissolved in a small quantity of water and the solution was shaken with activated carbon. Finally, the water was removed under vacuum in a water bath and the remaining viscous liquid brought to crystallization by treatment with hot alcohol. Colorless crystals which melt at 224° (uncor) were obtained. The substance was chromatographically pure. Titration of the tetrahydrochloride with standardized KOH and standardized AgNO₃ showed that it was slightly deficient in HCl. Further, it is worth noting that the pentahydrochloride of DMPAP could not be obtained under the experimental conditions of the preparation.

Anal. Calcd for $C_{19}H_{21}N_5 \cdot 4HCl$: C, 49.0; H, 5.4; N, 15.1; Cl, 30.4; mol wt, 465. Found: C, 48.4; H, 5.8; N, 15.3; Cl, 29.2; equiv wt, 457.

Di(2-picolyl)amine (DPA).—Pyridine-2-aldehyde (4.3 g, 0.04 mol) dissolved in 10 ml of methanol, was combined with 4.3 g (0.04 mol) of 2-picolylamine. After diluting the mixture with 70 ml of methanol, the solution was hydrogenated in the presence of 0.6 g of 10% Pd–C catalyst.

Hydrogen consumption (at 21° and 733 mm pressure) was 970 ml, which corresponds to 97% of the theoretical amount. After removal of the catalyst, hydrogen chloride was passed through the solution. Addition of acetone leads to the precipitation of the colorless trihydrochloride which melts at 204° (uncor). The product was chromatographically pure. Titration of the hydrochloride with standardized KOH or standardized AgNO₃ showed that it was slightly deficient in HCl.

Anal. Calcd for $C_{12}H_{13}N_3 \cdot 3HCl$: N, 13.9; Cl, 34.4; mol wt, 308. Found: N, 14.4; Cl, 32.8; equiv wt, 300.

N,N'-Bis(2-picolyl)ethylenediamine (BPEDA).—Bis(2-pyridinal)ethylenediimine (2.4 g, 0.01 mol), prepared according to Langenbeck, Reinisch, and Schonzart,[6] was dissolved in 60 ml of alcohol and the solution hydrogenated for 1–2 hr in the presence of 0.5 g of activated 10% Pd–C catalyst. Hydrogen consumption (at 20° and 730 mm pressure) was 442 ml and thus corresponded to 90% of the theoretical amount.

The catalyst was filtered off and the solvent removed under vacuum. The remaining viscous liquid was dissolved in ether, and the tetrahydrochloride was precipitated by passing hydrogen chloride through the solution.

Recrystallization from methanol–ether (8:2) yields colorless crystals which melt under decomposition at 223° (uncor). The product was chromatographically pure.

Anal. Calcd for $C_{14}H_{18}N_4 \cdot 4HCl$: N, 14.43; Cl, 36.53. Found: N, 14.44; Cl, 36.53.

N,N'-Bis(4-(5)-imidazolylmethyl)ethylenediamine (BIMEDA). (A). Bis(imidazole-4-(5)-aldehyde)ethylenediimine.—Imidazole-4-(5)-aldehyde (2 g, 0.02 mol), prepared from 4-(5)-hydroxymethylimidazole hydrochloride according to Totter and Darby[12] and Pyman,[13] and 0.9 g (0.01 mol) of ethylenediamine monohydrate were dissolved in 20 ml of water and the mixture boiled under reflux for 45 min. After cooling, the yellow precipitate was collected and recrystallized from hot water. Finally, the crystals were dried under vacuum over phosphorus pentoxide. Slightly yellow colored crystals were obtained which melt under decomposition at 225° (uncor).

Anal. Calcd for $C_{10}H_{12}N_6$: N, 38.87. Found: N, 38.71.

(B). N,N'-Bis(4-(5)-imidazolylmethyl)ethylenediamine.—

(12) J. R. Totter and W. J. Darby, *Org. Syn.*, **24**, 64 (1944).

(13) F. L. Pyman, *J. Chem. Soc.*, 186 (1916).

Bis(imidazole-4-(5)-aldehyde)ethylenediimine (2.2 g, 0.01 mol) was dissolved in 100 ml of alcohol and the solution hydrogenated in the presence of 0.4 g of activated 10% Pd–C catalyst. Within 1–2 hr, the theoretical amount of hydrogen had been absorbed. The catalyst was filtered off and an excess of solvent removed under vacuum. Hydrogen chloride was then passed through the solution and, after having been kept in the cold for several hours, the precipitated crystals were collected. Recrystallization from methanol yields colorless crystals which melt at 241° (uncor). The substance was chromatographically pure.

Anal. Calcd for $C_{10}H_{16}N_6 \cdot 4HCl$: N, 22.95. Found: N, 22.88.

N,N′-Bis(o-aminobenzyl)ethylenediamine (ABEDA). (A). **Bis-(o-nitrobenzaldehyde)ethylenediimine.**—o-Nitrobenzaldehyde (9 g, 0.06 mol) and 2.4 g (0.03 mol) of ethylenediamine monohydrate were dissolved in 40 ml of alcohol and the mixture boiled under reflux for several minutes. After cooling, crystals of the slightly colored Schiff base were collected. Recrystallization from alcohol and petroleum ether yields beige crystals melting at 110–112° (uncor).

Anal. Calcd for $C_{16}H_{14}N_4O_4$: N, 17.17. Found: N, 17.20. (The Schiff base decomposes quite rapidly in daylight. However, it can be kept in the dark without apparent decomposition for several weeks.)

(B). **N,N′-Bis(o-aminobenzyl)ethylenediamine.**—Bis(o-nitrobenzaldehyde)ethylenediimine (3.3 g 0.01 mol) was dissolved in 60 ml of ethyl acetate and the mixture added to 1 g of 10% Pd–C catalyst which had been activated with hydrogen. The mixture was reduced with hydrogen at a pressure slightly above atmospheric with gentle agitation. Hydrogen consumption (at 21° and 730 mm pressure) was 1806 ml, corresponding to 90% of the theoretical amount.

The catalyst was filtered off and the solvent removed under vacuum. The remaining substance was dissolved in ether and the tetrahydrochloride precipitated by passing hydrogen chloride through the solution. Recrystallization from alcohol–water yields colorless crystals which decompose without a defined melting point above 250°. The product was chromatographically pure. The tetrahydrochloride decomposes slowly in bright daylight. It can be kept for months in the dark without apparent decomposition.

Anal. Calcd for $C_{16}H_{22}N_4 \cdot 4HCl$ (mol wt 416): N, 13.46; Cl, 34.07. Found: N, 13.50; Cl, 33.78.

N,N′-Bis(o-hydroxybenzyl)ethylenediamine (HYBEDA).—Bis(salicylaldehyde)ethylenediimine (5.4 g, 0.02 mol), prepared according to Mason,[14] was dissolved in 100 ml of alcohol and the mixture hydrogenated for 5 hr in the presence of 0.5 g of activated 10% Pd–C catalyst. Hydrogen consumption (at 20° and 738 mm pressure) was 970 ml, corresponding to 97% of the theoretical amount. The catalyst was removed. After removal of the solvent under vacuum, the yellow residue was repeatedly recrystallized from alcohol and petroleum ether. The final product was colorless and melted at 122° (uncor) (lit.[15] 124°).

Anal. Calcd for $C_{16}H_{20}N_2O_2$: N, 10.29. Found: N, 10.25.

Reagents.—Metal chloride solutions were prepared from reagent grade materials purchased from Riedel de Haen Co. (Seelze, Hannover, Germany) and E. Merck Co. (Darmstadt, Germany). Metal concentrations were determined with the help of standardized ethylenediaminetetraacetic acid (EDTA) according to Schwarzenbach.[16]

Pyridine-2-aldehyde, pyridine-2,6-dialdehyde, and 2-picolylamine were purchased from Dr. F. Raschig Co., Ludwigshafen, Germany. o-Nitrobenzaldehyde was purchased from C. Roth Co. (Karlsruhe, Germany), while ethylenediamine monohydrate, salicylaldehyde, standardized CO_2-free potassium hydroxide, and standardized hydrochloric acid (both Titrisol) were obtained from E. Merck Co.

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(14) A. T. Mason, *Chem. Ber.*, **20**, 271 (1887).

(15) A. Funke and J. P. Fourneau, *Bull. Soc. Chim. France*, **9**, 806 (1942).

(16) G. Schwarzenbach, "Die Komplexometrische Titration" in "Die Chemische Analyse," Vol. 45, 3rd ed, F. Enke Co., Stuttgart, Germany, 1957.

β,β',β''-Triaminotriethylamine (tren) and N,N,N′,N′-tetrakis-(β-aminoethyl)ethylenediamine (penten) were gifts generously provided by Dr. F. Schneider.

Doubly distilled CO_2-free water was used throughout the investigation.

Determination of Proton Association and Stability Constants

Measurements.—Potentiometric titrations were performed using the Radiometer titrator TTT1 in connection with the titrigraph SBR2 (Radiometer, Copenhagen, Denmark). The pH of the solution was monitored with the Radiometer glass electrodes G 202 C (normal pH region) and G 202 B (alkaline pH region), respectively. The glass electrodes were standardized with either 0.05 M potassium hydrogen phthalate buffer, pH 4.01 (25°), or 0.01 M borate buffer, pH 9.18 (25°). A Radiometer saturated calomel electrode served as reference electrode.

The ionic strength, μ, of the experimental solutions was maintained at 0.1 M by adding calculated quantities of potassium chloride. All measurements were performed at 25°. A CO_2-free stream of nitrogen was passed through the solutions during titration in order to exclude carbon dioxide. Ligand solutions were prepared by dissolving the hydrochlorides in water; the normality of each was determined by titration with standardized KOH.

The proton association constants of the ligands, defined as $K_{H_nL} = (H_nL)/(H_{n-1}L)(H)$ ($n = 1, 2, 3,\ldots,$ p; with p being the maximum number of hydrogen ions attached to a molecule), were determined by titration of the protonated ligands with standardized KOH or HCl in the absence of the complexing metal ions. The hydrogen ion concentration was calculated from the measured pH as described below.

The formation constants of the metal chelates, $K_{ML} = (ML)/(M)(L)$, where (ML), (M), and (L) represent, respectively, the equilibrium concentrations of the 1:1 metal chelate, of the free metal ion, and of the free ligand in its most basic form, were determined by titration of the protonated ligands with KOH in the presence of the complexing metal ions. In instances where addition of the metal ions to a ligand resulted in a complete displacement of the hydrogen ions from the protonated polyamine, the so-called "competing ligand method," originally developed by Schwarzenbach,[17] had to be employed in order to measure the equilibrium concentration of the uncomplexed ligand in question.

Calcium ethylenediaminetetraacetate (Ca–EDTA), β,β',β''-triaminotriethylamine (tren),[18] and N,N,N′,N′-tetrakis(β-aminoethyl)ethylenediamine (penten),[19] respectively, served as competing ligands. Details of the measurements are described elsewhere.[1]

Calculations.—The measured pH was corrected for the solvent by using the mean activity coefficient of hydrochloric acid, f_{HCl}, in 0.1 M KCl. The mean

(17) H. Ackermann and G. Schwarzenbach, *Helv. Chim. Acta*, **32**, 1543 (1949).

(18) J. E. Prue and G. Schwarzenbach, *ibid.*, **33**, 963 (1950).

(19) G. Schwarzenbach and P. Moser, *ibid.*, **36**, 581 (1953).

activity coefficient of hydrochloric acid, in turn, was calculated with the help of the so-called Harned's rule,[20,21] $\log f_{HCl} = \log f_{oHCl} - ym_{KCl}$, which permits the evaluation of the mean activity coefficient of hydrochloric acid in a potassium chloride–hydrochloric acid mixture if the total ionic strength of the mixture remains constant. f_{oHCl} is the activity coefficient of pure hydrochloric acid in a concentration equal to the total ionic strength of the acid–salt mixture and m_{KCl} is the molality of potassium chloride in the mixture of the two strong electrolytes. Taking $f_{oHCl} = 0.7964$ (25°; $\mu = 0.1\ M$),[22] the parameter $y = 0.08$ (25°; $\mu = 0.1\ M$),[20] and $m_{KCl} = 0.1\ M$ (molarity), we obtain $f_{HCl} = 0.782$ (25°; $\mu = 0.1\ M$). Finally, pH $= -\log (H)f_{HCl}$.

Similarly, hydroxide ion concentrations (OH) were calculated using the value $K_w = 1.631 \times 10^{-14}$ (mol²/l.²) (25°; $\mu = 0.1\ M$)[23] for the ion product of water.

The proton association constants of the ligands as well as the stability constants of the metal chelates were calculated using well-known algebraic methods. In instances where the proton association constants had to be determined from overlapping buffer regions, graphical approximation methods[24,25] were employed. Details of the calculations are given elsewhere.[1,2]

Results and Discussion

Acid–Base Properties of the Ligands—Interpretation of the Titration Curves.

—It should be said at the outset that all but two of the polyamines investigated in this work are very weak bases; indeed, the completely protonated forms of the amines are unstable in aqueous solution under the conditions of our experiments. Thus, the tetrahydrochlorides of 2,6-dimethylenebis(N-2-picolylamino)pyridine (DMPAP), N,N'-bis(2-picolyl)ethylenediamine (BPEDA), and N,N'-bis-(o-aminobenzyl)ethylenediamine (ABEDA) dissociate at once into hydrochloric acid and the dihydrochlorides, and the trihydrochloride of di(2-picolyl)amine (DPA) exists to a large extent only as the monohydrochloride in water.

As an example, the neutralization curve of the tetrahydrochloride of DMPAP is shown in Figure 1 (curve a). From $q = 0$ to $q = 2$ (added base equivalents) free hydrochloric acid is neutralized as this part of the titration curve coincides with the neutralization curve of hydrochloric acid of identical concentration in 0.1 M KCl. In addition, the measured pH values from $q = 0$ to $q = 2$ are identical with the pH values calculated with the assumption that the tetrahydrochloride of DMPAP dissociates into the dihydrochloride and
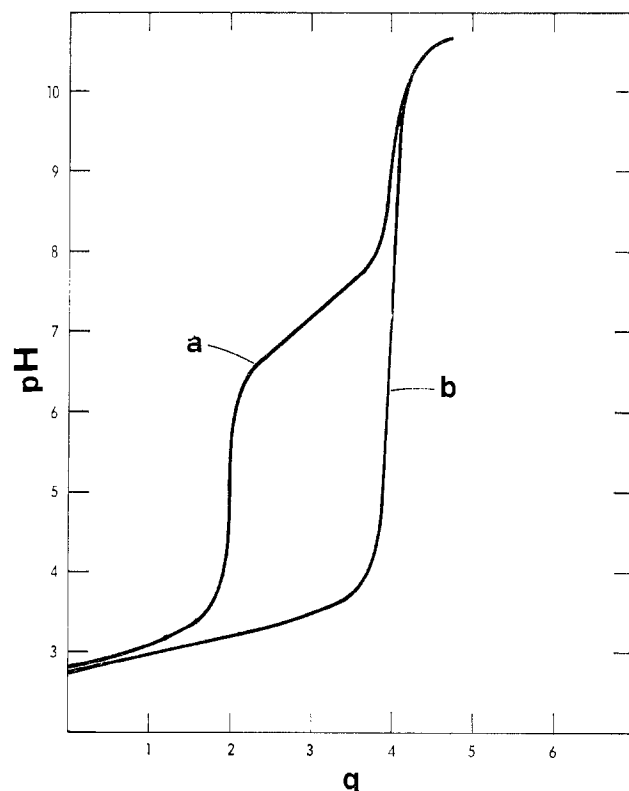
(20) H. S. Harned, *J. Am. Chem. Soc.*, **57**, 1865 (1935).

(21) G. Kortum, "Lehrbuch der Elektrochemie," 2nd ed, Verlag Chemie, Weinheim-Bergstrasse, 1957, pp 181–185.

(22) H. S. Harned and B. B. Owen, "The Physical Chemistry of Electrolytic Solutions," 3rd ed, Reinhold Publishing Corp., New York, N. Y., 1958, p 716.

(23) H. S. Harned and W. J. Hamer, *J. Am. Chem. Soc.*, **55**, 2194 (1933).

(24) G. Schwarzenbach, *Helv. Chim. Acta*, **33**, 947 (1950).

(25) F. J. C. Rossotti and H. Rossotti, "The Determination of Stability Constants and Other Equilibrium Constants in Solution," McGraw-Hill Series in Advanced Chemistry, McGraw-Hill Book Co., New York, Toronto, London, 1961.

Figure 1.—pH titration of 2,6-dimethylenebis(N-2-picolylamino)pyridine tetrahydrochloride (DMPAP) with potassium hydroxide: curve a, free ligand; curve b, ligand in the presence of an equimolar concentration of Zn(II). Concentration of ligand 0.001 M; ionic strength $\mu = 0.1\ M$ (KCl); q = added equivalents of potassium hydroxide.

HCl. The overlapping buffer region stretching from $q = 2$ to $q = 4$ corresponds to the reversible dissociation $H_2DMPAP \rightleftharpoons DMPAP + 2H$.

Similar neutralization curves were obtained for the ligands BPEDA, DPA, and ABEDA although here dissociation into HCl and the respective hydrochlorides was not as complete as in the case of DMPAP (*cf.* curve A, Figure 3).

In order to obtain the highly acidic proton association constants of BPEDA, DPA, and ABEDA, the ligand solutions were also titrated with HCl and the successive equilibrium constants were evaluated from the overlapping buffer regions at pH values between 2 and 1. Attempts to determine the constants K_{H_5L}, K_{H_4L}, and K_{H_3L} of DMPAP were unsuccessful.

Neutralization of the less acidic tetrahydrochloride of N,N'-bis(4-(5)-imidazolylmethyl)ethylenediamine (BIMEDA) and of the quite basic N,N'-bis(o-hydroxybenzyl)ethylenediamine (HYBEDA) (dihydrochloride) is shown in Figure 5 (curve A) and Figure 4 (curve A), respectively.

The proton association constants of all ligands are listed in Table I.

In general, the proton association constants could be determined with a precision of ± 0.02 pK unit or better. Somewhat less precise are the proton association constants of DPA and BPEDA: the variations range from ± 0.02 to ± 0.05 pK unit. Least precise
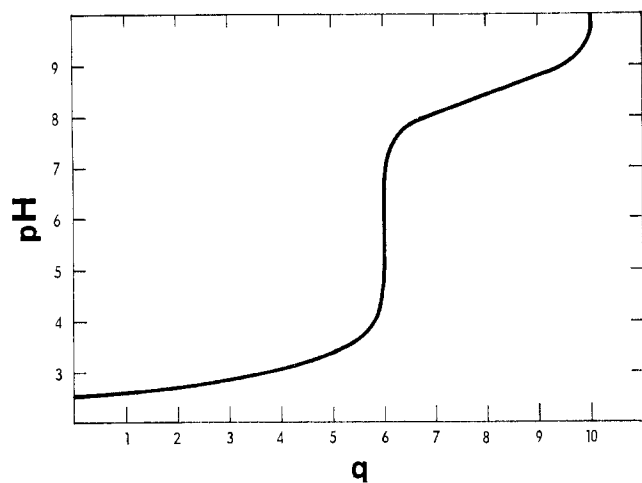
Figure 2.—pH titrations of an equimolar mixture of 2,6-dimethylenebis(N-2-picolylamino)pyridine tetrahydrochloride (DMPAP), N,N,N',N'-tetrakis(β-aminoethyl)ethylenediamine hexahydrochloride (penten), and Zn(II) with potassium hydroxide. Concentration of the ligands 0.001 M; ionic strength μ = 0.1 M (KCl); q = added base equivalents.
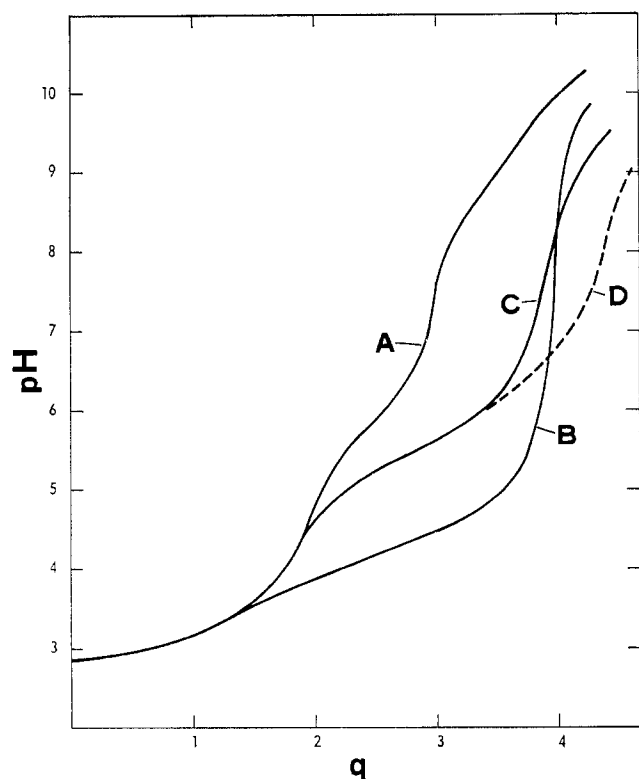

Figure 3.—pH titration of the tetrahydrochloride of N,N'-bis-(o-aminobenzyl)ethylenediamine (ABEDA) with potassium hydroxide: curve A, free ligand; curve B, equimolar mixture of ABEDA and Ni(II); curve C, equimolar mixture of ABEDA and Zn(II); curve D, equimolar mixture of ABEDA and Co(II) (curve C and curve D coincide up to $q \sim 3.5$). Concentration of the ligand and complexing metal ions 0.001 M; ionic strength μ = 0.1 M (KCl); q = added equivalents of KOH.

are the constants K_{H_4L} and K_{H_3L} of BPEDA. They vary to about ±0.1 pK unit.

The values for K_{HL} and K_{H_2L} of BPEDA (Table I) are in excellent agreement with the values $10^{8.23}$ and $10^{5.45}$ (1./mol), respectively, given by Lacoste and
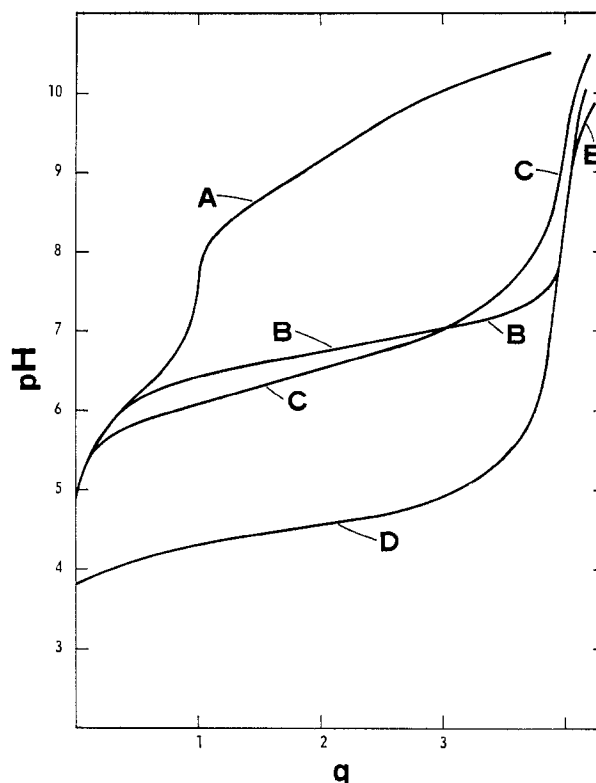

Figure 4.—pH titration of the dihydrochloride of N,N'-bis-(o-hydroxybenzyl)ethylenediamine (HYBEDA) with potassium hydroxide: curve A, free ligand; curve B, equimolar mixture of HYBEDA and Zn(II); curve C, equimolar mixture of HYBEDA and Ni(II); curve D, equimolar mixture of HYBEDA and Cu(II). Not shown is the neutralization curve of the dihydrochloride of HYBEDA in the presence of Co(II) as it is very similar to the Zn(II) curve. Concentration of the ligand and complexing metal ions 0.001 M; ionic strength μ = 0.1 M (KCl); q = added equivalents of KOH.

TABLE I
PROTON ASSOCIATION CONSTANTS OF DMPAP, BPEDA, DPA, ABEDA, BIMEDA, AND HYBEDA

Ligand	Log equilibrium constants				
	K_{H_5L}	K_{H_4L}	K_{H_3L}	K_{H_2L}	K_{HL}
DMPAP	...	...	....	6.86	7.55
DPA			1.75	2.41	7.27
BPEDA		1.8	2.0	5.47	8.28
ABEDA		2.00	2.32	5.90	9.00
BIMEDA		3.21	4.26	6.56	9.05
HYBEDA		6.17	8.37	9.80	10.50

Martell.[11] Larger deviations exist between their values for K_{H_3L} (K = $10^{1.81}$ (1./mol)) and K_{H_4L} (K = $10^{1.62}$ (1./mol)) and the corresponding values reported in Table I. Presumably, these deviations are due to differences in evaluating the constants, *i.e.*, using data uncorrected for the solvent.

It was shown by Holmes and Jones[26] and also by Anderegg[27] that the base strength of pyridine is lowered considerably upon substitution in the 2 position. It is reasonable to anticipate similar changes in the base strength of the heterocyclic polyamines DPA, BPEDA, and DMPAP. Thus, K_{HL} of DPA is the proton association constant of the secondary amino group while

(26) F. Holmes and F. Jones, *J. Chem. Soc.*, 2398 (1960).
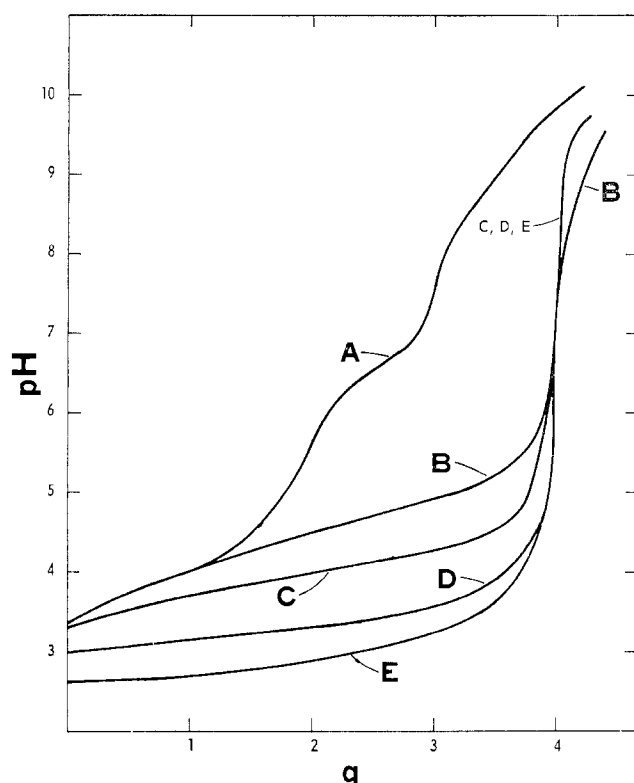(27) G. Anderegg, *Helv. Chim. Acta*, **43**, 414 (1960).

Figure 5.—pH titration of the tetrahydrochloride of N,N'-bis-(4-(5)-imidazolylmethyl)ethylenediamine (BIMEDA) with potassium hydroxide: curve A, free ligand; curve B, equimolar mixture of BIMEDA and Zn(II); curve C, equimolar mixture of BIMEDA and Co(II); curve D, equimolar mixture of BIMEDA and Ni(II); curve E, equimolar mixture of BIMEDA and Cu(II). Concentration of the ligand and complexing metal ions 0.001 M; ionic strength μ = 0.1 M (KCl); q = added equivalents of KOH.

K_{H_3L} and K_{H_3L} reflect the basicity of the two pyridine nitrogen atoms. Similarly, K_{HL} and K_{H_2L} of BPEDA and DMPAP reflect the base properties of the secondary amino groups whereas the other equilibrium constants are indicative of the large decrease in basicity of the pyridine nitrogens.

In the case of the chelating agents ABEDA and BIMEDA, K_{HL} and K_{H_2L} are also the proton association constants of the aliphatic amino groups while K_{H_3L} and K_{H_4L} of the two ligands are the equilibrium constants of the aromatic amino groups of ABEDA and of the aromatic ("pyridine") nitrogen atoms of the imidazolyl residues of BIMEDA.

Considering HYBEDA, it seems evident from the comparison of its structure and the structures of the other N,N'-disubstituted ethylenediamines that K_{HL} and K_{H_2L} are the proton association constants of the two phenolic hydroxyl groups while the other two equilibrium constants represent the base properties of the aliphatic amino groups. This interpretation is substantiated by the fact that in HYBEDA surprisingly strong intramolecular hydrogen bonds are formed involving participation of the phenolic hydroxyl groups and the unprotonated aliphatic amino groups.[28] In other words, as the phenolic hydrogen ions are the ones which are stabilized by hydrogen bonding, they

(28) H. H. Freedman, *J. Am. Chem. Soc.*, **83**, 2900 (1961).

will be also the last ones to leave the molecule. Thus, hydrogen bonding ultimately results in a weakening of the proton affinity of the aliphatic amino groups and increases the stability of the phenolic O–H bond.

Titration of the hydrochlorides of the various ligands in the presence of the ions Zn(II), Co(II), Ni(II), and Cu(II) with alkali yields neutralization curves which are shown in Figure 1 (curve b) and in Figures 3–5.

The stability constants of the 1:1 metal chelates are listed in Table II.

TABLE II
CHELATE FORMATION CONSTANTS OF DMPAP, DPA, BPEDA, ABEDA, BIMEDA, AND HYBEDA

Ligand	—————Log equilibrium constants—————			
	K_{ZnL}	K_{CoL}	K_{NiL}	K_{CuL}
DMPAP	12.0	14.8	...[a]	18.4
DPA	6.8	5.2	8.5	
BPEDA	11.4	12.0	14.4	
ABEDA	7.17	7.0[a]	10.00	
BIMEDA	10.39	11.43	14.02	16.5
HYBEDA	11.97	12.78	>13[a]	20.5

[a] Explanation in text.

The formation constants are precise to about ±0.03 log K unit. Larger deviations were observed in measurements involving the copper chelates of BIMEDA and HYBEDA. These constants vary about ±0.1 in log K. The stability constants of the heterocyclic polyamines DMPAP, DPA, and BPEDA are listed with only one significant decimal place as their numerical evaluation involved the use of complex formation data of other workers.[18,19]

In general, complex formation proceeds in accordance with the overall reaction

$$\text{M} + \text{H}_n\text{L} \rightleftharpoons \text{ML} + n\text{H}$$

with n being equal to 1, 2, or 4 depending on the ligand to be considered. At pH values above 9, there seem to be additional reactions involving the formation of hydroxo complexes. This is indicated by the fact that here the neutralization curves of the ligands in the presence of the complexing metal ions do not coincide with the titration curves of the metal-free compounds.

In the case of the heterocyclic polyamines DMPAP, DPA, and BPEDA, the above equilibrium is shifted almost completely to the right (*cf.* Figure 1, curve b). It is obvious that the binding constants of the metal ions cannot be determined by analysis of such neutralization curves since the concentration of the free hydrogen ions does not differ markedly from the total hydrogen concentration present. Accordingly, the ligands had to be titrated in the presence of a second competing ligand.

Figure 2 shows the neutralization curve of DMPAP in the presence of equimolar amounts of Zn(II) and equimolar amounts of N,N,N',N'-tetrakis(β-aminoethyl)ethylenediamine (penten) as the competing ligand. The stability constant of the Zn–DMPAP chelate was evaluated from the experimental data of the

buffer region stretching from $q = 6$ to $q = 10$ which corresponds to the metal exchange reaction

$$Zn(DMPAP) + H_4penten \rightleftharpoons Zn(penten) + 4H$$
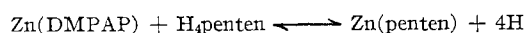
From $q = 0$ to $q = 6$, only free hydrochloric acid is neutralized: two equivalents result from the dissociation of the tetrahydrochloride of DMPAP into the dihydrochloride and free HCl, two additional equivalents come from the spontaneous dissociation of the hexahydrochloride of penten into HCl and the respective tetrahydrochloride, and, finally, two equivalents are liberated by complex formation of H_2DMPAP with Zn(II). Similar titration curves were obtained with the other metal ions in questions.

The stability constant of the Ni(II) chelate of DMPAP was not determined because of the slowness of the complex formation reaction. In fact, even after waiting several hours for each determination of hydrogen ion concentration, it was noted that no equilibrium was reached. Similar observations have been reported by other workers.[8,11]

Our data for the chelate formation of BPEDA with Zn(II) and Co(II) agree very well with the results obtained by Lacoste and Martell.[11] Their value for the stability constant of the Ni(II) chelate is, however, 1.7 pK units below the value listed in Table II.

In the case of the complex formation of ABEDA with Co(II) (Figure 3, curve D), the titration curve does not show the sharp inflection at the expected number of added base equivalents as observed with the other metal ions but continues to a point corresponding to approximately 0.3–0.5 additional equivalent of alkali (dashed line). At pH values above 6, the original pink color of the solution changes slowly and irreversibly to a light brown. Although titrations performed under conditions which supposedly excluded all trace amounts of oxygen impurities did not change the neutralization curve markedly, the most plausible explanation of the observed deviation is the assumption that Co(II) is being slowly oxidized to Co(III) at higher pH values. It is known that the stability of trivalent cobalt is greatly increased in the presence of complexing ligands, particularly nitrogen donors, and it is further known that Co(III) is more stable in basic than in acid media. It is noteworthy, however, that the neutralization curve of ABEDA in the presence of Co(II) yielded highly reproducible values for the stability constant of the cobalt chelate from $q = 2.0$ to $q = 3.3$. It is for this reason that the formation constant is listed in Table II.

An exact value for the stability constant of the Ni(II) chelate of HYBEDA could not be obtained. Although Ni(II) reacts with the ligand by displacing four hydrogen ions in one step (Figure 4, curve C), the calculation yields values for the stability constant which are seemingly pH dependent. The titration curve C

of Figure 4 indicates that complexing takes place over a somewhat broader pH range than does, for instance, the titration curve B with zinc ions. As the titration curve B is a curve which fits the theory, the additional broadness of curve C could be explained if there was some contribution by complexes which were partially protonated as well as by the complex Ni(HYBEDA). Attempts to evaluate the formation constants of such partially protonated complexes, however, were unsuccessful; no further studies have been made to investigate the complex formation with nickel ions more closely.

Conclusion.—The most striking feature of the present investigation is the fact that the heterocyclic amines DMPAP, DPA, and BPEDA bind metal ions much more strongly than one would expect from the hydrogen ion binding data (Table I). Indeed, it is readily shown that they are considerably better sequestering agents at pH values below 8 than the analogous basic aliphatic polyamines tetraethylenepentamine, β,β'-diaminodiethylamine, and β,β'-diamino-N,N'-diethylethylenediamine.

Ordinarily, the tendency of an electron donor to bind metal ions decreases with decreasing basicity, and for sufficiently similar donors (*e.g.*, nitrogen compounds) there exists a parallel between metal binding and proton affinity. However, as was shown by Anderegg,[27] this correlation has to be modified for ligands which, for instance, contain the pyridine ring.

At present, we are unable to offer a reasonable explanation for this interesting chelating behavior. It has been suggested that pyridine belongs to a class of ligands which can engage in *synergic* $\sigma-\pi$ bonding.[29] This bond type should be less dependent on the availability of σ electrons as here the flux of electrons is primarily directed from the metal to the ligand. Direct experimental evidence for such bonding, however, has been virtually absent.

A similar if less pronounced disparity between proton affinity and metal binding is shown by BIMEDA whereas the decreased stability of the chelates of ABEDA is a true reflection of the lowered basicity of the ligand. There can be no doubt, however, that the aromatic amino groups of ABEDA participate in complex formation as, for instance, N,N'-difurfurylethylenediamine,[30] a strictly bidentate chelating agent of almost identical basicity, forms a 1:1 Ni(II) complex whose stability constant is about 5 log K units below the value of the nickel chelate of ABEDA. In other words, this is the chelate stability to be expected if ABEDA would coordinate with the metal ion only *via* the aliphatic amino groups of the ethylenediamine residue.

(29) F. A. Cotton and G. Wilkinson, "Advanced Inorganic Chemistry," 2nd ed, Interscience Publishers, New York, London, Sydney, 1966, pp 719, 755; also see ref 8, 27.

(30) E. Hoyer, *Z. Anorg. Allgem. Chem.*, **297**, 167 (1958).