

New Complexanes. XIX.

Complex-forming Properties of the Ethylenediamine-*N,N'*-diacetic-*N,N'*-(2,2'-dialkanecarboxylic) Acids

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The dissociation constants of three complexanes of above-mentioned type as well as the stability constants of their chelates with 24 central atoms are presented. The ethylenediamine-*N,N'*-diacetic-*N,N'*-(2,2'-diisovaleric) acid has shown the complex-forming properties which are considerably different in comparison to EDTA.

The effect of alkyl and isoalkyl substituents on the properties of ethylenediaminetetraacetic acid functioning as a model complex-forming ligand has been studied in another complete group of ditopic, disubstituted complex-forming agents of the type of ethylenediamine-*N,N'*-diacetic-*N,N'*-(2,2'-dialkanecarboxylic) acids. This group represents one of the variants of alkyl and isoalkyl substituted EDTA which is essentially constituted by the representatives of two homologous series of these complexanes (*n*-series and iso-series).

The physico-chemical constants characterizing the acid-base and chelate-forming properties of diethyl-(EDDB α DA), dipropyl-(EDDV α DA), and diisopropyl-(EDDIV α DA) derivatives have been determined potentiometrically and polarographically. These problems are in close connection with our preceding publications [1, 2] in which we have described the dimethyl derivative EDDP α DA. In experimental part we deal with the determination of the dissociation constants of individual tetracarboxylic acids as well as stability constants of their chelates with alkaline earth cations (Mg²⁺, Ca²⁺, Sr²⁺, Ba²⁺), bivalent cations (Cd²⁺, Cu²⁺, Mn²⁺, Pb²⁺, Zn²⁺, Co²⁺), and lanthanides for $I = 0.10$ (KNO₃) and 20°C, in addition to the synthesis of these complexanes. We present only the resulting constants and in all other details, especially in the case of physico-chemical measurements, we refer to above-mentioned papers.

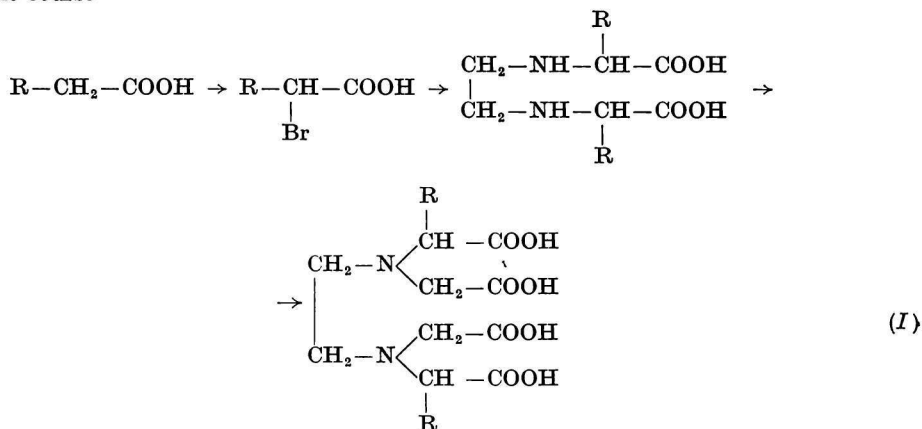
Abbreviations:

EDDP α DA	ethylenediamine- <i>N,N'</i> -diacetic- <i>N,N'</i> -(2,2'-dipropionic) acid.
EDDB α DA	ethylenediamine- <i>N,N'</i> -diacetic- <i>N,N'</i> -(2,2'-dibutyric) acid.
EDDV α DA	ethylenediamine- <i>N,N'</i> -diacetic- <i>N,N'</i> -(2,2'-divaleric) acid.
EDDIV α DA	ethylenediamine- <i>N,N'</i> -diacetic- <i>N,N'</i> -(2,2'-diisovaleric) acid.
EDDB α	ethylenediamine- <i>N,N'</i> -(2,2'-dibutyric) acid.
EDDV α	ethylenediamine- <i>N,N'</i> -(2,2'-divaleric) acid.
EDDIV α	ethylenediamine- <i>N,N'</i> -(2,2'-diisovaleric) acid.
„tren“	tris(2-aminoethyl)amine.

Experimental

Synthesis of the investigated chelate-forming agents

The complexanes were prepared in a three step synthesis according to following schematic course



where R: CH_3-CH_2- , $\text{CH}_3-\text{CH}_2-\text{CH}_2-$, $\begin{array}{l} \text{CH}_3 \\ \diagdown \\ \text{CH}- \\ \diagup \\ \text{CH}_3 \end{array}$

The α -bromobutyric acid was prepared in the first step according to *Fischer and Monneyrat* [3], α -bromovaleric and α -bromoisovaleric acids analogously according to *Schleischer* [4]. In following two steps the α -bromo-acids were subjected to a condensation with ethylenediamine in alkaline medium, the resulting dicarboxylic acids of complexane type (EDDB α , EDDV α , and EDDIV α , respectively) were isolated and by a subsequent condensation with bromoacetic acid transformed into corresponding complexanes. Owing to analogy between the preparations of two derivatives the alternative data are in parentheses and the common text remains without change. For elementary analyses as well as physico-chemical measurements the recrystallized preparations of complexanes were used.

A. Preparation of the ethylenediamine- N,N' -diacetic- N,N' -(2,2'-dibutyric) and ethylenediamine- N,N' -diacetic- N,N' -(2,2'-divaleric) acids

EDDB α (EDDV α)

33 g α -bromobutyric acid (36 g α -bromovaleric acid) is dissolved in 70% ethyl alcohol and under intensive stirring and cooling neutralized with 21 g KHCO_3 under formation of potassium salt. This solution is dropped under constant stirring into a mixture of 6 g ethylenediamine of anal. grade and 21 g KHCO_3 pending 2 hours. In the course of reaction the temperature is raised gradually up to 85°C at which the condensation continues for another 6–8 hours. After cooling and filtration the solution is acidified by 30% CH_3COOH to pH 5–6. A white and in water little soluble microcrystalline substance is separated. By repeated transformation into bipotassium salt with KOH and acidifying by 30% CH_3COOH a preparation of 99.90% purity can be obtained.

Yield: 18 g 78% EDDB α (16.5 g 64% EDDV α).

For EDDB α C₁₀H₂₀O₄N₂ (232.29) calculated: 51.66% C, 8.68% H, 12.06% N; found: 51.58% C, 8.76% H, 12.01% N.

For EDDV α C₁₂H₂₄O₄N₂ (260.34) calculated: 55.36% C, 9.29% H, 10.76% N; found: 55.27% C, 9.24% H, 10.69% N.

EDDB α DA (EDDV α DA)

19 g bromoacetic acid (2 M excess) neutralized with 7 N-KOH is added to 7.7 g EDDB α (8.7 g EDDV α) which have been transformed into bipotassium salt by 7 N-KOH. The solution is heated at 80–85°C for 6–8 hours and the alkalinity of solution is maintained at pH 10–11 by adding 7 N-KOH. The condensation having been finished the complexane is disengaged by acidifying with 25% HCl to pH 1–2.

Yield: 3.6 g 31% EDDB α DA (3.4 g 26% EDDV α DA).

For EDDB α DA C₁₄H₂₄O₈N₂ (348.36) calculated: 48.27% C, 6.95% H, 8.04% N; found: 48.08% C, 7.21% H, 7.82% N.

For EDDV α DA C₁₆H₂₈O₈N₂ · H₂O (394.43) calculated: 48.77% C, 7.67% H, 7.11% N; found: 48.31% C, 7.58% H, 7.28% N.

B. Preparation of the ethylenediamine-*N,N'*-diacetic-*N,N'*-(2,2'-diisovaleric) acid

EDDIV α

30 g α -bromoisovaleric acid is neutralized with 7 N-KOH under cooling and stirring. Then 5 g ethylenediamine anal. grade is added and the temperature is raised to 45–50°C. During 1 1/2–2 hours an equivalent amount of 7 N-NaOH is put in dropwise. The alkalinity of solution being maintained at pH 10–11. Then the temperature of reaction mixture is raised to 90°C and the condensation still proceeds for 8 hours. EDDIV α is isolated analogously to the preparation of EDDB α in the form of a white substance which could be purified by reprecipitation via bipotassium salt.

Yield: 4.6 g 21% EDDIV α .

For EDDIV α C₁₂H₂₄O₄N₂ (260.34) calculated: 55.36% C, 9.29% H, 10.76% N; found: 55.13% C, 9.41% H, 10.61% N.

EDDIV α DA

4.4 g EDDIV α is converted under stirring by 7 N-NaOH into bisodium salt and subsequently a solution containing 9.5 g Br-CH₂-COOH neutralized with 7 N-NaOH is added. The condensation runs for 6–8 hours at 85–90°C and pH 10–11. The free complexane is isolated after acidifying the reaction mixture with 25% HCl to pH 1–2.

Table 1

Negative values of dissociation constant logarithms
I = 0.10 (KNO₃); t = 20°C

Acid	pK ₁	pK ₂	pK ₃	pK ₄
EDTA [5]	2.00	2.67	6.16	10.26
EDDP α DA [1]	1.9 ± 0.1	2.68 ± 0.05	6.65 ± 0.02	10.42 ± 0.04
EDDB α DA	1.8 ± 0.1	2.69 ± 0.03	6.09 ± 0.02	10.42 ± 0.01
EDDV α DA	1.9 ± 0.1	2.79 ± 0.03	6.15 ± 0.02	10.47 ± 0.03
EDDIV α DA	1.9 ± 0.1	3.02 ± 0.03	5.60 ± 0.03	10.38 ± 0.03

Yield: 0.9 g 13% EDDIV α DA.

For EDDIV α DA C₁₆H₂₈O₆N₂ · H₂O (394.43) calculated: 48.77% C, 7.67% H, 7.11% N;
found: 48.79% C, 7.45% H, 7.00% N.

Dissociation constants

The dissociation constants were evaluated from the neutralization curves of 1×10^{-3} M solutions of acids in a usual way. For illustration the neutralization curve of EDDIV α DA is presented in Fig. 1. Table 1 gives the dissociation constants which have been found.

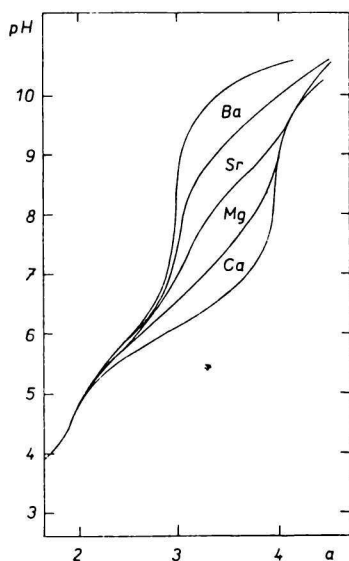


Fig. 1. Neutralization curve of 1×10^{-3} M-EDDIV α DA in the presence of 1×10^{-2} M-Ca²⁺, Mg²⁺, Sr²⁺, and Ba²⁺ ions, respectively.

α = mole KOH/mole EDDIV α DA.

Stability constants of chelates

The stability constants of complexes with alkaline earths have been evaluated by using the neutralization curves of 1×10^{-3} M complexane solutions containing a 10-fold excess of metal ion concentration. Their course for EDDIV α DA is given in Fig. 1.

On the other hand, the stability constants of Cu(II) and Cd(II) chelates have been estimated potentiometrically by the method of exchange equilibria with „tren“. Other complexes of EDDB α DA and EDDV α DA have been evaluated polarographically by the method of exchange equilibrium systems. In this case the values corresponding to Cd(II) complexes have been used as a basis for their determination. Owing to a small stability of complexes of EDDIV α DA with lanthanides and some bivalent ions the evaluation by the method with „tren“ applying an exchange with Cu(II) ions has been chosen. Higher lanthanides (Gd—Lu) have also been evaluated polarographically and in this case the value of Cu(II) complex with EDDIV α DA has been used as a basis. All stability constants are summarized in Table 2.

Table 2

Stability constants
 $I = 0.10$ (KNO₃); $t = 20^\circ\text{C}$

M	log K_M			
	EDDB α DA	EDDV α DA	EDDIV α DA*	EDDIV α DA
Ca	9.02 ± 0.02*	9.24 ± 0.02*	6.05 ± 0.03	—
Mg	7.83 ± 0.02*	7.96 ± 0.02*	5.20 ± 0.04	—
Sr	6.95 ± 0.02*	7.13 ± 0.02*	4.12 ± 0.04	—
Ba	5.81 ± 0.02*	5.97 ± 0.02*	3.30 ± 0.04	—
Cd	15.26 ± 0.02*	15.34 ± 0.06*	12.34 ± 0.02	—
Cu	18.76 ± 0.03*	18.89 ± 0.04*	—	—
Cu	18.64 ± 0.16	18.76 ± 0.16	16.07 ± 0.02	—
Pb	16.46 ± 0.10	16.57 ± 0.10	—	14.18 ± 0.12
Zn	16.04 ± 0.07	16.10 ± 0.07	13.07 ± 0.05	—
Co	15.93 ± 0.07	16.00 ± 0.07	—	—
Mn	13.19 ± 0.08	13.23 ± 0.09	9.75 ± 0.03	—
La	14.13 ± 0.13	14.12 ± 0.14	10.78 ± 0.05	—
Ce	14.77 ± 0.11	14.77 ± 0.11	11.54 ± 0.05	—
Pr	15.09 ± 0.11	15.11 ± 0.12	11.93 ± 0.05	—
Nd	15.35 ± 0.11	15.38 ± 0.11	12.09 ± 0.05	—
Sm	16.00 ± 0.11	16.07 ± 0.11	12.87 ± 0.05	—
Eu	16.31 ± 0.12	16.39 ± 0.12	13.23 ± 0.05	—
Gd	16.48 ± 0.11	16.60 ± 0.11	13.39 ± 0.05	13.47 ± 0.16
Tb	17.13 ± 0.14	17.16 ± 0.14	14.07 ± 0.05	14.00 ± 0.12
Dy	17.58 ± 0.15	17.63 ± 0.15	14.41 ± 0.05	14.45 ± 0.07
Ho	17.85 ± 0.16	17.83 ± 0.16	14.70 ± 0.07	14.71 ± 0.09
Er	18.19 ± 0.18	18.16 ± 0.17	14.91 ± 0.07	14.99 ± 0.08
Tm	18.45 ± 0.21	18.45 ± 0.19	15.20 ± 0.07	15.31 ± 0.07
Yb	18.70 ± 0.21	18.75 ± 0.21	15.38 ± 0.07	15.55 ± 0.07
Lu	18.90 ± 0.23	18.92 ± 0.22	15.50 ± 0.05	15.77 ± 0.06

* The values marked with asterisk were measured potentiometrically.

Discussion

As to the acid-base properties, substitution in methylcarboxyl groups effects only a slight change in the pK values of studied acids belonging to the n -series in comparison to the value of EDTA. EDDIV α DA shows a relatively greatest change because the more intense interaction of carboxyl groups due to the steric effect of isopropyl group raises the difference between pK_2 and pK_1 . The shift of pK_3 into acid region is also due to a closer approach of both ammonium groups. The pK_4 values are approximately the same for both series and a little greater than those of EDTA.

The stability constants of the complexes with alkaline earth elements (Fig. 2, Tab. 2) are lower for all acids studied though it should not be expected according to pK_4 values. That indicates a steric hindrance for chelating which is most evident in case of EDDIV α DA, the stability constant drop of which reaches 4 log K units on the average. There is also a certain relationship common for all acids investigated to be observed, namely an increase in the difference between the stability constants of Mg(II) and Sr(II) complexes.

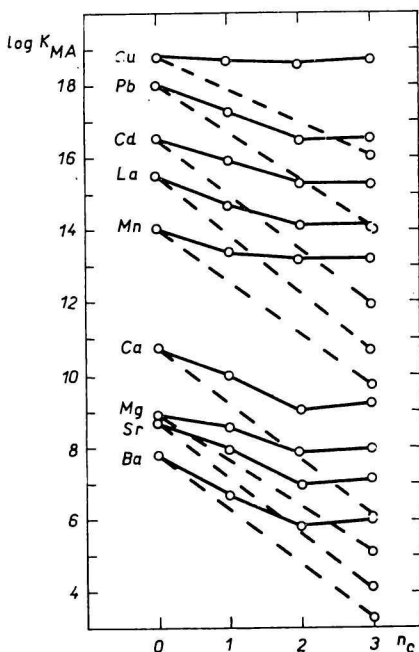


Fig. 2. Discontinuous relationship between the stability constants of some complexes and the number of carbon atoms in an alkyl- or isoalkyl-substituent R(I) of the carboxymethyl group of EDTA; $\log K_{MA} = F_1(n_c)$.
— *n*-series; - - iso-series.

To illustrate the stability constant change for individual complexanes we have plotted the discontinuous relationship between the stability constant logarithms of some selected complexes and the number of carbon atoms in alkyl substituent R of

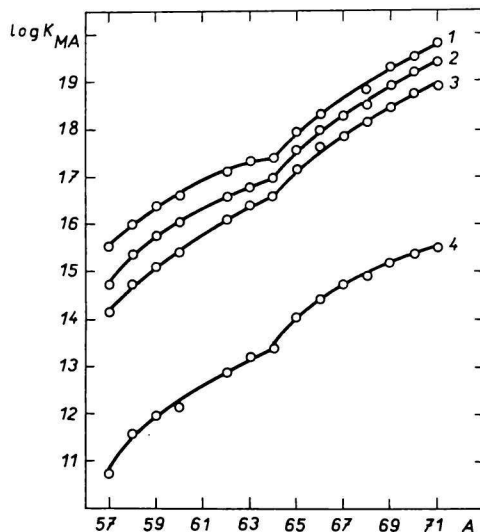


Fig. 3. Logarithms of chelate stability constants of the studied complexanes as a function of the atomic number of complex central atom; $\log K = F_2(A)$.
1. EDTA [6, 7]; 2. EDDP α DA [2]; 3. EDDB α DA (\cong EDDV α DA); 4. EDDIV α DA.

methylcarboxyl group of EDTA (Fig. 2). These plots show that in n -series a fall of stability constants takes place with the extension of carbon chain and their values approach a definite limiting value which is practically represented by the complexes of $\text{EDDB}\alpha\text{DA}$. Among the ions under investigation a particular exception is represented by Cu(II) complexes the stability constants of which are almost equal in the whole n -series. In case of $\text{EDDIV}\alpha\text{DA}$, a considerable fall of stability constants occurs for all ions studied.

The situation in the group of lanthanides is to be seen in Fig. 3. The individual curves 1—4 show the logarithms of stability constants of their complexes with EDTA, $\text{EDDP}\alpha\text{DA}$, $\text{EDDV}\alpha\text{DA}$ ($\cong \text{EDDB}\alpha\text{DA}$), and $\text{EDDIV}\alpha\text{DA}$ as a function of atomic number of the lanthanide representing the central atom of complex. From these plots it is evident that not only the character of stability constants increasing

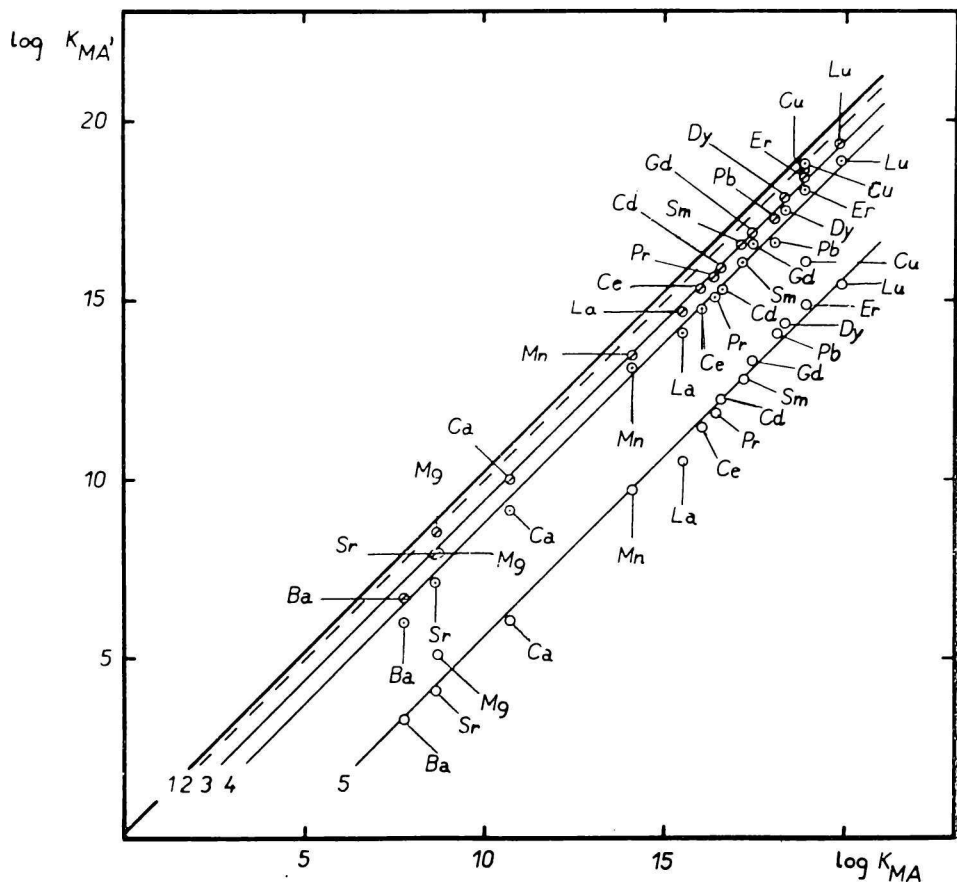


Fig. 4. Logarithms of stability constants as a function of the corresponding values of EDTA; $\log K_{MA'} = F_3(\log K_{M-EDTA})$.

1. EDTA; 2. theoretical curve; 3. $\text{EDDP}\alpha\text{DA}$; 4. $\text{EDDB}\alpha\text{DA}$ ($\cong \text{EDDV}\alpha\text{DA}$);
5. $\text{EDDIV}\alpha\text{DA}$.

from La to Lu but also the compass of about 4.7 units of $\log K$ between the first and last lanthanide remain unchanged in this group of complexanes. All agents studied form complexes which are more labile in comparison to EDTA this phenomenon being most conspicuous in case of EDDIV α DA.

The chelate-forming properties of complexanes studied are also evaluated on the basis of the thermodynamic relationship according to *Irving and Rossotti* [7] which is helpful for a comparison of stability constant logarithms of two or several sufficiently related agents:

$$\log K_{MA'} = \log K_{MA} + (\log K_{HA'} - \log K_{HA}). \quad (1)$$

In this equation $\log K_{MA'}$ and $\log K_{MA}$ are the corresponding couples of logarithms of stability constants for the chelates formed with A and A' agents and the stated complex central atom M whereas $\log K_{HA'}$ and $\log K_{HA}$ denote the pK_4 values of individual tetracarboxylic acids. The theoretical relationship is thus a straight line with the slope equal to one and the intercept $q = pK_{4(HA')} - pK_{4(HA)}$. The difference between the complex-forming properties of the investigated agents is thus given quantitatively by the difference of pK_4 values *i.e.* the change of their acid base properties.

In this way the stability constants of EDDP α DA, EDDV α DA (\doteq EDDB α DA), and EDDIV α DA are plotted in Fig. 4 as functions of the corresponding stability constants of EDTA chelates. The stability constants found for each complexane cover a considerably wide range — a compass of 12 $\log K$ units. With respect to the scale used in the plot and sufficient proximity of pK_4 values of investigated agents, the curve *I* indicates on the basis of relationship (1) the position of theoretically expected values* of stability constants which should thus manifest a little greater stability than complexes with EDTA and small differences among themselves for all complexes studied. A linear relationship with unit slope (curves 3—5) and a drop in stability constants, namely by half a decimal order for EDDP α DA, by one decimal order for EDDB α DA and EDDV α DA, and even by four decimal orders for EDDIV α DA in comparison to EDTA or to the expected relationship following only from the change of acid-base properties confirm the steric effect due to alkyl or isoalkyl substitution.

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