modifications of zirconia.[13] The stronger metal–chlorine bonds deduced for the analogous nickel and manganese complexes favor decomposition to anhydrous chlorides as observed.[34]

(34) F. Ephraim, "Inorganic Chemistry," P. C. L. Thorne and E. R. Roberts, Ed., Interscience Publishers, Inc., New York, N. Y., 1947, p. 269.

[CONTRIBUTION OF DEPARTMENT OF CHEMISTRY OF CLARK UNIVERSITY]

Thermodynamics of Metal Chelate Formation. I. The Third and Fourth Dissociation Constants of Ethylenediaminetetraacetic Acid
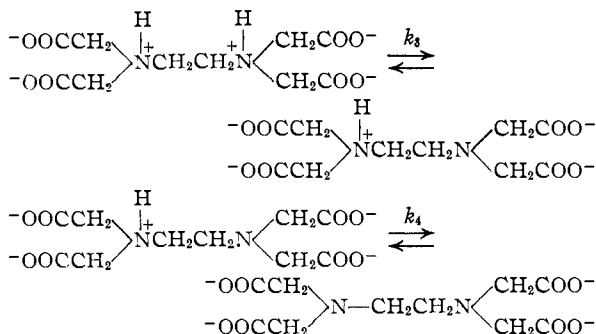
BY F. F. CARINI AND A. E. MARTELL

The potentials of the hydrogen–silver–silver chloride cell have been measured in buffer solutions containing acid salts of ethylenediaminetetraacetic acid. The e.m.f. data obtained without liquid junction were extrapolated to infinite dilution with the aid of the Debye–Hückel limiting law, and the thermodynamic equilibrium constants associated with the dissociation of the third and fourth protons were determined. The standard free energy changes for these reactions at 0, 5, 10, 15, 20, 25 and 30° were calculated, and the corresponding values of $\Delta H°$ and $\Delta S°$ applying over this temperature range are reported.

In order to carry out a potentiometric study of the thermodynamics of reactions between metal ions and the ethylenediaminetetraacetate anion, it is first necessary to study the thermodynamic changes associated with the combination of the anion with hydrogen ions. Since it has been shown in a previous publication[1] that it is possible to calculate the stabilities of the alkaline earth chelates from potentiometric measurements involving only the third and fourth ionization constants of ethylenediaminetetraacetic acid, it was decided to first restrict our investigation to the determination of these thermodynamic equilibrium constants over a range of temperatures.

With the exception of the work mentioned above, no thermodynamic constants have been determined for this amino acid, and no studies have been made of the effect of temperature on the equilibria. Previous investigations by Schwarzenbach and Ackermann[2] and by Cabell[3] were carried out at 25° and in a neutral salt medium of 0.1 ionic strength. In addition to usefulness in the study of complexing of metal ions, the heats and entropies of ionization of ethylenediaminetetraacetic acid are interesting in view of the complex structure and high charge of the basic substances involved. The equilibria under investigation may be represented by

(1) F. F. Carini and A. E. Martell, THIS JOURNAL, **74**, 5745 (1952).
(2) G. Schwarzenbach and H. Ackermann, Helv. Chim. Acta, **30**, 1798 (1942).
(3) M. J. Cabell, A. E. R. E. Report C/R 813, Ministry of Supply, Harwell, Berks., England, 1951.

The differences between the third and fourth dissociation constants are too large in view of present methods of predicting dissociation constants of organic substances. It was hoped that the thermodynamic changes involved would help to explain this discrepancy.

Experimental

The method employed for the determination of thermodynamic dissociation constants consisted of the extrapolation to zero ionic strength of the electromotive force of cells without liquid junction containing a buffer system consisting of appropriate ethylenediaminetetraacetate anions. The cells employed may be divided into two general classes

I. Pt–H₂, K₂H₂V(m₁), K₃HV(m₂), KCl(m₃). AgCl–Ag

II. Pt–H₂, K₃HV(m₁), K₄V(m₂), KCl(m₃), AgCl–Ag

where H₄V represents ethylenediaminetetraacetic acid.

Cell I, which contained the di- and tripotassium salts of ethylenediaminetetraacetic acid was used for the evaluation of k_3, and cell II, containing the tri- and tetrapotassium salts of ethylenediaminetetraacetic acid, was employed for the determination of k_4. The electromotive forces of these cells were measured from 0 to 30°. The values for 0° were evaluated by extrapolation of data taken at slightly higher temperatures.

Materials and Equipment.—The ethylenediaminetetraacetic acid was obtained through the courtesy of the Bersworth Chemical Company, Framingham, Massachusetts. It was further purified by two successive recrystallizations from water. The buffer solutions employed in cells of type I and II were made up by adding to the purified ethylenediaminetetraacetic acid the required amount of carbonate-free standard potassium hydroxide solution, prepared by the method of Schwarzenbach and Biedermann,[4] and standardized against potassium acid phthalate in the usual manner. The potassium chloride used was freed from bromide contamination by recrystallization from water and 95% ethanol as outlined by Pinching and Bates.[5]

The silver–silver chloride electrodes were prepared by the method of Shedlovsky and MacInnes,[6] and the platinum–hydrogen electrodes were made according to the directions outlined in Weissberger.[7] Tank hydrogen was first passed through a deoxo purifier, a presaturator, and then through

(4) G. Schwarzenbach and W. Biedermann, Helv. Chim. Acta, **31**, 331 (1948).
(5) G. Pinching and R. Bates, J. Research Natl. Bur. Standards, **37**, 311 (1946).
(6) T. Shedlovsky and D. A. MacInnes, THIS JOURNAL, **58**, 1970 (1936).
(7) A. Weissberger, "Physical Methods of Organic Chemistry," Second Edition, Vol. II, Interscience Publishers, Inc., New York, N. Y., 1949, p. 1722.

TABLE I

E.M.F. MEASUREMENTS (MV.)

m_3	0°	5°	10°	15°	20°	25°	30°

Cell I, $m_1:m_2:m_3 = 1:1:3.20$

m_3	0°	5°	10°	15°	20°	25°	30°
$6.61(10)^{-4}$	518.49	525.12	531.36	537.48	543.90	550.28	557.34
$8.09(10)^{-4}$	513.24	519.71	525.46	532.22	538.37	544.78	551.44
$1.319(10)^{-3}$	499.91	506.03	512.21	518.22	523.90	530.11	536.47
$1.693(10)^{-3}$	491.40	497.53	503.11				
$3.312(10)^{-3}$	474.61	479.99	485.36	490.38	496.10	501.73	507.55
$3.390(10)^{-3}$	472.83	477.67	482.89				
$4.053(10)^{-2}$	414.14	417.53	421.84	425.45	429.00	433.19	437.62

Cell II, $m_1:m_2:m_3 = 1:4:25$

m_3	0°	5°	10°	15°	20°	25°	30°
$1.452(10)^{-2}$	889.30	894.37	899.59	903.73	908.11	912.23	916.10
$2.070(10)^{-2}$	876.89	881.79	885.99	890.29	894.32	898.21	901.79
$2.542(10)^{-2}$	869.36	874.12	878.91	882.63	887.17	890.16	893.49
$2.917(10)^{-2}$	864.26	868.99	873.74	877.31	880.94	884.54	888.19
$3.993(10)^{-2}$	853.53	857.84	861.89	865.88	869.37	872.71	875.86

the experimental solution. The gases were removed from the system under a head of a few centimeters of water. The electromotive force of the cell was measured with the aid of a Leeds and Northrup Type K potentiometer and a sensitive galvanometer. For each measurement at least two platinum electrodes and a number of silver–silver chloride electrodes were employed, and electrodes which disagreed by more than 0.1 millivolt were discarded. The electromotive force of the cell was reproducible to ±0.05 millivolt. The temperature of the experimental solution was maintained constant within ±0.02°. The glass vessel used for the measurements was described in a previous publication.[1] The measured e.m.f. values obtained for cells I and II at various temperatures and ion concentrations are presented in Table I.

Treatment of Data.—Both cells I and II, corrected to standard pressure in the usual way, may be given in the general form

$$Pt-H_2(1 \text{ atm.}), H^+(a_{H^+}), Cl^-(a_{Cl^-}), AgCl-Ag$$
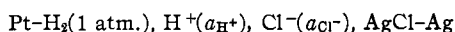
The electromotive force of this cell is given by

$$E = E_0 - \frac{RT}{F} \ln a_{H^+} \gamma_{Cl^-} m_{Cl^-} \quad (1)$$

where the symbols employed have their usual meaning. For the third dissociation constant

$$H_2V^{-2} \rightleftharpoons H^+ + HV^{-3}$$

$$k_3 = \frac{a_{H^+} \cdot a_{HV^{-3}}}{a_{H_2V^{-2}}} \quad (2)$$

Substitution of (2) into (1) and rearrangement gives

$$\frac{(E - E_0)F}{2.30RT} + \log m_{Cl^-} = -\log \frac{k_3 \, a_{H_2V^{-2}} \gamma_{Cl^-}}{a_{HV^{-3}}} \quad (3)$$

By expressing the two left-hand terms of equation 3 by the symbol p_wH, according to usual practice, and splitting of the activity terms into molality and activity coefficient terms, equation (3) becomes

$$p_wH + \log \frac{m_{H_2V}}{m_{HV}} + \log \frac{\gamma_{H_2V^{-2}} \cdot \gamma_{Cl^-}}{\gamma_{HV^{-3}}} = pk_3 \quad (4)$$

where the activity coefficients are expressed by the Debye–Hückel relationship

$$-\log f_1 = \frac{A Z_1^2 u^{1/2}}{1 + Ba^* u^{1/2}} + \text{higher terms}^8 \quad (5)$$

The values of A and B have been given by Manov, Bates, Hamer and Acree.[8] The other terms of equation 5 have their usual meaning. This relationship was employed to evaluate the activity coefficient expression of equation 4. Thus, it was possible to evaluate all terms on the left side of equation 4 with the exception of the parameter a^*, for which various values were assumed. The sum of these terms was plotted as a function of the square root of ionic strength and extrapolated to infinite dilution to evaluate k_3.

The equilibrium constant k_4 is defined by the expression

$$HV^{-3} \rightleftharpoons H^+ + V^{-4}$$

$$k_4 = \frac{a_{H^+} \cdot a_{V^{-4}}}{a_{HV^{-3}}} \quad (6)$$

The evaluation of this constant was carried out in a manner similar to that used for k_3. However, in this case, it was necessary to take into consideration the hydrolysis of the V^{-4} ion. At the pH values employed for the experimental solution, it is possible to assume that the concentration of hydroxide ion resulting from the ionization of water is negligible. Hence, it follows that $m_{V^{-4}} = m_{K_4V} - m_{OH^-}$ and $m_{HV^{-3}} = m_{K_3HV} + m_{OH^-}$. The value of m_{OH^-} was evaluated by means of the expression $\log m_{OH^-} = \log K_w^* + p_wH$, according to the method of Harned and Owen.[9] The relationship analogous to equation (4) used for the determination of k_4 is

$$p_wH + \log \frac{m_{K_3HV} + m_{OH^-}}{m_{K_4V} - m_{OH^-}} + \log \frac{\gamma_{HV^{-3}} \cdot \gamma_{Cl^-}}{\gamma_{V^{-4}}} = pk_4 \quad (7)$$

In the extrapolation of equation 4 to infinite dilution, values of the distance of closest approach, a^*, of equation 5 were used which gave straight lines with the smallest slopes. Equation 7 was extrapolated in a similar manner. The most satisfactory values of a^* for extrapolation of the terms of equation 4 was 2.4, while the corresponding value of a^* for the extrapolation of equation 7 was 1.3. A higher term $\beta\mu^2$, with $\beta = 9.0$ was necessary in equation 7 to obtain a linear extrapolation for determination of pk_4. The graphical extrapolations of equations 4 and 7 to give pk_3 and pk_4 are given in Figs. 1 and 2, respectively.

Discussion of Results

The values obtained for the thermodynamic quantities ΔF^0, ΔH^0, ΔS^0 associated with the reactions investigated are listed in Table II.

TABLE II

THERMODYNAMIC CHANGES FOR DISSOCIATION OF ETHYLENEDIAMINETETRAACETIC ACID

t, °C.	pk_3	ΔF_3^0, kcal./mole	pk_4	ΔF_4^0, kcal./mole
0	6.527	8.15	11.308	14.13
5	6.476	8.24	11.234	14.29
10	6.425	8.32	11.159	14.45
15	6.369	8.41	11.084	14.61
20	6.320	8.49	11.014	14.77
25	6.273	8.56	10.948	14.93
30	6.236	8.64	10.883	15.09

(8) G. Manov, R. Bates, W. Hamer and S. Acree, THIS JOURNAL, **65**, 1765 (1943).

(9) H. Harned and B. Owen, "The Physical Chemistry of Electrolytic Solutions," Second Edition, Reinhold Publ. Corp., New York, N. Y., 1950, p. 485.
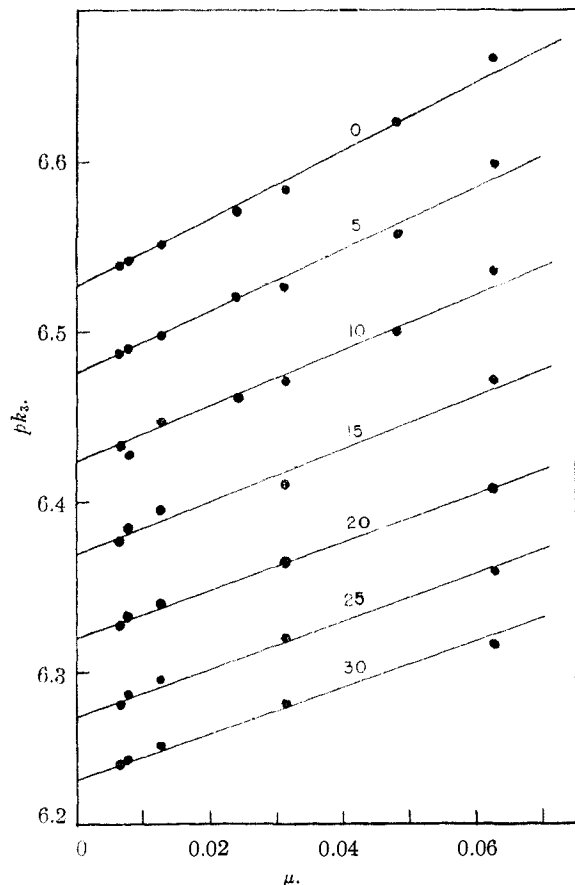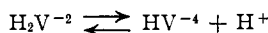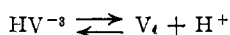
Fig. 1.—Determination of pk_3: extrapolation of e.m.f. data of equation 4 to infinite dilution; μ = ionic strength.

For the reaction

$$H_2V^{-2} \rightleftarrows HV^{-4} + H^+$$

$\Delta H_3° = +3.69$ kcal./mole; $\Delta S_3° = -16.4$ e.u./mole

For the reaction

$$HV^{-3} \rightleftarrows V_4 + H^+$$

$\Delta H_4° = +5.34$ kcal./mole; $\Delta S_4° = -32.2$ e.u./mole

Previous studies[2,3] of the dissociation constants of ethylenediaminetetraacetic acid involved measurement of "concentration" constants, k_c, which are related to the thermodynamic constants of this investigation by the equation

$$k = \frac{a_{V^{-n}} \cdot a_{H^+}}{a_{V^{-n+1}}} = \frac{c_{V^{-n}} \cdot c_{H^+}}{c_{V^{-n+1}}} \cdot \frac{\gamma_{V^{-n}} \cdot \gamma_{H^+}}{\gamma_{V^{-n+1}}} = k_c \frac{\gamma_{V^{-n}} \cdot \gamma_{H^+}}{\gamma_{V^{-n+1}}} \quad (8)$$

where c represents molal concentration, n may be 1, 2, 3 or 4 and V^{-n} represents ionized forms of ethylenediaminetetraacetic acid having 3, 2, 1 or 0 ionizable hydrogens, respectively. The values of pk_3 and pk_4 found in this investigation are considerably greater than the concentration constants reported by Schwarzenbach and Ackermann[2] and by Cabell.[3] This is to be expected since the quantity $\gamma_{V^{-n}} \cdot \gamma_{H^+}/\gamma_{V^{-n+1}}$ should always be less than unity. Combination of equations 4 and 8 with the elimination of k_3 gives the following expression for the concentration constant, k_3^c

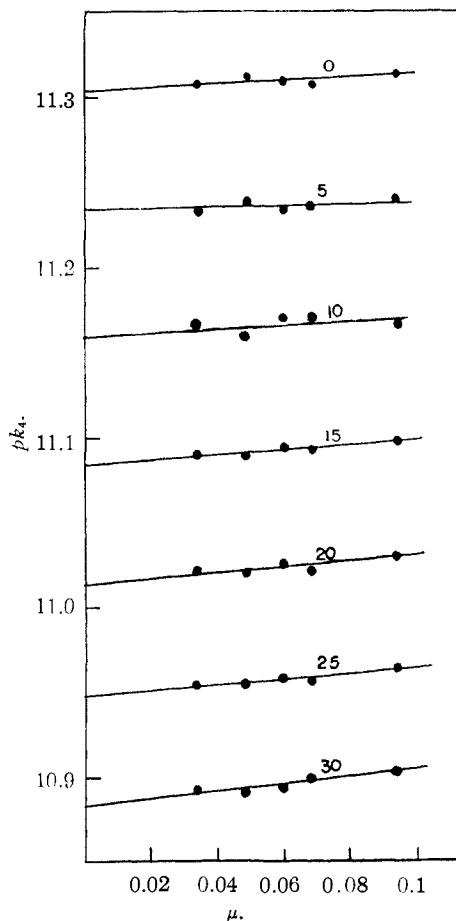$$k_3^c = p\mathrm{wH}_{(3)} + \log \frac{m_{H_2V^{-2}}}{m_{HV^{-3}}} + \log \gamma_{HCl} \quad (9)$$

Fig. 2.—Determination of pk_4: extrapolation of e.m.f data of equation 7 to infinite dilution; μ = ionic strength.

Similarly, combination of equations 7 and 8 gives a relationship for k_4^c

$$k_4^c = p\mathrm{wH}_{(4)} + \log \frac{m_{HV^{-3}}}{m_{V^{-4}}} + \log \gamma_{HCl} \quad (10)$$

or

$$k_4^c = p\mathrm{wH}_{(4)} + \log \frac{m_{K_3HV} + m_{OH^-}}{m_{K_4V} - m_{OH^-}} + \log \gamma_{HCl} \quad (11)$$

where $p\mathrm{wH}_{(3)}$ refers to the definition of $p\mathrm{wH}$ in terms of pk_3 according to equation 3 while $p\mathrm{wH}_{(4)}$ refers to $p\mathrm{wH}$ defined in a similar way in terms of pk_4. These equilibrium constants, listed in Table III, are useful for calculation of the degree of dissociation of ethylenediaminetetraacetic acid in solutions having known electrolyte concentration.

TABLE III

CONCENTRATION CONSTANTS

t, °C.	pk_3		pk_4		
	$\mu = 0.01$	$\mu = 0.05$	$\mu = 0.01$	$\mu = 0.05$	$\mu = 0.1$
0	6.41	6.37	11.08	10.81	10.67
5	6.35	6.27	11.00	10.73	10.60
10	6.30	6.20	10.93	10.66	10.53
15	6.25	6.14	10.85	10.58	10.45
20	6.21	6.09	10.78	10.51	10.38
25	6.14	6.04	10.71	10.44	10.30
30	6.10	6.00	10.64	10.37	10.24

The equilibrium constants listed in Table III show a considerable decrease as the salt concentra-

tion is decreased, in qualitative agreement with the results reported by Carini and Martell.[1] A direct comparison with the previous work is not possible, however, since the acid dissociation constants reported were not concentration constants but rather "hybrid" constants of the form $a_{H^+}c_{H^+}/c_{V^{-n+1}}$. Further, these data were obtained at constant acid concentration, the ionic strength being varied by adjusting the KCl concentration. In the present work the ratio of concentrations of the important ionic species present was kept the same as the ionic strength was varied. A change in the ratios of the components may vary the activity coefficient of a particular component even though the ionic strength remains constant. In view of these considerations, it is not surprising that there is considerable difference in both the slopes and the absolute values of the pk_3' and pk_4' vs. μ plots for the concentration constants of the present work and the hybrid constants reported previously. Although the concentration constant, pk_3, for the third dissociation at 20° and at an ionic strength of 0.1 does not appear in Table III, it is certainly lower than 6.24 and 6.16, the values reported by Schwarzenbach and Ackermann[2] and by Cabell,[3] respectively. Some disagreement is expected since the activity coefficients of the highly charged ions involved are very sensitive to a change in the ionic atmosphere. In this case the ratios of the ionic components differ from those employed by Schwarzenbach and Ackermann and Cabell. This alone would alter the concentration constant even though the ionic strengths are the same. Also, the activity coefficient of HCl, assumed to be constant in the above calculations, must vary slightly with change in ratio of the ionic components. Variation of the unknown liquid junction potential in Cabell's measurements must also have an important influence on the concentration constants reported. For the same reason, the small deviation between our value of 10.38 for pk_4 at 20° and 0.1 ionic strength, and the values reported by Schwarzenbach and Ackermann[2] and Cabell,[3] 10.26 and 10.32, respectively, is not unexpected. The values reported in Table II for the thermodynamic dissociation constants k_3 and k_4 are considerably different from the values reported by Carini and Martell on the basis of extrapolation of log k values to infinite dilution. The difference is due mainly to (1) a more valid method of extrapolation in the present paper in that the Debye–Hückel relationship is employed in guiding the extrapolation to infinite dilution, and (2) uncertainties in the extrapolation in the previous work resulting from lack of data at low ionic strength.

Within experimental error, the values of ΔH^0 and ΔS^0 of the third and fourth dissociation constants in Table I are constant over the entire range from 0 to 30°. The quantity ΔH^0 differed by less than 0.01 kcal. over this temperature range, while ΔS^0 varied by less than 0.1 e.u. per mole.

It is interesting to note the extremely low values of ΔH^0 as compared to other ammonium-type dissociations. Heats of dissociation of the last ammonium proton to dissociate from glycine, β-alanine, ethylenediamine, trimethylamine and dimethylamine are 10.6, 11.6, 13.1, 9.0 and 12.0 kcal. per mole, respectively, while the corresponding entropy changes are -9.4, -8.3, -1.8, -14.3 and -9.0 e.u., respectively.[10] The values of ΔH^0 found in the present investigations are roughly half of what may be considered to be the normal value based on the examples cited. As might be expected, the values of ΔS^0 reported for ammonium-type dissociation reactions of ethylenediaminetetraacetic acid are very large and negative. An unfavorable entropy change is to be expected in view of the effect of increasing nitrogen-substitution observable in the examples given. Furthermore, the fact that the dissociation of ammonium protons from ethylenediaminetetraacetic acid results in the formation of a more negative ion of high charge would also favor an entropy increase.

The values of the third dissociation constants listed in Table I are among the lowest ever given for an aliphatic ammonium proton. It is the same order of magnitude as the constants reported by other investigators[2,3] for ethylenediaminetetraacetic acid, and not very much different from the value of pk_3 of ethylenediaminediaceticdipropionic acid.[11] Although this abnormally low value of the third dissociation constant has not yet been explained on theoretical grounds, it is seen that it may be correlated with the abnormally low value of ΔH_3^0 of this dissociation step. The unusually low values of ΔH_3^0 and ΔH_4^0, and the corresponding large decreases of entropy are of particular interest in view of the high affinity of this amino acid for alkaline earth ions. Measurement of heats and entropies for the reactions of this and similar amino acids with various metal ions is now in progress, and preliminary results will be reported soon.

WORCESTER, MASS.

(10) H. Irving, Paper No. 4, "A Discussion in Co-ordination Chemistry," Report No. BRL/146, Butterwick Research Laboratories. "The Frythe," Welwyn, Herts., May, 1951.

(11) S. Chaberek, Jr., and A. E. Martell, THIS JOURNAL, 74, 6228 (1952).