The Infrared Spectra of Ethylenediaminetetra-acetic Acid and its Di- and Tetra-sodium Salts.

By D. Chapman.

[Reprint Order No. **6028**.]

The infrared spectra of solid ethylenediaminetetra-acetic acid and its di- and tetra-sodium salts have been obtained between 650 and 3500 cm.$^{-1}$; they do not support the mode of ionisation of the acid previously suggested. The spectrum of the disodium salt suggests the presence of both carboxylic acid and carboxylate ion groups in the molecule, whereas only carboxylate ion groups should occur. A new mode of ionisation for the acid is suggested consistent with this evidence.

ETHYLENEDIAMINETETRA-ACETIC ACID is one of many polycarboxylic amino-acids which are becoming increasingly important because of their stable complexes with metal ions. Since complex stability has been partly related to the proton affinity of these acids (Martell and Calvin, " Chemistry of the Metal Chelate Compounds," Prentice-Hall, New York, 1952, p. 159), a clear picture of the mode of ionisation of the acids could lead to a better understanding of metal complex formation.

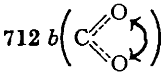
The negative logarithms of the dissociation constants of ethylenediaminetetra-acetic acid are 2·0, 2·7, 6·2, and 10·3 at 20° for successive protons (Schwarzenbach and Ackermann, *Helv. Chim. Acta*, 1947, **30**, 1798). This sequence of acid strengths was explained by supposing that a double betaine structure of the acid is formed. Thus, the first two, strongly acid, protons ionise from the carboxyl groups, and the third, of intermediate character, and the fourth, only feebly acidic, ionise from the respective nitrogen atoms. In order to explain the remarkable intermediate value of pK_3 the existence of a hydrogen bridge was invoked joining the two nitrogen atoms, the difference between pK_3 and pK_4 being attributed to the energy produced on formation of the bridge (cf., however, Carini and Martell, *J. Amer. Chem. Soc.*, 1953, **75**, 4814).

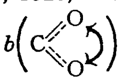
If this mode of ionisation is correct, there should be no evidence of carboxyl groups in the infrared spectrum of the disodium salt and only carboxylate-ion group frequencies should appear. In order to confirm this, the infrared spectrum of this salt has been studied. To aid interpretation, the spectra of the acid and its tetrasodium salts were also recorded.

Experimental.—The sample of ethylenediaminetetra-acetic acid used was an analytical reagent (Messrs. Hopkin and Williams). The disodium salt was a B.D.H. laboratory reagent recrystallised. The tetrasodium salt was obtained by adding the requisite amount of sodium hydroxide to a solution of the disodium salt in water, and precipitation with alcohol.

Apparatus and Technique.—A Grubb-Parsons double-beam spectrometer with rock-salt prism was used. The crystalline specimens were dispersed in Nujol between rock-salt plates. The spectra of the di- and tetra-sodium salt were obtained both before and after heating them over phosphoric oxide at 110°. Spectra were obtained from 3500 to 650 cm.$^{-1}$. The results are given in the figure and the following table (where ν is in cm.$^{-1}$, w = weak, and vw = very weak).

Acid: **2933** (Nujol), **2659** (associated OH), **1698** ($C{=}O$), **1460** (Nujol), **1414** ($CH_2{\cdot}CO_2H$), **1370** (Nujol), **1345**, **1318** (CO_2H), **1259** (vw), **1237** (vw), **1214** (w), **1135** (w), **1091** (w), **1054**, **1043**, **1006**, **983**, **967**, **870**, **778** (broad region), **714**.

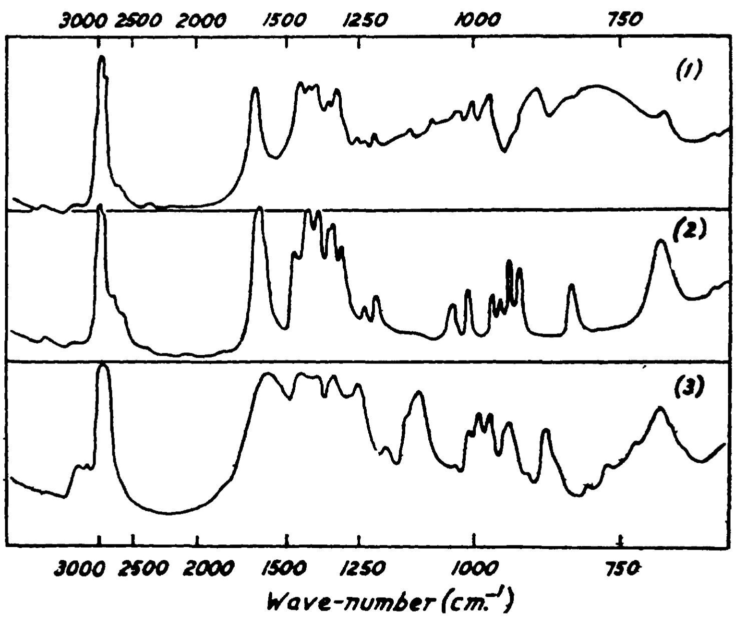
Disodium salt: 2933 (Nujol), 2713, 2596 (assoc. OH), 1668 (C=O), 1637 ν_a(O$\cdots$C$\cdots$O), 1460 (Nujol), 1398, 1370 (Nujol), 1327, 1315 (CO_2H), 1286, 1223, 1195, 1056, 1020, 959, 937, 919, 900, 811, 712 δ mode.

Tetrasodium salt: 3434, 3197 (H_2O of crystn.), 2933 (Nujol), 1597 ν_a(O$\cdots$C$\cdots$O), 1443 (Nujol), 1372 (Nujol), 1325, 1251, 1185, 1137, 1115, 1012, 988, 958, 914, 880 (w), 849, 786 (w), 762 (w), 734 (w), 709 δ mode.

Discussion

The infrared spectra of a great number of simple amino-acids have been obtained, and the positions of the absorption bands of the ionised carboxyl group fairly well established.

Infra-red spectra of: (1) *ethylenediaminetetra-acetic acid*; (2) *disodium dihydrogen ethylenediaminetetra-acetate*; (3) *tetrasodium ethylenediaminetetra-acetate.*



Thompson, Nicholson, and Short (*Discuss. Faraday Soc.*, 1950, **9**, 222) suggest the narrow range of 1600—1590 cm.$^{-1}$, and Fuson, Josien, and Powell (*J. Amer. Chem. Soc.*, 1952, **74**, 1) suggest the range 1600—1560 cm.$^{-1}$ for this band. In the case of dicarboxylic amino-acids both the ionic and the non-ionic carbonyl bands are reported to appear (Bellamy, " The Infra-red Spectra of Complex Molecules," Methuen, London, 1954, p. 207).

In view of these data it is noteworthy that ethylenediaminetetra-acetic acid does not have an ionised carboxyl group as would be expected if the molecule had a betaine structure. The frequency of the carboxyl band in the acid is at 1698 cm.$^{-1}$, showing the carboxyl groups to be quite normal, and presumably associated by hydrogen bonding. That the acid does not possess a typical betaine structure in the solid state suggests that the tendency of the molecule to form a zwitter-ion is less than in simple amino-acids such as glycine or alanine, although an alternative explanation might be that there is preferential hydrogen bonding for this molecule in the crystal.

The spectrum of disodium dihydrogen ethylenediaminetetra-acetate shows a number of significant features (see figure). On Schwarzenbach and Ackermann's mode of ionisation, the salt should have four carboxylate groups and no un-ionised carboxyl groups. There should therefore be one strong band between 1560 and 1600 cm.$^{-1}$ due to the asymmetric stretching frequency $\nu_a(\mathrm{O{\cdots}C{\cdots}O})$ of the ionised carboxyl group. The spectrum of the hydrated disodium salt shows two bands at 1686 and 1637 cm.$^{-1}$ and two strong OH stretching bands in the 3300-cm.$^{-1}$ region. After heating of the compound over phosphoric oxide *in vacuo* the 3300 and the 1686-cm.$^{-1}$ band vanish, showing these bands to be due to water of crystallisation. The remainder of the spectrum is unaltered. A band at 1668 cm.$^{-1}$ as well as the 1637-cm.$^{-1}$ band can now be clearly observed, however. The frequency of the 1668-cm.$^{-1}$ band is rather high to be assigned to an ionised carboxyl asymmetric stretching frequency, and even the 1637-cm.$^{-1}$ band is a little higher in frequency than the range 1600—1560 cm.$^{-1}$ (Fuson, Josien, and Powell, *loc. cit.*) given for the normal ionised carboxyl group in amino-acids. The high-frequency 1668-cm.$^{-1}$ band and the small shift in frequency of this band from that observed in the acid (1698 cm.$^{-1}$) are therefore taken to indicate the presence of un-ionised carboxyl groups in the disodium salt.

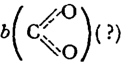
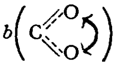
The spectrum of the tetrasodium salt shows a strong broad band with maximum absorption at 1590 cm.$^{-1}$. This band can clearly be assigned to the asymmetric stretching mode of the ionised carboxyl group $\nu_a(\mathrm{O{\cdots}C{\cdots}O})$. In this molecule all four carboxyl groups must be ionised. The difference in the carbonyl absorption frequency for the di- and the tetra-sodium salt confirms the existence of un-ionised carboxyl groups in the disodium salt.

Further confirmation is obtained in the high-frequency region of the spectrum of the disodium salt, where a breadth of absorption typical of associated carboxyl groups (Davies, *J. Chem. Phys.*, 1940, **8**, 577) is observed. Such absorption is also observed in the spectrum of the acid but not in the tetrasodium salt. Absorption at 3434 and 3197 cm.$^{-1}$ is clearly due to residual water of crystallisation in the tetrasodium salt since after it has been heated, the intensity of these bands decreases.

The regions 1400 and 1250 cm.$^{-1}$ are reported to be useful for further characteristic carboxylic acid vibration (Bellamy, *loc. cit.*). Vibrations in this region arise from a C–O vibration coupled with an OH in-plane deformation vibration. Absorption in the 1400-cm.$^{-1}$ region also occurs, however, when a CH_2 group is adjacent to a CO group (Francis, *J. Chem. Phys.*, 1951, **19**, 942). The band observed near 1414 cm.$^{-1}$ in ethylenediaminetetra-acetic acid will therefore be due both to the coupled C–O vibration and to the CH_2-modified deformation modes. This region is of limited use in the present problem, however, since the symmetrical stretching mode of the ionised carboxyl group also gives rise to absorption in this region, and will occur in both the di- and the tetra-sodium salt.

A band near 1250 cm.$^{-1}$ is reported in a considerable number of acids (Flett, *J.*, 1951, 962). The frequency range for the band is 1210—1320 cm.$^{-1}$, although Hadzi and Sheppard (*Proc. Roy. Soc.*, 1953, *A*, **216**, 247) quote the narrow range 1300 ± 15 cm.$^{-1}$ for the acids they examined. In the spectrum of ethylenediaminetetra-acetic acid the strong band at 1318 cm.$^{-1}$ is assigned to this carboxyl band, since it is the only strong band in the 1210—1320 cm.$^{-1}$ range. A band occurs at 1315 cm.$^{-1}$ in the spectrum of the disodium salt.

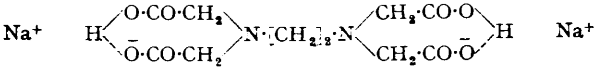
Since the disodium salt contains both carboxyl and carboxylate ion structures, and the acid itself is un-ionised, it might be expected that the spectrum of the disodium salt would be more or less a superposition of the spectra of the acid and the tetrasodium salt. The limitation to this is set by the intramolecular interaction between the carboxyl and carboxylate groups. To a certain extent this simple picture holds, although the difference (23 cm.$^{-1}$) between the $\nu(\mathrm{C{=}O})$ and $\nu_a(\mathrm{O{\cdots}C{\cdots}O})$ frequencies for the disodium salt is rather small:

Acid	1698	—	1318	—
4Na	—	1597	—	709
2Na	1668	1637	1315	712
Assignment	$\nu(\mathrm{C{=}O})$	$\nu_a(\mathrm{O{\cdots}C{\cdots}O})$	2*b*  (?)	*b* 

In a similar study of potassium hydrogen bisphenylacetate (Davies and Thomas, *J.*, 1951, 2858) a much greater $\nu\mathrm{C{=}O} - \nu_a(\mathrm{O{\cdots}C{\cdots}O})$ difference was observed and "superposition " was in general better. However, owing to displacements, etc., which can occur in the solid state, the simple picture seems entirely adequate.

Since the disodium salt does not possess a double betaine structure, a new mode of ionisation consistent with this must be found. Flett (*loc. cit.*) has shown that, of nine acids with carbonyl frequencies below **1680** cm.$^{-1}$, seven formed internal hydrogen bonds. Since the high-frequency carbonyl band in the disodium salt is at **1668** cm.$^{-1}$, it seems reasonable to suppose that the two remaining protons in the disodium salt are each linked between a carboxyl and a carboxylate ion. An analogous situation exists in maleic acid where, in the ion formed by half-dissociation, the carboxyl and carboxylate group attract each other, being linked by a hydrogen bond. This stabilises the ion (cf. Speakman, *J.*, **1949**, 3357).

The mode of ionisation proposed is therefore the following. The first and the second proton are removed from opposite ends of the molecule, which then acts to a first approximation as two dibasic acids. The disodium salt will then have the structure:



The third proton will be removed from between the carboxyl–carboxylate link, and pK_3 will therefore be higher than pK_1 or pK_2. At this stage the fourth proton will tend to migrate to the nearby nitrogen atom, since now the zwitter-ion structure will be more probable and the possibility of having two positive charges on neighbouring nitrogen atoms does not occur. Thus pK_4 will be high, corresponding to the energy required to remove a proton from a nitrogen atom. In this manner the almost equal acid strength for pK_1 and pK_2, the intermediate value for pK_3, and the high value for pK_4 are satisfactorily explained.

It is presumably the nearness of the two nitrogen atoms which prevents the double-betaine structure being formed in the disodium salt, owing to the resultant repulsion which would arise if a positive charge were to develop on each nitrogen atom; and so it is to be expected that, in the higher homologues of ethylenediaminetetra-acetic acid, as the number of methylene groups between the nitrogen atoms increases, so will the tendency for formation of the double-betaine structure, and for the nitrogen atoms to hold the third and the fourth proton. The value of pK_3 will therefore increase in these higher homologues up to that of pK_4, the molecule tending more to act like (say) two methyliminodiacetic acid molecules where pK_1 and pK_2 are given as 2·1 and 9·65 respectively (Martell and Calvin, *loc. cit.*). This is consistent with the experimental values for the ionisation constants of these homologues (Schwarzenbach and Ackermann, *Helv. Chim. Acta*, **1948**, **31**, 1029). The experimental values show that the pK_3 increases from 6·6 in ethylenediaminetetra-acetic acid to 9·5 in pentamethylenediaminetetra-acetic acid.

RESEARCH DEPARTMENT, UNILEVER LTD.,
PORT SUNLIGHT, CHESHIRE.

[*Received, January 11th*, 1955.]
