CCCCXXXI.—*Neutral Salt Addition Compounds of β-Alanine.*

By HAROLD KING and GEORGE VICTOR RUTTERFORD.

THE capacity of the α-amino-acids, $NH_2{\cdot}CHR{\cdot}CO_2H$, to form additive compounds with neutral salts is now well established. Several types of additive compound arise and the only consistent interpretation of the various types is their formulation by co-ordination of the alkali or alkaline-earth metal to the oxygen or oxygen atoms of the carboxyl group of the amino-acid. It is not known whether the α-amino-group, characteristic of the majority of naturally occurring amino-acids, exerts any specific influence on the additive capacity, and to decide this, the amino-acid, β-alanine, $NH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$, has been used as the organic component. β-Alanine has, in addition, a high aqueous solubility, a factor favourable for the isolation from aqueous solutions of additive compounds of lesser solubility. This acid has given a series of additive compounds of types similar to those obtained from glycine and other α-amino-acids. The following table shows the compounds which have been realised experimentally.

	Li.	Na.	Ca.	Sr.	Ba.
Cl	$A,LiCl,1\frac{1}{2}H_2O$	—	$A_2,CaCl_2,2H_2O$	$A,SrCl_2,4H_2O$	—
Br	$A,LiBr,1\frac{1}{2}H_2O$	—	$A,CaBr_2,4H_2O$ $A_2,CaBr_2,3H_2O$	$A,SrBr_2,4H_2O$	$A,BaBr_2,2H_2O$
I	$A,LiI,1\frac{1}{2}H_2O$ $A_2,LiI,1\frac{1}{2}H_2O$	A,NaI	$A,CaI_2,4H_2O$	$A,SrI_2,4H_2O$	—

A = β-alanine.

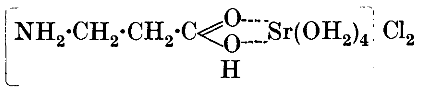
They are all of two types and might be represented as amphi-salts, those from calcium bromide, for example, receiving the formulations

$$Br\ \{NH_3{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2{\cdot}CaBr \text{ and}$$

$$Br\ \{NH_3{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2CaCO_2{\cdot}CH_2{\cdot}CH_2{\cdot}NH_3\}\ Br$$

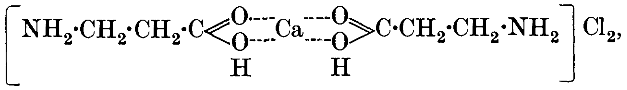
Such a view could not, however, be extended to include well-established types such as $B_3,CaBr_2$, where B is glycine or sarcosine (Pfeiffer, Klossmann, and Angern, *Z. physiol. Chem.*, 1924, **133**, 22; Anslow and King, *Biochem. J.*, 1928, **22**, 1253), B_4,SrI_2 and B_4,BaI_2, where B is glycine (P., K., and A., *loc. cit.*), and such a well-defined compound as $B_5(CaI_2)_2,11H_2O$, where B is betaine, which crystallises in the cubic system (A. and K., *loc. cit.*). The fact that the anhydrides of the α-amino-acids, the diketo-piperazines, form additive compounds with neutral salts also speaks against the amphi-salt formulation (Pfeiffer, " Organische Molekülverbindungen," 1922, 111).

The only consistent method of representing all these various types is to regard the oxygen atoms (or atom) of the carboxyl groups as forming the point of attachment of the inorganic addenda. The commonest type shown in the table above under strontium is also the commonest type observed with *N*-dimethylaminoacetic acid and alkaline-earth halides (A. and K., *loc. cit.*). When it is borne in mind that strontium has a co-ordination number of 6 in $[Sr(OH_2)_6]Cl_2$ the conclusion seems irresistible that the same holds true in the commonest type of additive compound, which would be written



$$\left[\mathrm{NH_2{\cdot}CH_2{\cdot}CH_2{\cdot}C}{<}\begin{matrix}\mathrm{O}\cdots\\ \underset{\mathrm{H}}{\mathrm{O}}\cdots\end{matrix}\mathrm{Sr(OH_2)_4}\right]\mathrm{Cl_2}$$

The second type of compound observed with β-alanine, of which three examples are recorded in the table, would be formulated



$$\left[\mathrm{NH_2{\cdot}CH_2{\cdot}CH_2{\cdot}C}{<}\begin{matrix}\mathrm{O}\cdots\\ \underset{\mathrm{H}}{\mathrm{O}}\cdots\end{matrix}\mathrm{Ca}\begin{matrix}\cdots\mathrm{O}\\ \cdots\underset{\mathrm{H}}{\mathrm{O}}\end{matrix}{>}\mathrm{C{\cdot}CH_2{\cdot}CH_2{\cdot}NH_2}\right]\mathrm{Cl_2},$$

an element of uncertainty arising in the allocation of the water molecules in individual cases.

EXPERIMENTAL.

Preparation of β-Alanine.—β-Bromopropionic acid was prepared in 68% yield by the elegant method of Jacobs and Heidelberger (*J. Amer. Chem. Soc.*, 1917, **39**, 191) from ethylene cyanohydrin and hydrobromic acid. The bromo-acid (25 g.) was added slowly to ammonia solution (250 c.c., *d* 0·88) in a pressure bottle fitted with a rubber bung which could be wired in. The contents were heated at 70° for 12 hours, then concentrated to a small volume, diluted with water (600 c.c.), and boiled with freshly precipitated lead hydroxide until all the ammonia and most of the bromide had been removed. The filtrate was assayed for its bromide content and then treated with the calculated amount of freshly precipitated silver oxide. The bromide-free filtrate was treated with hydrogen sulphide to remove traces of lead and silver, filtered, and concentrated to a thick syrup. This was dissolved by warming in absolute alcohol (75 c.c.) and on keeping at 0° gave a 62% yield of β-alanine.

Preparation of Additive Compounds.

In the first instance equimolecular proportions of the components were dissolved together in water and the solution was concentrated on the water-bath until, on cooling, a crop of crystals was obtained of undoubted homogeneous appearance. To avoid the known decomposing action of water on certain of these additive compounds the products were never washed; in most cases they were collected on hardened paper, quickly rubbed on porous plate, and analysed. In certain cases where very viscous or syrupy solutions were obtained the whole contents were transferred to porous plate. Water of crystallisation was never determined directly, but was calculated on the analyses. Owing to the difficulty of removing the last traces of viscous solutions, the analyses sometimes show more than the usual divergence from the theoretical values.

β-*Aminopropionic Acid Lithium Chloride Sesquihydrate.*—This compound crystallised in flattened needles from a solution containing the components in equimolecular proportion (Found: Cl, 22·9; N, 8·6. $C_3H_7O_2N,LiCl,1\frac{1}{2}H_2O$ requires Cl, 22·4; N, 8·8%).

β-*Aminopropionic acid lithium bromide sesquihydrate* was obtained similarly in flattened needles (Found: Br, 39·0; N, 6·9. $C_3H_7O_2N,LiBr,1\frac{1}{2}H_2O$ requires Br, 39·4; N, 6·9%). A second crop from the mother-liquors had the same composition.

β-*Aminopropionic Acid Lithium Iodide Sesquihydrate.*—From a solution of the components in equimolecular proportion a crop of crystals of homogeneous appearance was obtained with an analytical ratio I : N = 1 : 1·46. The mother-liquors, now relatively richer in iodide, deposited on concentration fine silky needles (Found: I, 50·4; N, 5·3. $C_3H_7O_2N,LiI,1\frac{1}{2}H_2O$ requires I, 50·8; N, 5·6%).

*Di-*β-*aminopropionic Acid Lithium Iodide Sesquihydrate.*—On addition of more β-alanine to the mother-liquors of the previous preparation a crop of fine silky needles was obtained (Found: I, 36·7; N, 8·1. $2C_3H_7O_2N,LiI,1\frac{1}{2}H_2O$ requires I, 37·4; N, 8·3%).

β-*Aminopropionic acid sodium iodide* was obtained in clusters of fine needles (Found: I, 52·4; N, 5·9. $C_3H_7O_2N,NaI$ requires I, 53·1; N, 5·9%).

*Di-*β-*aminopropionic Acid Calcium Chloride Dihydrate.*—This substance can only be obtained from a solution of the components in equimolecular proportion with great difficulty owing to the viscous nature of the concentrated solutions. It crystallises slowly in transparent needles (Found: Cl, 21·6; N, 7·2. $2C_3H_7O_2N,CaCl_2,2H_2O$ requires Cl, 21·8; N, 8·6%).

β-*Aminopropionic Acid Calcium Bromide Tetrahydrate.*—On concentration of an aqueous solution of the components in equimolecular proportion tufts of needles of homogeneous appearance were obtained which proved on analysis to be mixed crystals of two addition compounds. The mother-liquors on concentration gave needles of the more usual type (Found : Br, 43·8 ; N, 3·8. $C_3H_7O_2N,CaBr_2,4H_2O$ requires Br, 44·3 ; N, 3·9%). When the original components were mixed in the molecular ratio of two of β-alanine to one of calcium bromide, *di-β-aminopropionic acid calcium bromide trihydrate* separated in needles (Found : Br, 36·9 ; N, 6·1. $2C_3H_7O_2N,CaBr_2,3H_2O$ requires Br, 37·0; N, 6·5%). On recrystallisation from water it gave the same compound (Found : Br, 36·8 ; N, 6·3%).

β-Aminopropionic acid calcium iodide tetrahydrate crystallises readily in rods (Found : I, 55·1 ; N, 3·3. $C_3H_7O_2N,CaI_2,4H_2O$ requires I, 55·8 ; N, 3·1%).

β-Aminopropionic acid strontium chloride tetrahydrate crystallises in fine needles (Found : Cl, 22·2 ; N, 4·8. $C_3H_7O_2N,SrCl_2,4H_2O$ requires Cl, 22·2 ; N, 4·4%).

β-Aminopropionic acid strontium bromide tetrahydrate crystallises readily in plates (Found : Br, 38·3 ; N, 3·5. $C_3H_7O_2N,SrBr_2,4H_2O$ requires Br, 39·1 ; N, 3·4%).

β-Aminopropionic acid strontium iodide tetrahydrate, obtained under similar conditions, crystallises in stout needles (Found : I, 49·7 ; N, 2·7. $C_3H_7O_2N,SrI_2,4H_2O$ requires I, 50·5 ; N, 2·8%).

β-Aminopropionic Acid Barium Bromide Dihydrate.—Equimolecular proportions of the components were concentrated in aqueous solution and two crops of barium bromide were removed as the least soluble component. When the syrupy mother-liquors were kept, clusters of needles separated (Found : Br, 37·3 ; N, 3·7. $C_3H_7O_2N,BaBr_2,2H_2O$ requires Br, 37·8 ; N, 3·4%).

No addition compounds were obtained with the following salts : barium chloride, sodium chloride, sodium bromide, potassium chloride, potassium bromide, and potassium iodide. From the last five mentioned, the characteristic plates of β-alanine were obtained, often crystallising side by side with cubic crystals of the inorganic salt.

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