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PREPARATION AND SOME PROPERTIES OF N,N'-DIETHYLETHYLENE DIAMINE-N,N'-DIACETIC ACID AND N',N'-DIETHYLETHYLENEDIAMINE-N,N'-DIACETIC ACID, INCLUDING ABILITY OF THE FORMER TO ASSOCIATE WITH LANTHANONS AND YTTRIUM

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SUMMARY

N,N'-diethylethylenediamine-N,N'-diacetic acid and N',N'-diethylethylenediamine-N,N'-diacetic acid were prepared via a classical cyanomethylation process and subsequently isolated by displacement cation-exchange chromatography. N,N'-diethylethylenediamine-N,N'-diacetic acid melted with decomposition at 205–208° and N',N'-diethylethylenediamine-N,N'-diacetic acid at 175–177°. Successive pK_1 and pK_2 values measured at 25° and $\mu = 0.10$ (KNO_3) for N,N'-diethylethylenediamine-N,N'-diacetic acid and N',N'-diethylethylenediamine-N,N'-diacetic acid were, respectively, 6.31, 10.42 and 4.71, 11.65. $\log K_{LnCh^+}$ values of 7.1, 6.9, 7.0, 7.0, 6.9, 7.0, 7.1, 7.1, 7.1 and 6.8 were determined by a potentiometric method for $Ch = (\text{anion of N,N'-diethylethylenediamine-N,N'-diacetic acid})^{2-}$ and $Ln = Eu^{3+}$, Gd^{3+} , Tb^{3+} , Dy^{3+} , Ho^{3+} , Er^{3+} , Tm^{3+} , Yb^{3+} , Lu^{3+} and Y^{3+} , respectively. Because the pK_2 value of N',N'-diethylethylenediamine-N,N'-diacetic acid was so high (11.65), the formation constants of its $LnCh^+$ species could not be ascertained below pH 7. The high pK_2 value of unsymmetrical N',N'-diethylethylenediamine-N,N'-diacetic acid has been rationalized by classical arguments.

INTRODUCTION

Although ethylenediamine-N,N'-diacetic (*unsym.*-EDDA) and ethylenediamine-N,N'-diacetic (*sym.*-EDDA) acids have been studied as complexants for a few metal ions, little is known regarding N',N'- and N,N'-dialkyl substituted ethylenediamine-diacetic acids. *Unsym.*-EDDA was investigated in 1955 by SCHWARZENBACH *et al.*¹ as a complexant for alkaline earth and first row transition metal(II) cations (also Cd^{2+} , Hg^{2+} and Pb^{2+}). *Sym.*-EDDA was studied in 1952 by CHABEREK AND MARTELL² as a complexant for divalent Mg, Co, Ni, Cu, Zn and Cd cations, and in 1962 by THOMPSON³ as a complexant for the trivalent lanthanons and yttrium. It was the

fact that THOMPSON reported a much smaller change in $\log K_{LnCh^+}$ from $Ln = La$ to $Ln = Lu$ for *sym.*-EDDA than for EDTA as Ch that triggered an interest in N,N' - and N',N' -diakyl substituted EDDAs. It was hoped that steric effects produced by alkyl substituents might augment the small values of $\Delta \log K_{LnCh^+}$ for adjacent pairs of lanthanons.

Further search revealed that N,N' -dimethylethylenediamine- N,N' -diacetic acid had been characterized⁴, but not the N',N' -dimethyl entity. No references were found regarding N,N' -diethylethylenediamine- N,N' -diacetic acid (I) and N',N' -diethylethylenediamine- N,N' -diacetic acid (II), although N,N' -di(2-hydroxyethyl)ethylenediamine- N,N' -diacetic and N',N' -di(2-hydroxyethyl)ethylenediamine- N,N' -diacetic acids^{5,6} have been studied cursorily.

The following describes a comparative study made in this laboratory with respect to preparation, isolation and some properties of I and II.

EXPERIMENTAL

Reagents

The intermediates used to prepare I and II, namely, N,N' -diethylethylenediamine and N,N' -diethylethylenediamine, were procured better than 98% pure from Aldrich Chemical Company, Inc. All other materials were of Analytical Reagent grade purity.

General preparative procedure

Syntheses of I and II were accomplished by the classical carboxylation of SMITH *et al.*⁷ involving reaction of amines with formaldehyde and sodium cyanide in the presence of NaOH or KOH. The products were isolated from the reaction mixture by the cation-elution process described by POWELL AND JOHNSON⁸ in their preparation of N' -methylethylenediamine- N,N,N' -triacetic acid.

N,N'-diethylethylenediamine- N,N' -diacetic acid. 58.1 g of N,N' -diethylethylenediamine, 125 ml of *tert.*-butyl alcohol and 125 ml of water were heated under reflux over a period of 10 h while 200 ml of an aqueous solution containing 57 g of NaCN and 3.5 g of NaOH and 200 ml of diluted aqueous formaldehyde (100 ml 37% H_2CO and 100 ml of H_2O) were added simultaneously at slow rates. The reaction mixture was then refluxed an additional 20 h, cooled to room temperature and acidified to pH 1.2 with 30% H_2SO_4 . The acidified mixture was boiled for 4 h, cooled to room temperature and passed into a 2-in. diameter, 4-ft. long, columnar bed of H^+ -form, 40-50 mesh, Dowex 50W-X8, cation-exchange resin. The sorbed amino acid was eluted down the bed and through a second bed of this kind with 0.1 *M* aqueous ammonia. The effluent solution containing product was collected in ten 900-ml fractions, each of which was evaporated to 25 ml and stirred into 100 ml of absolute ethanol. The solid which separated was filtered off and dried at 105°. The combined material melting at 205-208°, apparent molecular weight 234.7 (calculated 232.28), weighed 52.3 g (yield 45%) and analyzed 50.9% C, 9.0% H, 12.1% N and 28% O (calculated: 51.72% C, 8.62% H, 12.06% N and 27.60% O).

N',N'-diethylethylenediamine- N,N' -diacetic acid. A batch of II was prepared from N,N' -diethylethylenediamine by the process described above. In this case the combined material melted at 174-177°, had an apparent molecular weight of 237.6

and was analyzed as 51.5% C, 9.1% H, 12.1% N and 27.3% O. The yield was calculated to be 44%.

Ionization constants of acids I and II

The first and second ionization constants of I and II were determined independently at 25° and $\mu = 0.10(\text{KNO}_3)$ by measuring the pHs resulting when series of solutions were prepared (each containing 10.00 ml of 0.0500 M amino acid and

TABLE I

APPARENT IONIZATION CONSTANTS OF I AND II AT $\mu = 0.10 (\text{KNO}_3)$ AND 25°

<i>Acid</i>	pK_1	pK_2
I (sym.)	6.31	10.42
II (unsym.)	4.71	11.65

varying amounts of 0.1176 M KOH and 1.67 M KNO_3) and diluted to 200.0 ml at 25.0°. The pH measurements were made with a Beckman Research pH Meter, Model 1019 (see Table I).

Determination of stability constants of some 1:1 lanthanon N,N' -diethylethylenediamine- N,N' -diacetate chelate species

The stabilities of 1:1 lanthanon chelate species of reagent I were measured at 25° and $\mu = 0.10(\text{KNO}_3)$ using the procedure described previously by POWELL *et al.*¹¹. \bar{n} values ranging from about 0.2 to 0.6 were achieved in each case for some lanthanons (Eu^{3+} through Lu^{3+}) and yttrium in the buffer pH region 5.6–5.9. It was not possible to elicit reliable information from the data obtained, regarding possible formation of any 1:2 species.

CONCLUSIONS

The data in Table II reveal that the lanthanons and yttrium form substantially

TABLE II

STABILITIES OF THE 1:1 CHELATE SPECIES FORMED BETWEEN I AND SOME LANTHANONS AND YTTRIUM AT 25° AND $\mu = 0.10 (\text{KNO}_3)$

<i>Metal ion</i>	$\log K_{LnCh}^+$	$\log K_{Ln(sym.-EDDA)}^{+11}$
Eu^{3+}	7.0	8.38
Gd^{3+}	6.9	8.13
Tb^{3+}	7.0	8.18
Dy^{3+}	7.0	8.31
Ho^{3+}	6.9	8.42
Er^{3+}	7.0	8.59
Tm^{3+}	7.1	8.75
Yb^{3+}	7.1	8.93
Lu^{3+}	7.1	9.09
Y^{3+}	6.8	7.78

¹¹ Data of THOMPSON⁵.

weaker (less stable) chelates with N,N' -diethylethylenediamine- N,N' -diacetate anion than with *sym.*-EDDA³. Also revealed is an unprecedented lack of selectivity exhibited by the anion of I toward individual rare-earth cations.

The most significant fact revealed by this investigation perhaps is that the anion of the unsymmetrical acid II exhibits a seventeen-fold greater affinity for the first proton while manifesting a forty-fold lesser affinity for a second proton than the anion of the symmetrical acid I does. A similar effect (although of lesser magnitude) is observed in comparing *sym.*-EDDA with *unsym.*-EDDA (see Table III).

The *unsym.*-EDDA anion appears to have a three-fold greater affinity for the first proton and an eight-fold lesser affinity for the second proton than the anion of *sym.*-EDDA.

This observed enhanced affinity exhibited by homologous unsymmetrically substituted EDDA anions for the first proton and an attenuated affinity for a second proton reflects the fact that the unsymmetrical EDDA entities inherently have their donor atoms in a more favorable arrangement to closely approach the first proton

TABLE III

IONIZATION CONSTANTS OF THE ISOMERIC (*sym.* AND *unsym.*) ETHYLENEDIAMINEDIACETIC ACIDS

<i>Acid</i>	<i>Temperature</i>	pK_1	pK_2	<i>Ref.</i>
<i>sym.</i> -EDDA	25°	6.48	9.57	3
<i>unsym.</i> -EDDA	20°	5.58	11.05	1

than do the symmetrical EDDA entities. If a proton is considered to have four tetrahedrally arrayed coordination sites (as in the ice structure or in the hypothetical hydronium ion, $H_3O_4^+$), it is seen that two of the sites can be occupied by N atoms and that the other two sites are then accessible to two O donor atoms when the acetate groups are joined to the same N atom. When one acetate group is on each N, however, fixing the two N atoms (by their lone pair electrons) about a proton leads to possible asymmetry in arrangement of groups about each N. When the acetate groups extend from opposite sides of the plane established by the five membered ($-N-C-C-N-H-$) ring, an O atom of each carboxyl group can occupy its own tetrahedral site, but when both acetate groups extend from the same side of the plane (a statistically equal possibility) a site is accessible to only one carboxylate O donor atom at a time. It is obvious then that the symmetric ligand should hold a single proton less tightly than the corresponding unsymmetric ligand.

That both diethyl substituted ligand anions form stronger attachments to the first proton than the unsubstituted (*sym.*- and *unsym.*-) EDDA anions may be attributed to the electron releasing effect of alkyl groups on amines (which makes the nitrogen lone pair(s) of electrons more accessible for bonding). Note that it is this enhanced attraction for H^+ (plus a lower affinity for Ln^{3+} cations) that has prevented measurement of lanthanon N,N' -diethylethylenediamine- N,N' -diacetate stabilities below pH 7 and has rendered determination of lanthanon N,N' -diethylethylenediamine- N,N' -diacetate stabilities considerably less certain than the corresponding EDDA chelate stabilities determined and reported by THOMPSON³.

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