65. *The Extent of Dissociation of Salts in Water. Part XII. Calcium Salts of Some Amino-acids and Dipeptides.*

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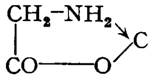
The calcium ion has a marked tendency to associate with the anions of α-amino-acids in the following way: $Ca^{\cdot\cdot} + A' = CaA^{\cdot}$. The stabilities of a number of such association products of calcium with amino-acids and dipeptides are reported and discussed.

In a previous paper (*J.*, 1938, 277) it was shown that the aminoacetate anion, like the anions of α-hydroxy-acids, has a strong tendency to associate with the calcium ion in aqueous solution, and it was suggested that a chelate structure  $\begin{matrix} CH_2\text{–}NH_2 \\ | \\ CO\text{——}O \end{matrix} \rangle Ca^{\cdot}$ was possibly responsible for this. We have now extended this work to a number of other amino-acids and dipeptides at 25°, using the same method as before: the enhanced solubility of calcium iodate in a solution of the sodium salt of the amino-acid gives, after correction for interionic effects, a direct measure of the association of calcium with the added anion.

EXPERIMENTAL.

Materials.—Calcium iodate hexahydrate was prepared, and the solubility measurements were made, in the manner described previously (*J.*, 1938, 273, 277). Where only small amounts of saturating salt were available, as with the dipeptides and di-iodotyrosine, a smaller saturator was used, and the titrations were carried out on 10-ml. samples of the saturated solution.

The purity of the acids and dipeptides was checked by carrying out differential potentiometric titrations of their solutions against standard sodium hydroxide, using an "alki" electrode for pH's greater than 9, and applying the corrections of Jordan and Taylor (*J.*, 1946, 994). Stock solutions of the sodium salts were then made up in accordance with the observed end-points.

Sodium aminoacetate.

m.	*s.*	*K.*
0	7·84	—
28·35	9·55	0·037
56·70	10·81	0·037
74·70	11·40	0·039
149·4	13·77	0·036
		Mean 0·037

Sodium α-aminopropionate.

m.	*s.*	*K.*
19·62	8·96	0·057
21·08	8·99	0·060
31·63	9·45	0·058
42·17	9·85	0·059
52·72	10·24	0·058
63·27	10·61	0·057
73·80	10·92	0·058
84·35	11·26	0·056
98·64	11·58	0·060
109·6	11·70	0·060
		Mean 0·058

Sodium salt of serine.

m.	*s.*	*K.*
11·22	8·62	0·034
21·10	9·20	0·036
56·10	10·68	0·040
		Mean 0·037

Sodium salt of glycylglycine.

m.	*s.*	*K.*
11·55	8·51	0·060
13·06	8·56	0·053
23·10	9·04	0·053
34·85	9·55	0·060
48·52	10·05	0·061
		Mean 0·057

Sodium salt of alanylglycine.

m.	*s.*	*K.*
61·22	9·83	0·22

Sodium salt of leucylglycine.

m.	*s.*	*K.*
52·55	9·61	0·20

Sodium salt of tyrosine.

m.	*s.*	*K.*
19·09	9·02	0·028
32·20	9·69	0·038
35·89	9·98	0·034
		Mean 0·033

Sodium salt of di-iodotyrosine.

m.	*s.*	*K.*
18·64	9·17	0·028
41·89	10·44	0·029
		Mean 0·029

Sodium hippurate.

m.	*s.*	*K.*
24·15	8·76	0·42
25·14	8·81	0·35
48·36	9·45	0·35
50·22	9·48	0·37
		Mean 0·37

Monosodium glutamate.

m.	*s.*	*K.*
22·22	8·87	0·071
23·00	9·06	0·060
44·50	9·86	0·065
46·47	9·92	0·067
90·26	11·05	0·068
92·85	11·14	0·068
		Mean 0·067

Disodium glutamate.

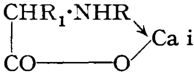
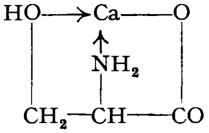
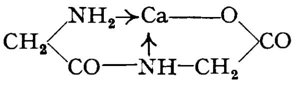
m.	*s.*	*K.*
5·62	8·68	0·0092
11·42	9·34	0·0096
21·43	10·42	0·0080
22·49	10·44	0·0083
		Mean 0·0088

Results.—These are given in the table. Col. 1 shows the concentration of the added salt, and col. 2 the measured solubility of calcium iodate hexahydrate, both in millimols. per litre. Col. 3 gives the calculated dissociation constant, $K = f_{Ca}f_A[Ca][A]/f_{CaA}[CaA]$, [A] being the concentration of the added anion. The calculations were made as in the earlier papers. The saturated solution contains $Ca^{\cdot\cdot}$, IO_3', $Na^{\cdot}$, A', and their possible association products, $CaIO_3^{\cdot}$, $NaIO_3$ and $CaA^{\cdot}$; NaA was assumed to be completely dissociated. The composition of the solutions was obtained by successive approximations from the known dissociation constants of $CaIO_3$, $K = 0{\cdot}13$, and of $NaIO_3$, $K = 3{\cdot}0$ and from the solubility product $\{Ca^{\cdot\cdot}\}\{IO_3'\}^2 = 7{\cdot}119 \times 10^{-7}$, using Davies's activity equation (*J.*, 1938, 2093). In the case of the disodium glutamate solutions, which are extensively hydrolysed, allowance had also to be made for the species OH', $CaOH^{\cdot}$, HG' and $CaHG^{\cdot}$ (G representing the doubly charged glutamate ion).

Discussion.

Greenwald (*J. Physical Chem.*, 1939, **43**, 379) has studied the association between magnesium and aminoacetate (glycine) ions, and has concluded that the formulation : $Mg^{\cdot\cdot} + 2G' \rightleftharpoons MgG_2$ fits the data better than does $Mg^{\cdot\cdot} + G' \rightleftharpoons MgG^{\cdot}$; this is contrary to the assumption we have used here and in the earlier paper quoted above. The data available to Greenwald were not very numerous or concordant, and our long series of solubility measurements with alanine was carried out to test the two possibilities more thoroughly. It will be seen that the *K* values derived for the $CaAl^{\cdot}$ ion leave little to be desired as regards constancy, and we conclude that up to a concentration of 0·1M. the tendency for association to go beyond the first stage is negligibly small. This agrees with what has been found previously for the association between the calcium ion and the anions of α-hydroxy-acids (*J.*, 1939, 279).

Of the eleven series of measurements reported in the Table, those involving the glutamic acid salts must be considered separately. The value $K = 0{\cdot}0088$ for calcium glutamate comes between the dissociation constants found by Topp and Davies (*J.*, 1940, 87) for calcium succinate (0·010) and calcium adipate (0·0064); there is no evidence that the amino-group exerts any influence in this case. In the monosodium glutamate solutions the anion is believed to be mainly $CO_2'{\cdot}CH_2{\cdot}CH_2{\cdot}CH(NH_3^{\cdot}){\cdot}CO_2'$, and this, in its association with the calcium ion, is not comparable with the other anions studied. In seeking for relationships between dissociation constant and structure, the data for tyrosine and di-iodotyrosine should also be excluded from the comparison. Both these compounds contain phenolic groups, and although the apparent constants reported in the table seem satisfactory, it is probable that neither is really a true constant for a single dissociation process, since the solutions studied will contain both $CO_2'{-}CH(NH_2){-}R{-}OH$ and $CO_2'{-}CH(NH_3^{\cdot}){-}R{-}O'$ (where R represents the remainder of the molecule).

The remaining seven constants all refer to univalent cations which will dissociate into $Ca^{\cdot\cdot}$ and ions of formula $NHR{\cdot}CHR_1{\cdot}CO_2'$. They cover a ten-fold range, from $K = 0{\cdot}037$ for the glycine salt, which is certainly abnormally weak, to $K = 0{\cdot}37$ for the hippurate, where the benzoylated amino-group would not be expected to exert any influence, and which is almost completely dissociated in dilute solution. So far as the figures go, they are consistent with the following two hypotheses: (*a*) that the tendency to form a chelate structure  is rapidly reduced by weighting the glycine molecule with extraneous groups R or R_1; and (*b*) that the possibility of a tridentate configuration will enhance the tendency to associate with the calcium ion; this would account for the low constants found for serine and glycylglycine, where the structures  and  would be possible.

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