# Constitution of Glycocoll and its Derivatives.

## (Appendix: General theory and Nomenclature of Amido-acids.)

By

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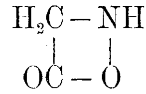
Glycocoll, the prototype of that large and important class of compounds generally called amido-acids, is usually represented as amido-acetic acid, $H_2N.CH_2.COOH$, in spite of an abundance of facts which show that it must be considered as an internal ammonium salt of the constitution,

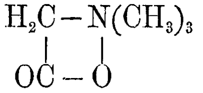


$$\begin{array}{l} H_2C - NH_3 \\ \;\;| \qquad\; | \\ OC - O \end{array} ;$$

and the object of this paper is to strengthen the evidence in support of the latter view and, at the same time, to deprecate the almost universal employment of the open formula in describing the reactions of this compound.

The view that glycocoll is constituted as an internal ammonium salt was first suggested by Erlenmeyer and Sigel (*Lieb. Ann.*, **176**, 349 [1875]), in order to account for the perfect neutrality of this compound towards litmus ; it may also be advanced to explain the high melting point of glycocoll and its insolubility in alcohol and ether. A similar view of the constitution of taurin had already been put forward by Erlenmeyer.

The great analogy in properties between glycocoll and anhydrous betaïn (trimethyl-glycocoll) on the one hand, and the close relationship between the latter and choline on the other, a relationship which establishes the constitution,



$$\begin{array}{l} H_2C-N(CH_3)_3 \\ \;\;\,|\qquad| \\ OC-O \end{array} ,$$

for anhydrous betaïn, give a further support to the correctness of the closed formula.

Again, the observation made by Marckwald, Neumark, and Stelzner (*Ber.*, **24**, 3279 [1891]), that glycocoll does not readily react with mustard oils to form derivatives of thio-urea, contrary to the behaviour of all primary amines, speaks against the commonly adopted open formula for glycocoll.

All other properties of this compound are in perfect accordance with the constitution of the internal ammonium salt, and there is not a single reaction which needs to be expressed by the open formula ; on the contrary, there are several, as will be shown later on, which can not be explained by it.

In spite of the evident claim of the internal ammonium theory to be exclusively adopted, it is astonishing to find that there are most eminent authors who do not recognise it frankly and make common use of it, and others who even disregard it altogether.(1) While insist-

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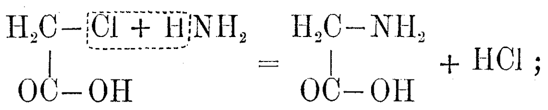
(1) Beilstein (*Handbuch :* 2 Aufl., I, 1182-1183 [1893]) does not even mention the closed formula. Roscoe and Schorlemmer (*Treatise :* 2 Ed., III, Pt. 2 [1890]) say in one place (p. 20) that glycocoll must be considered as an ammonium salt, but in describing its reactions they expressly use the open formula (pp. 20 and 100) ; alkyl glycocolls are, on the other hand, represented by the closed formula. V. Meyer and Jacobson (*Lehrbuch :* I, 828 [1893]) seem to be greatly in favour of the internal ammonium theory, but do not use it consistently ; in fact, like

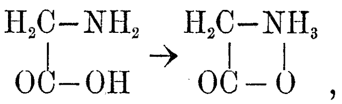
ing upon the analogy between glycocoll and its trimethyl derivative, they represent the one by the open, and the other by the closed, formula. This inconsistency on their part is, I think, to be attributed partly, at any rate, to the erroneous manner in which the modes of formation of glycocoll have been hitherto represented.

Thus, the production of glycocoll by the action of ammonia upon chloracetic acid is always regarded as if taking place by the direct replacement of chlorine by the amidogen group—



$$\begin{array}{l} H_2C-\boxed{Cl+H}NH_2 \\ \quad | \\ OC-OH \end{array} = \begin{array}{l} H_2C-NH_2 \\ \quad | \\ OC-OH \end{array} + HCl\,;$$

it, therefore, requires a further strain of mind to represent glycocoll as an internal ammonium salt,



$$\begin{array}{l} H_2C-NH_2 \\ \quad | \\ OC-OH \end{array} \rightarrow \begin{array}{l} H_2C-NH_3 \\ \quad | \qquad | \\ OC-O \end{array} ,$$

and it is this awkwardness, no doubt, which has had much to do in making authors hesitate in adopting the closed formula.

The above universally employed representation of the mode of formation of glycocoll is, however, erroneous, inasmuch as it does not take into account the evident fact that ammonium chloracetate must first be produced. In order to obtain glycocoll by this method, an excess of ammonia must be employed, which not only goes to neutrallise chloracetic acid but also to form an ammonium chloride,

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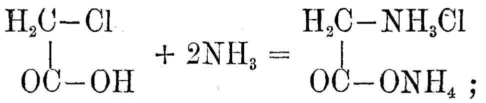
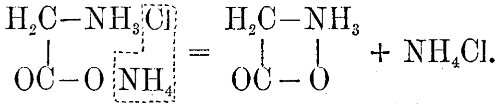
Roscoe and Schorlemmer, they only employ the open formula in describing the modes of formation of glycocoll. Mono- and dimethyl glycocolls are represented by the open, and trimethyl glycocoll by the closed, formula. Strecker and Wislicenus (*Text Book:* English Translation, 416 [1885]) are more decidedly inclined to this theory; but still they are not quite consistent, in one or two places using the open formula and in several others the closed double formula. The only work I have seen where the internal ammonium theory is exclusively adopted, though on an insufficient ground, is the article on Glycocoll, contributed by Hell to the *Neues Handwörterbuch* der Cheime, III, 446 [1878].



$$\begin{array}{l} H_2C-Cl \\ | \\ OC-OH \end{array} + 2NH_3 = \begin{array}{l} H_2C-NH_3Cl \\ | \\ OC-ONH_4 \end{array} ;$$

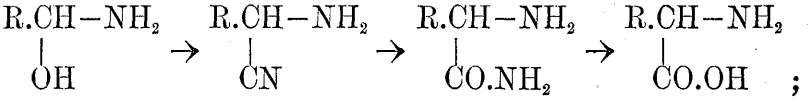
the latter part of this change being analogous to that which occurs between ammonia and alkyl halides. This ammonium compound must, then, be regarded as decomposing into glycocoll and ammonium chloride by the action of heat :



$$\begin{array}{l} H_2C-NH_3\boxed{Cl} \\ | \\ OC-O\boxed{NH_4} \end{array} = \begin{array}{l} H_2C-NH_3 \\ |\qquad | \\ OC-O \end{array} + NH_4Cl.$$

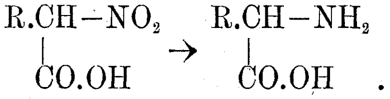
The conception of the mode of formation of glycocoll here advanced is not a matter of speculation, but is only an expression of actual facts, and it *necessarily* leads to the internal ammonium theory of the constitution of this compound ; for, if we regarded glycocoll as $H_2N.CH_2.COOH$, we should have to assume that the highly acid group, COOH, remains unneutrallised by ammonia even in the presence of an excess of the latter !

Again, it may be observed that in describing various other modes of formation of glycocoll and of the "amido-acids" generally, the fact is almost always either concealed or forgotten that it is the hydrochlorides or other analogous compounds which are first obtained. Thus, it is stated that "amido-acids" are formed by heating a mixture of aldehyde-ammonias and hydrogen cyanide with hydrochloric acid, the changes which occur being indicated by some such scheme as follows :



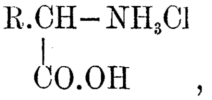
$$\begin{array}{l} R.CH-NH_2 \\ | \\ OH \end{array} \rightarrow \begin{array}{l} R.CH-NH_2 \\ | \\ CN \end{array} \rightarrow \begin{array}{l} R.CH-NH_2 \\ | \\ CO.NH_2 \end{array} \rightarrow \begin{array}{l} R.CH-NH_2 \\ | \\ CO.OH \end{array} ;$$

or, that they are produced by reducing nitro-acids with tin and hydrochloric acid :



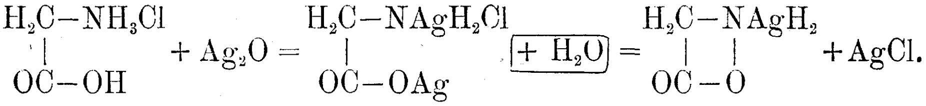
$$\begin{array}{l}\mathrm{R.CH-NO_2}\\ |\\ \mathrm{CO.OH}\end{array} \rightarrow \begin{array}{l}\mathrm{R.CH-NH_2}\\ |\\ \mathrm{CO.OH}\end{array} .$$

" Amido-acids " are, however, *not* produced in these reactions ; it is their hydrochlorides,

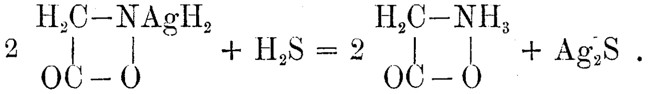


$$\begin{array}{l}\mathrm{R.CH-NH_3Cl}\\ |\\ \mathrm{CO.OH}\end{array} ,$$

which are actually obtained. In order to prepare the " amido-acid " itself, glycocoll for example, the hydrochloride is digested with silver oxide (or litharge), and the silver-glycocoll decomposed by sulphuretted hydrogen. The changes which occur in these operations are in accordance with the following scheme :

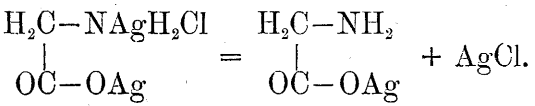


$$\begin{array}{l}\mathrm{H_2C-NH_3Cl}\\ |\\ \mathrm{OC-OH}\end{array} + \mathrm{Ag_2O} = \begin{array}{l}\mathrm{H_2C-NAgH_2Cl}\\ |\\ \mathrm{OC-OAg}\end{array} \boxed{+\mathrm{H_2O}} = \begin{array}{ll}\mathrm{H_2C} & \mathrm{-NAgH_2}\\ | & |\\ \mathrm{OC} & \mathrm{-O}\end{array} + \mathrm{AgCl}.$$



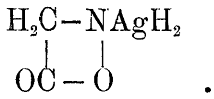
$$2\begin{array}{ll}\mathrm{H_2C} & \mathrm{-NAgH_2}\\ | & |\\ \mathrm{OC} & \mathrm{-O}\end{array} + \mathrm{H_2S} = 2\begin{array}{ll}\mathrm{H_2C} & \mathrm{-NH_3}\\ | & |\\ \mathrm{OC} & \mathrm{-O}\end{array} + \mathrm{Ag_2S} .$$

It may be thought, however, that the separation of silver chloride occurs, not in the manner indicated above, but as follows :



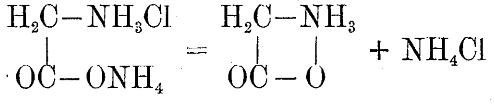
$$\begin{array}{l}\mathrm{H_2C-NAgH_2Cl}\\ |\\ \mathrm{OC-OAg}\end{array} = \begin{array}{l}\mathrm{H_2C-NH_2}\\ |\\ \mathrm{OC-OAg}\end{array} + \mathrm{AgCl}.$$

Against this objection, it may be pointed out that the properties of silver-glycocoll cannot, as will be shown later on, be accounted for by regarding it as an amido-acetate, but that all its reactions are most satisfactorily explained by the formula,



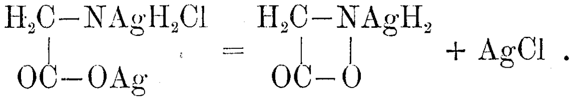
$$\begin{array}{ccc} H_2C & - & NAgH_2 \\ | & & | \\ OC & - & O \end{array} .$$

Moreover, there is a complete parallelism between the two equations :



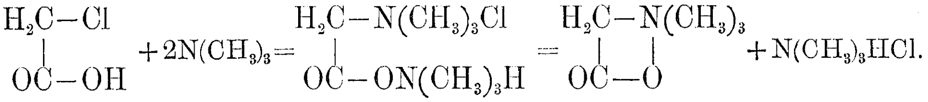
$$\begin{array}{ccc} H_2C & - & NH_3Cl \\ | & & \\ OC & - & ONH_4 \end{array} = \begin{array}{ccc} H_2C & - & NH_3 \\ | & & | \\ OC & - & O \end{array} + NH_4Cl$$

and



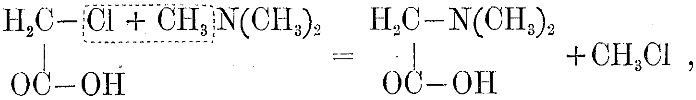
$$\begin{array}{ccc} H_2C & - & NAgH_2Cl \\ | & & \\ OC & - & OAg \end{array} = \begin{array}{ccc} H_2C & - & NAgH_2 \\ | & & | \\ OC & - & O \end{array} + AgCl .$$

The synthetic formation of anhydrous betaïn from trimethylamine and chloracetic acid (Liebreich: *Ber.*, **2**, 167 [1869]) can be expressed in a manner perfectly analogous to that indicated for glycocoll :

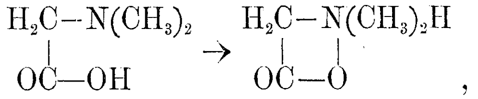


$$\begin{array}{ccc} H_2C & - & Cl \\ | & & \\ OC & - & OH \end{array} + 2N(CH_3)_3 = \begin{array}{ccc} H_2C & - & N(CH_3)_3Cl \\ | & & \\ OC & - & ON(CH_3)_3H \end{array} = \begin{array}{ccc} H_2C & - & N(CH_3)_3 \\ | & & | \\ OC & - & O \end{array} + N(CH_3)_3HCl.$$

If, however, we attempted to represent the above change in a manner analogous to that by which the formation of glycocoll is usually represented—

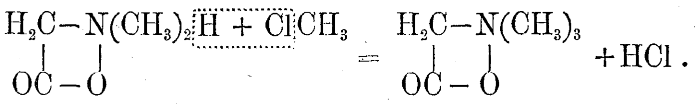


$$\begin{array}{ccc} H_2C & - & \boxed{Cl + CH_3}N(CH_3)_2 \\ | & & \\ OC & - & OH \end{array} = \begin{array}{ccc} H_2C & - & N(CH_3)_2 \\ | & & \\ OC & - & OH \end{array} + CH_3Cl ,$$



$$\begin{array}{ccc} H_2C & - & N(CH_3)_2 \\ | & & \\ OC & - & OH \end{array} \rightarrow \begin{array}{ccc} H_2C & - & N(CH_3)_2H \\ | & & | \\ OC & - & O \end{array} ,$$

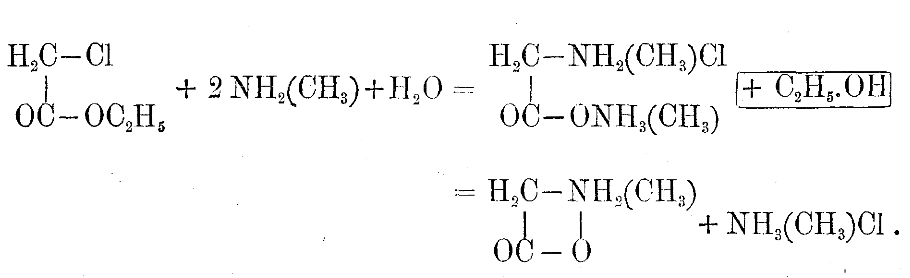
we should misrepresent the actual fact, inasmuch as dimethyl-glycocoll is thus made to be the product instead of betaïn, unless, indeed, we assume that methyl chloride, supposed to be liberated during the first stage of the reaction, goes to interact with dimethyl-glycocoll, producing betaïn and hydrogen chloride :



$$\begin{array}{l} H_2C-N(CH_3)_2\boxed{H + Cl}CH_3 \\ \;\,|\qquad| \\ OC-O \end{array} = \begin{array}{l} H_2C-N(CH_3)_3 \\ \;\,|\qquad| \\ OC-O \end{array} + HCl\,.$$

This assumption, which has no merit as an explanation over that already given, is, moreover, hardly warranted by facts. For, even if we suppose that dimethyl-glycocoll is first formed and then changed into trimethyl-glycocoll by interaction with methyl chloride, it is difficult to imagine that this interaction would be so complete that none of the interacting bodies should be left unaltered. The fact, then, that by the action of trimethylamine upon chloracetic acid, betaïn is produced unmixed with dimethyl-glycocoll goes to deprive the ground of the assumption necessitated above of any probability and, therefore, to corroborate the view here advocated as to the mode of formation of glycocoll and its trimethyl derivative.

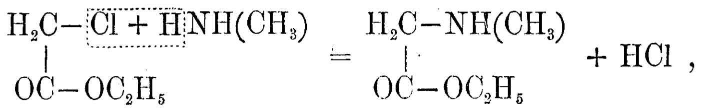
The consideration of the mode of formation of sarkosine (mono-methyl-glycocoll), a body which Volhard synthetically obtained by the action of methylamine upon ethyl chloracetate (*Lieb. Ann.*, **123**, 261 [1862]), leads to the same conclusion. The reaction is expressed as follows, according to the view here urged :



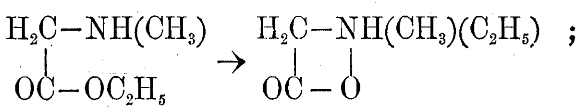
$$\begin{array}{l} H_2C-Cl \\ \;\,| \\ OC-OC_2H_5 \end{array} + 2\,NH_2(CH_3)+H_2O = \begin{array}{l} H_2C-NH_2(CH_3)Cl \\ \;\,| \\ OC-ONH_3(CH_3) \end{array} \boxed{+\ C_2H_5.OH}$$

$$= \begin{array}{l} H_2C-NH_2(CH_3) \\ \;\,|\qquad| \\ OC-O \end{array} + NH_3(CH_3)Cl\,.$$

If, however, we attempted as before to represent the above change in the way commonly adopted in the case of glycocoll, we should have



$$\begin{array}{l} H_2C-\boxed{Cl + H}NH(CH_3) \\ \;\;| \\ OC-OC_2H_5 \end{array} = \begin{array}{l} H_2C-NH(CH_3) \\ \;\;| \\ OC-OC_2H_5 \end{array} + HCl \ ,$$

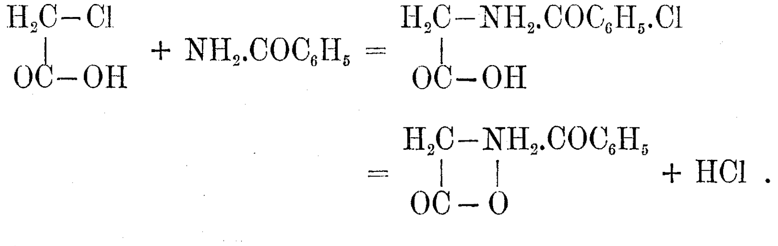


$$\begin{array}{l} H_2C-NH(CH_3) \\ \;\;| \\ OC-OC_2H_5 \end{array} \rightarrow \begin{array}{l} H_2C-NH(CH_3)(C_2H_5) \\ \;\;|\;\;\;\;\;| \\ OC-O \end{array} \ ;$$

and in order to avoid the misrepresentation here involved that methyl-ethyl-glycocoll is produced instead of sarkosine, we should have to make an assumption similar to that made in the case of betaïn, an assumption which is not supported by facts.

It is, then, that property, characteristic of the class of compounds under consideration, of producing internal ammonium salts, which alone can satisfactorily explain the mode of formation of sarkosine and betaïn. This consideration gives a fresh confirmation of the correctness of the closed formula for glycocoll, unless we disregard the evident analogy which exists between it and its methyl derivatives.

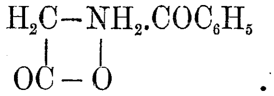
The mode of formation of hippuric acid by the action of benzamide upon chloracetic acid has also to be represented in a manner analogous to that above advanced for glycocoll and its methyl derivatives, thus :



$$\begin{array}{l} H_2C-Cl \\ \;\;| \\ OC-OH \end{array} + NH_2.COC_6H_5 = \begin{array}{l} H_2C-NH_2.COC_6H_5.Cl \\ \;\;| \\ OC-OH \end{array}$$

$$= \begin{array}{l} H_2C-NH_2.COC_6H_5 \\ \;\;|\;\;\;\;\;| \\ OC-O \end{array} + HCl \ .$$

This way of regarding the formation of hippuric acid makes it also a ring compound, a conclusion which is not contradicted by facts ; on the contrary, very slight solubility of this compound in cold alcohol and ether, its feeble acid character, and its almost neutral taste rather go to support this view of its constitution. That it does possess an acid character, feeble as it is, is easily accounted for by the presence of the benzoyl group, which imparts to the amidic hydrogen the property of being more easily replaced by metals generally than in the case of glycocoll ; and it is scarcely necessary to mention that there are many well known non-carboxylic compounds, uric acid for example, which possess acid characters. Again, the fact that all attempts hitherto made to obtain what may be called hippuryl chloride, $COCl.CH_2.NH.COC_6H_5$, have been attended with failure, goes towards upsetting the accepted view that it is a carboxylic compound, an argument which, indeed, may be used for denying carboxylic constitution to all the so-called amido-acids. In one word, the name benzoyl-glycocoll, already in common use, expresses its constitution perfectly—

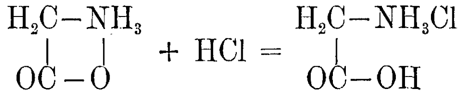


$$\begin{array}{l} H_2C-NH_2.COC_6H_5 \\ \quad\;| \qquad | \\ OC-O \end{array}.$$

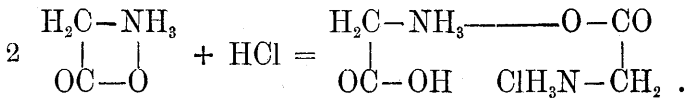
Passing, now, from the modes of formation of glycocoll and its derivatives, let us consider some of its transformations and discuss the constitution of the compounds thereby produced.

A. *Addition compounds.* That, although glycocoll and its derivatives must be regarded as closed bodies, its addition compounds should possess an open constitution is easy to admit, remembering that a nitrogen atom is not yet known to be capable of combining with more than five monovalent radicals. The ordinary or hydrated betaïn, $COOH.CH_2.N(CH_3)_3.OH$, and the corresponding chloride, $COOH.CH_2.N(CH_3)_3.Cl$, are bodies of this kind. Their formation presents, therefore, no difficulties with the closed formula for glycocoll.

(a) *Combination with acids :*

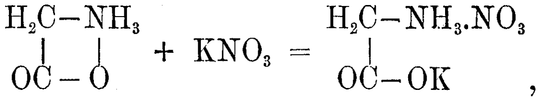


$$\begin{array}{c}H_2C-NH_3\\ |\qquad|\\ OC-O\end{array} + HCl = \begin{array}{l}H_2C-NH_3Cl\\ \;\;|\\ OC-OH\end{array}$$



$$2\begin{array}{c}H_2C-NH_3\\ |\qquad|\\ OC-O\end{array} + HCl = \begin{array}{l}H_2C-NH_3\text{———}O-CO\\ \;\;|\qquad\qquad\qquad\quad\;|\\ OC-OH\quad ClH_3N-CH_2\end{array} .$$

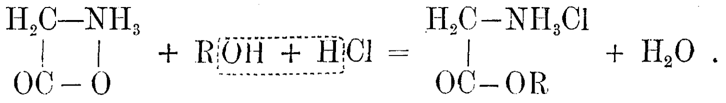
(b) *Combination with metallic salts :*



$$\begin{array}{c}H_2C-NH_3\\ |\qquad|\\ OC-O\end{array} + KNO_3 = \begin{array}{l}H_2C-NH_3.NO_3\\ \;\;|\\ OC-OK\end{array} ,$$

whereas with the open formula for glycocoll, we must assume, in this case, that a double decomposition first takes place with formation of potassium amido-acetate and nitric acid and that, then, the latter unites to the amidogen group, unless we give the irrational formula, $COOH.CH_2.NH_2.K.NO_3$, to this compound.

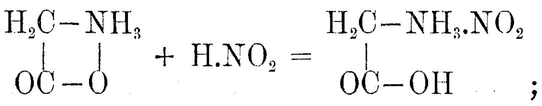
(c) *Conversion into the hydrochloride of an amido-acetic ester :*



$$\begin{array}{c}H_2C-NH_3\\ |\qquad|\\ OC-O\end{array} + R\boxed{OH + H}Cl = \begin{array}{l}H_2C-NH_3Cl\\ \;\;|\\ OC-OR\end{array} + H_2O .$$

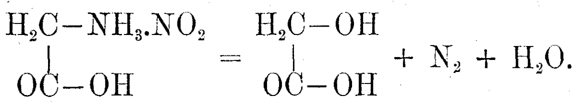
(d) *Conversion into glycollic acid :*

Although this change is usually regarded as consisting in the direct replacement of the amidogen group by hydroxyl and, therefore, may appear as offering a difficulty to the closed formula, the first action of nitrous acid must be admitted to be analogous to that which occurs between glycocoll and hydrochloric acid, namely the formation of an addition compound—



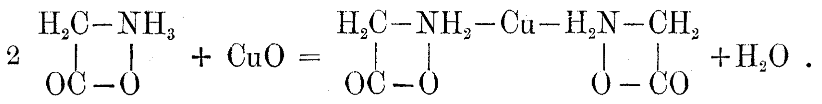
$$\begin{array}{c}H_2C-NH_3\\ |\qquad|\\ OC-O\end{array} + H.NO_2 = \begin{array}{l}H_2C-NH_3.NO_2\\ \;\;|\\ OC-OH\end{array} ;$$

the latter, then, decomposes, under the conditions of the experiment, into glycollic acid, nitrogen, and water :



$$\begin{array}{l}H_2C-NH_3.NO_2\\ \ \ |\\ OC-OH\end{array} = \begin{array}{l}H_2C-OH\\ \ \ |\\ OC-OH\end{array} + N_2 + H_2O.$$

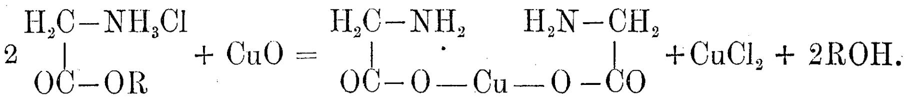
B. *Metallic derivatives.* Among the derivatives of glycocoll one, which is best known and most characteristic, is the *copper* compound. The deep blue colour of this body and its solubility in alkalies distinguish it from ordinary carboxylic salts of copper, and lead us to the conclusion that it is most probably a cuprammonium compound, a conception which can be readily expressed by the following scheme :



$$2\begin{array}{l}H_2C-NH_3\\ \ \ |\quad\ \ |\\ OC-O\end{array} + CuO = \begin{array}{l}H_2C-NH_2-Cu-H_2N-CH_2\\ \ \ |\quad\ \ |\qquad\qquad\quad |\quad\ \ |\\ OC-O\qquad\qquad\quad O-CO\end{array} + H_2O\ .$$

If we attempted to represent the copper compound as an ammoniated derivative by help of the open formula and gave it the constitution $Cu(NH.CH_2.COOH)_2$, we should have to make the baseless assumption that the hydrogen of the carboxyl group remains unreplaced by copper even in the presence of an excess of cupric oxide. If, on the other hand, we regarded the copper derivative as $(H_2N.CH_2.COO)_2Cu$, looking upon glycocoll as a carboxylic compound (an acid) because it dissolves oxide of copper and some other metallic oxides, we might argue that ammonium chloride or even ammonia itself is also an acid !

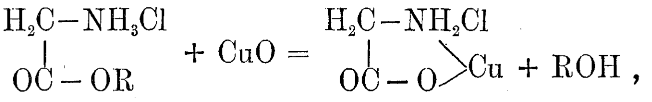
Reference must here be made to two important papers bearing upon the question : one by Curtius and Goebel (*J. prakt. Chem.*, **37**, 150 [1888]), the other by Kraut (*Lieb. Ann.*, **266**, 292 [1891]). By digestion of the hydrochloride of an amido-acetic ester with an excess of freshly precipitated cupric oxide, Curtius and Goebel obtained a copper compound which they represent by the formula, $COOR.CH_2.NH-Cu-NH.CH_2.COOR$; whilst Kraut denies the existence of such a compound and shows, by a careful experimental study, that the interaction between the hydrochloride of an amido-acetic ester and cupric oxide occurs according to the equation :



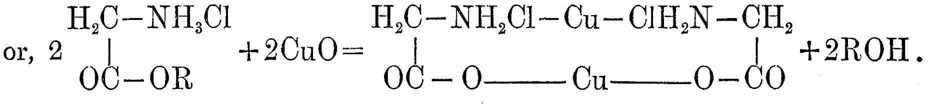
$$2\begin{array}{l}H_2C-NH_3Cl\\ \quad |\\ OC-OR\end{array} + CuO = \begin{array}{l}H_2C-NH_2 \qquad\qquad H_2N-CH_2\\ \quad | \qquad\qquad\qquad\qquad\qquad |\\ OC-O-Cu-O-CO\end{array} + CuCl_2 + 2ROH.$$

Kraut concludes from this that it is the hydrogen of the hydroxyl, not that of the amidogen, which is replaced by copper.

It must be observed, however, that what Kraut obtained is a double copper compound, having the composition, $CuCl_2.(H_2N.CH_2.COO)_2Cu$, or more simply, as he himself puts it, $H_2N.CH_2.COO\,CuCl$; but he does not give any explanation of the formation of this *double* salt in support of his views. I think a satisfactory explanation of the formation and existence of this double salt can be readily obtained by supposing that cupric oxide displaces an equivalent of an alcohol from the hydrochloride of an amido-acetic ester, according to the equation,



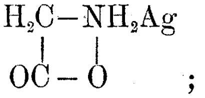
$$\begin{array}{l}H_2C-NH_3Cl\\ \quad |\\ OC-OR\end{array} + CuO = \begin{array}{l}H_2C-NH_2Cl\\ \quad | \qquad \searrow\\ OC-O \nearrow Cu\end{array} + ROH,$$



$$\text{or, } 2\begin{array}{l}H_2C-NH_3Cl\\ \quad |\\ OC-OR\end{array} + 2CuO = \begin{array}{l}H_2C-NH_2Cl-Cu-ClH_2N-CH_2\\ \quad | \qquad\qquad\qquad\qquad\qquad\quad |\\ OC-O \text{———} Cu \text{———} O-CO\end{array} + 2ROH.$$

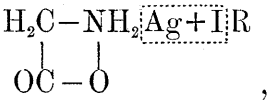
The view here advanced as to the constitution of the copper compound obtained by Kraut is in perfect harmony with his experimental data; at the same time, it shows that his conclusion that copper must be wholly carboxylated is groundless.

Turning now to the *silver* derivative, the metallammonium theory gives it the constitution,



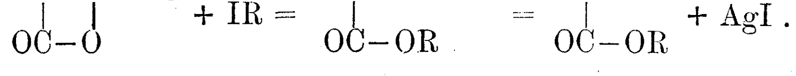
$$\begin{matrix} H_2C & - & NH_2Ag \\ | & & | \\ OC & - & O \end{matrix} \quad ;$$

and although the formation of amido-acetic esters by the action of alkyl iodides upon it is brought forward against this view (Kraut: *op. cit.*, 310), I see no ground whatever for this argument. Representing, as is usually done, the action of alkyl iodides upon silver-glycocoll, as if direct replacement of silver by alkyl radicals took place,



$$\begin{matrix} H_2C & - & NH_2\boxed{Ag+I}R \\ | & & | \\ OC & - & O \end{matrix} \quad ,$$

the formation of amido-acetic esters, $H_2N.CH_2.COOR$, would, indeed, offer a difficulty to the metallammonium theory; but the action in this case, as in other analogous cases, must be regarded as primarily of an additive nature, the unstable addition compound, then, decomposing into silver iodide and the ester, under the conditions of the experiment:



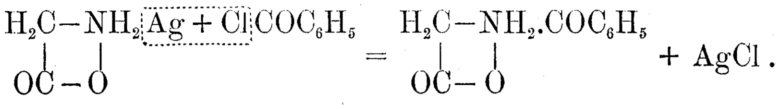
$$\begin{matrix} H_2C - NH_2Ag \\ | \quad\; | \\ OC - O \end{matrix} + IR = \begin{matrix} H_2C - NH_2AgI \\ | \qquad\quad \\ OC - OR \end{matrix} = \begin{matrix} H_2C - NH_2 \\ | \qquad \\ OC - OR \end{matrix} + AgI \, .$$

The formation of amido-acetic esters, and not alkyl-glycocolls, by the action of alkyl iodides upon silver-glycocoll is a strong argument against the *metallamido-acetic acid theory* ($MHN.CH_2.COOH$), but it does not touch the metallammonium theory.

The formation of hippuric acid by the action of benzoyl chloride upon silver (or zinc) glycocoll is, on the other hand, a death-blow to the *metallic amido-acetate theory* ($H_2N.CH_2.COOM$) ; it is this reaction which has led many eminent chemists to regard metallic derivatives of glycocoll as $MHN.CH_2.COOH$, and to represent the formation of hippuric acid accordingly :

$$COOH.CH_2.NH\boxed{Ag + Cl}COC_6H_5 = COOH.CH_2.NH.COC_6H_5 + AgCl.$$

As already pointed out, however, there are reasons to believe that hippuric acid is benzoyl-glycocoll, and its formation is, therefore, no more easily expressed by the scheme above given than by



$$\begin{array}{l} H_2C-NH_2\boxed{Ag + Cl}COC_6H_5 \\ \;\,| \quad\;\; | \\ OC-O \end{array} = \begin{array}{l} H_2C-NH_2.COC_6H_5 \\ \;\,| \quad\;\; | \\ OC-O \end{array} + AgCl.$$

It must be observed that an opening of the ring, as in the case of the action of alkyl iodides upon silver-glycocoll, could not occur here, because both the radicals, Cl and $COC_6H_5$, are negative.

The metallic amido-acetate theory can furnish no satisfactory explanation of the formation of hippuric acid by the action of benzoyl chloride upon silver-glycocoll, nor can the metallamido-acetic acid theory that of the production of amido-acetic esters by the action of alkyl iodides upon silver-glycocoll. Both theories are imperfect, inasmuch as each considers only one set of facts ; the *metallammonium theory*, on the contrary, takes complete account of the reactions of the derivatives under consideration and, at the same time, meets the objections and requirements of the other two theories.

With regard to other metallic derivatives, such as those containing *mercury*, *cadinum*, *zinc*, *magnesium*, and *lead*, they are no doubt constituted like the copper or the silver derivative. Those containing the metals of the alkaline earths—*barium*, *strontium*, and *calcium*—have only been recently obtained in definite and crystalline states (Kraut:

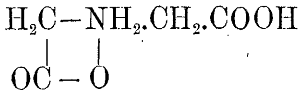
*op. cit*, 299). Horsford (*Lieb. Ann.*, **60**, 33 [1846]) and, more recently, Curtius (*J. prakt. Chem.*, **26**, 159 [1882]) attempted in vain to prepare these bodies in the pure state; it is only by mixing concentrated aqueous solutions of glycocoll and an alkaline earth, pouring the mixture into alcohol, and leaving the precipitated oil for some days in contact with the mother liquor that Kraut was able to obtain them in a pure and crystalline condition. The evident difficulties, under which these bodies are formed, mark them off from ordinary carboxylic salts, a circumstance which shows that they are probably also metallammonium compounds. The comparative ease with which derivatives containing copper, silver, mercury, &c. are formed and the difficulties, which attend the preparation of those containing the metals of the alkaline earths, and which increase still more in the case of those containing alkali metals (these derivatives, in fact, do not seem to have been isolated as yet), speak again in favour of the metallammonium theory; inasmuch as metals like copper, silver, and mercury are eminently characterised by the ease with which they form ammoniated derivatives. In opposition to Kraut's words, " Ich halte daher sämmtliche Metallverbindungen des Glycocolls für wahre amidoessigsaure Salz," I would rather say that *all metallic derivatives of glycocoll are metallammonium compounds.*

The above examination of the modes of formation and transformation of glycocoll irresistably leads to the internal ammonium theory of its constitution; there is, however, one other point which must be considered before going further. The point in question is the relation between glycocoll and the so-called diglycolamidic and triglycolamidic acids. The latter compounds are usually represented by $HN(CH_2.COOH)_2$ and $N(CH_2.COOH)_3$ respectively, and glycocoll and these two bodies are compared to mono-, di-, and triethylamine; this relation is even regarded as an argument for the open formula for glycocoll (Kraut: *op. cit.*, 309). It is to be observed, however, that di- and triglycolamidic acids behave respectively as mono- and dibasic acids towards alkalies and alkaline earths, the composition of their anhydrous salts containing alkali metals and metals of the alkaline earths(2) being

| Diglycolamidates. | Triglycolamidates. |
|---|---|
| $NH_4.C_4H_6NO_4$ | $(NH_4)_2.C_6H_7NO_6$ |
| $Ba.(C_4H_6NO_4)_2$ | $K_2 . C_6H_7NO_6$ |
| | $Ba. C_6H_7NO_6$ (3) . |

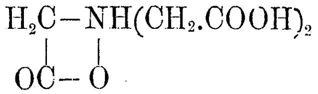
It is only those of their derivatives containing copper, silver, zinc, or lead(4)-metals more or less characterised by the ease with which they form ammoniated compounds—which may be regarded as dibasic ($M'_2.C_4H_5NO_4$) and tribasic ($M'_3.C_6H_6NO_6$) salts respectively. These facts are unexplicable by the accepted constitution of di- and triglycolamidic acids, but receive an ample and ready explanation from the following formulae:

Diglycolamidic acid.



$$\begin{array}{l} H_2C-NH_2.CH_2.COOH \\ \;\,|\quad\;\; | \\ OC-O \end{array}$$

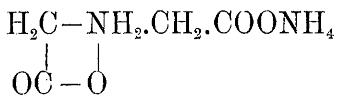
Triglycolamidic acid.



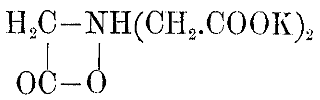
$$\begin{array}{l} H_2C-NH(CH_2.COOH)_2 \\ \;\,|\quad\;\; | \\ OC-O \end{array}$$

;

the constitution of their salts or metallic derivatives being



$$\begin{array}{l} H_2C-NH_2.CH_2.COONH_4 \\ \;\,|\quad\;\; | \\ OC-O \end{array}$$



$$\begin{array}{l} H_2C-NH(CH_2.COOK)_2 \\ \;\,|\quad\;\; | \\ OC-O \end{array}$$

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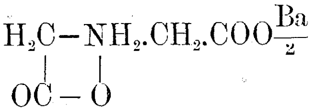
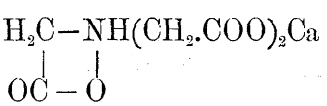
(2) For the composition of these and other salts, see Heintz: *Lieb. Ann.*, **122,** 269; **124,** 297; **156,** 54; Lüddecke: *Ibid.*, **147,** 272; Beilstein: *Handbuch*, 3 Aufl., I, 1191-1192.

(3) Barium forms another salt of the composition $Ba_3(C_6H_6NO_6)_2$, but it readily changes into the above dibasic salt on addition of acetic acid

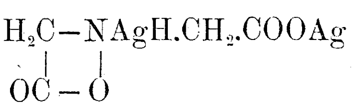
(4) A dibasic salt of lead of the composition $Pb. C_6H_7NO_6$ is also known.



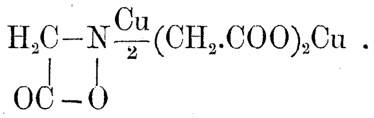
$$\begin{array}{l} H_2C-NH_2.CH_2.COO\frac{Ba}{2} \\ \;|\quad\;\;| \\ OC-O \end{array}$$



$$\begin{array}{l} H_2C-NH(CH_2.COO)_2Ca \\ \;|\quad\;\;| \\ OC-O \end{array}$$



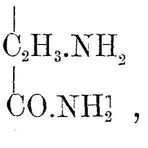
$$\begin{array}{l} H_2C-NAgH.CH_2.COOAg \\ \;|\quad\;\;| \\ OC-O \end{array}$$



$$\begin{array}{l} H_2C-N\frac{Cu}{2}(CH_2.COO)_2Cu\ . \\ \;|\quad\;\;| \\ OC-O \end{array}$$

A word must now be said with regard to the term "amido-acids."(5) This term which is so generally employed should, in accordance with the internal ammonium theory, be dropped from chemical nomenclature and replaced by the word *glycocolls*, at least in the case of the so-called amido-carboxylic acids. This designation is to be recommended, because it is not new, and is to be preferred to other difficult names which might be suggested as expressing constitution. Moreover, a particular glycocoll may be easily specified by prefixing *acetic*, *propionic*, &c.; alanine would thus be *propionic glycocoll*. These expressions have to be distinguished from those, which are already in use to designate derivatives of a particular glycocoll, such as acetyl-glycocoll (aceturic acid) and benzoyl-glycocoll (hippuric acid). We may also use such expressions as "glycocollic constitution," "glycocollyl group—$CO_2NH_3$—," &c. without confusion or other inconvenience.

Asparagin and aspartic acid, as well as all other similar bodies, such as glutamin, glutamic acid, leucine, leucic acid, &c. must be looked upon as glycocollyl compounds. Thus, asparagin which is usually regarded as "amido-succinamic acid,"



$$\begin{array}{l} CO.OH \\ | \\ C_2H_3.NH_2 \\ | \\ CO.NH_2\ , \end{array}$$

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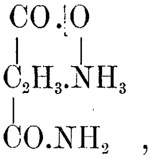
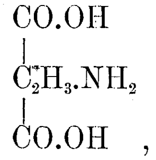
(5) In the new edition of his Handbuch, Beilstein changes it into "amino-acids," but very little is gained by the alteration.

is exceedingly like glycocoll both in its physical and chemical properties, and does not possess any acid character. It ought, consequently, to be represented by the formula,



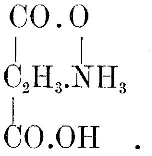
$$\begin{array}{l} \mathrm{CO.O} \\ | \quad\;\; | \\ \mathrm{C_2H_3.NH_3} \\ | \\ \mathrm{CO.NH_2} \end{array} ,$$

and called *succinamic glycocoll.* Aspartic acid, generally expressed in name and formula as " amido-succinic acid,"



$$\begin{array}{l} \mathrm{CO.OH} \\ | \\ \mathrm{C_2H_3.NH_2} \\ | \\ \mathrm{CO.OH} \end{array} ,$$

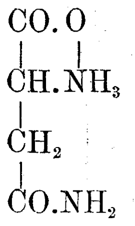
must in reality be considered as monobasic, inasmuch as its so-called normal salts containing alkali metals are easily decomposed by carbonic acid, and the only salts known in a definite state are the so-called acid salts. This body must, therefore, be regarded as *succinic glycocoll*, and represented by the formula,



$$\begin{array}{l} \mathrm{CO.O} \\ | \quad\;\; | \\ \mathrm{C_2H_3.NH_3} \\ | \\ \mathrm{CO.OH} \end{array} .$$

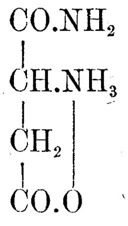
The fact that a mono-ethyl ester is obtained by direct etherification of aspartic acid also goes to support this view of its constitution.

The above consideration leads to the prediction not only of the existence of two chemically isomeric asparagins, as is predicted by the current view,



$$\begin{array}{l} \mathrm{CO.O} \\ \mathrm{CH.NH_3} \\ \mathrm{CH_2} \\ \mathrm{CO.NH_2} \end{array}$$

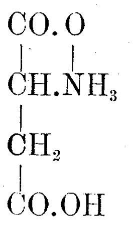
and



$$\begin{array}{l} \mathrm{CO.NH_2} \\ \mathrm{CH.NH_3} \\ \mathrm{CH_2} \\ \mathrm{CO.O} \end{array}$$

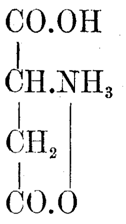
,

but also of aspartic acids—



$$\begin{array}{l} \mathrm{CO.O} \\ \mathrm{CH.NH_3} \\ \mathrm{CH_2} \\ \mathrm{CO.OH} \end{array}$$

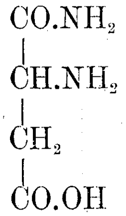
and



$$\begin{array}{l} \mathrm{CO.OH} \\ \mathrm{CH.NH_3} \\ \mathrm{CH_2} \\ \mathrm{CO.O} \end{array}$$

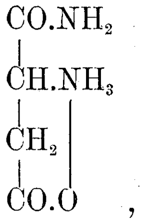
,

each of which is further capable of existing as dextro-rotatory, laevo-rotatory, and racemoid modifications. It must be frankly acknowledged, however, that all the aspartic acids known at present appear to possess one and the same constitution, the two active acids obtained from the ordinary and the sweet asparagins being optical isomers, and all the inactive aspartic acids obtained in various ways being identical among themselves and also with that produced on mixing the two active acids in equal quantities (Piutti : *Ber.*, **19**, 1684 [1886]; Engel: *Bull.*, **50**, 150 [1888]). There are, however, certain points in the chemistry of asparagin and aspartic acid, which require further investigation. The singular fact that, of the two asparagins which are regarded to be optical isomers, one is tasteless and the other exceedingly sweet, the fact also that these two active asparagins, mixed in equal quantities, do not produce an inactive racemoid compound, are some of the points above referred to. Moreover, the inactive asparagin obtained from monoethyl α—aspartate (m. p. 165°) and which, from its mode of formation, has to be represented by the formula,



$$\begin{array}{l} CO.NH_2 \\ | \\ CH.NH_2 \\ | \\ CH_2 \\ | \\ CO.OH \end{array}$$

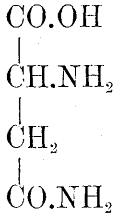
or rather



$$\begin{array}{l} CO.NH_2 \\ | \\ CH.NH_3 \\ | \quad | \\ CH_2 \; | \\ | \quad | \\ CO.O \end{array},$$

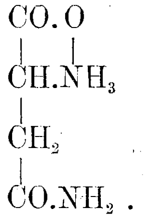
has not yet been resolved into active components; but since van't Hoff's theory does not admit of the existence of an inactive amesotomic compound in the case of bodies containing only one asymmetric carbon atom, the mesotomism of the above inactive asparagin has yet to be achieved. It is not unlikely that the new active asparagins thus obtained would yield active aspartic acids different from those known at present.

It is to be observed that the inactive asparagin is here assumed to be *chemically* isomeric with the two known active asparagins (*Cf.* Victor Meyer and Jacobson, *loc. cit.*), and since the former possesses the constitution above given, the latter should be



$$\begin{array}{l} CO.OH \\ | \\ CH.NH_2 \\ | \\ CH_2 \\ | \\ CO.NH_2 \end{array}$$

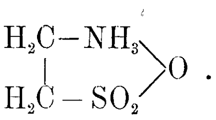
or rather



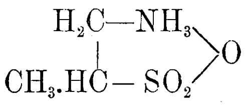
$$\begin{array}{l} CO.O \\ | \quad | \\ CH.NH_3 \\ | \\ CH_2 \\ | \\ CO.NH_2 \end{array}.$$

It is probable, however, that the inactive asparagin will prove to be the racemoid compound of the two known active asparagins, in which case an asparagin possessing the latter constitution has yet to be discovered. Our non-acquaintance of a second aspartic acid presents, therefore, no greater difficulties to the acceptance of the view here advocated as to the constitution of aspartic acids than our non-acquaintance of a second aspargin presents to the current theory. From this point of view, the existence of new aspartic acids is again, at least, as probable as that of new asparagins. Time will show whether these predictions are verified or not by actual facts.

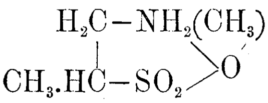
Returning to the question of nomenclature, the generic name *taurins* should be used in the case of the so-called amido-sulphonic acids, and different taurins distinguished by prefixing the names of the divalent hydrocarbon radicals. Thus, "β-amido-ethyl sulphonic acid," or "amido-isethionic acid," terms which are intended to express the constitution of common taurin, should be replaced by *ethylene-taurin* (or simply, *taurin*) in accordance with the formula,



The "β-methyl taurin" and the "β-ν-dimethyl taurin," described by Gabriel (*Ber.*, **22**, 2988 [1889]), would be respectively *propylene-taurin* and *methyl propylene-taurin*, and expressed by the formulae,

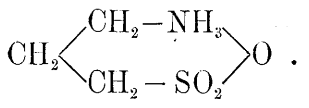


and



;

whilst the "γ-amido-propyl sulphonic acid" (Gabriel and Lauer: *Ber.*, **23**, 92 [1890]) should be named *trimethylene-taurin*, and expressed by the formula,



The above examples would, I hope, suffice to show that the nomenclature of the "amido-acids" here suggested is capable of general application.

I have much pleasure, in conclusion, in tendering my best thanks to Dr. E. Divers, F.R.S., for kindly looking over this paper.