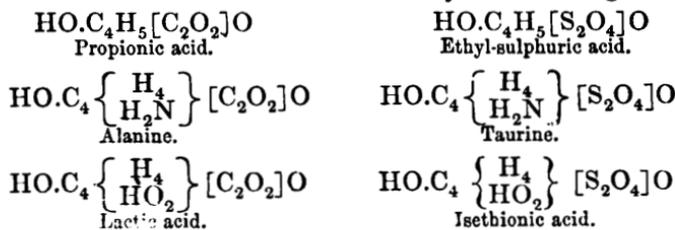


XIX.—*On the Chemical Constitution and Artificial Formation of Taurine.*

By HERMANN KOLBE, of Marburg.

SOME years ago, Strecker* made the interesting observation that isethionate of ammonia, when heated to 210° C., gives off water, and is converted into taurine. By this discovery, as well as by the more recent observation of Gibbs,† that taurine treated with nitrous acid is reconverted into isethionic acid, the existence of intimate relations between taurine and isethionic acid was placed beyond doubt; but the question relating to the chemical constitution of taurine, with which that of isethionic acid is closely connected, still remained undecided. That taurine is not the amide of isethionic acid, is sufficiently shown by its behaviour with hydrate of potash, which does not eliminate ammonia from it till heated to the melting point, and then completely decomposes it.

I believe that I have found the key to the solution of this problem, by an experimental confirmation of the conjecture which I threw out a short time ago,‡ that taurine is related to isethionic acid in the same manner as alanine to lactic acid. In the same sense that the two last-mentioned bodies may be regarded as derivatives of ethyl-carbonic (propionic) acid, that is to say, alanine as amido-ethyl-carbonic acid, and lactic acid as oxy-ethyl-carbonic acid,—so likewise may taurine and isethionic acid be viewed as derivatives of ethyl-sulphuric acid, namely taurine as amido-ethyl-sulphuric acid, and isethionic acid as oxy-ethyl-sulphuric acid: these relations are exhibited by the following formulæ :



* Ann. Ch. Pharm. xci, 101.

† Jahresbericht der Chemie, xi, 550.

‡ Ann. Ch. Pharm. cxii, 241.

To the assumption that taurine and alanine are so nearly related to each other as these formulæ indicate, it may be objected that taurine does not possess the power which is common to glycocine, alanine, leucine, aspartic acid, amidobenzoic acid, and amido-acids in general, of forming saline compounds both with bases and with acids. But independently of the fact that the organic derivatives of sulphuric acid differ in many points from those of carbonic acid, the following consideration is of especial importance in connection with the present inquiry.

It must, in the first place, be presumed that, by the introduction of amidogen into the ethyl-molecule, the acid properties of ethyl-sulphuric acid will be weakened in the same degree as in alanine, the body derived in like manner from ethyl-carbonic (propionic) acid. But inasmuch as ethyl-sulphuric acid is a stronger acid than propionic acid, it is not surprising that even the weak basic properties of amidated propionic acid should be wanting in the amidated ethyl-sulphuric acid.* On the other hand, this latter acid might be expected to exhibit properties which have not hitherto been actually observed in taurine. Guided by these considerations, I have made several experiments with pure taurine prepared from ox-bile, the results of which I will here briefly communicate.

Taurine dissolved in fuming hydrochloric or strong nitric acid, crystallizes unaltered from the solution on evaporation; moreover, it does not increase in weight when exposed to an atmosphere of dry hydrochloric acid gas, either at ordinary temperatures or when heated. In order to determine whether taurine, like alanine, is capable of forming crystalline compounds with salts, I mixed the concentrated aqueous solutions of equivalent quantities of taurine and chloride of potassium, and abandoned the solution to spontaneous evaporation: pure taurine then crystallized out first, and afterwards chloride of potassium. Neither does the hydrochloric acid solution of taurine yield any compound with bichloride of platinum, alcohol added to the solution producing a precipitate of pure taurine.

It appears therefore that taurine does not exhibit the basic properties possessed by other amido-acids; but, on the other hand, it is by no means destitute of the power of uniting with

* Methyl-sulphuric acid, the analogue of acetic acid, does not yield marsh-gas when treated with soda-lime; neither does benzyl-sulphuric acid, the analogue of benzoic acid, yield benzole when thus treated. Other examples of these differences of character are afforded by the observations lately communicated by Vogt (*Ann. Ch. Pharm.* cxix, 143), and Keller (*ibid.*, 153).

bases; and, although I have not succeeded in preparing salts of taurine in the solid form, the following experiments show that it is really capable of forming such compounds.

A saturated aqueous solution of taurine, in which absolute alcohol immediately produces a copious precipitate, is not precipitated, or even clouded, by a mixture of absolute alcohol and ammonia; but if the solution be then exposed to the air till the ammonia is volatilized, the taurine separates in beautiful crystals. Neither is a concentrated aqueous solution of taurine containing free potash, precipitated by absolute alcohol—a property which may be successfully applied to the separation of taurine from other compounds insoluble in alcohol. Carbonic acid, passed into the solution, separates the taurine in its original state.

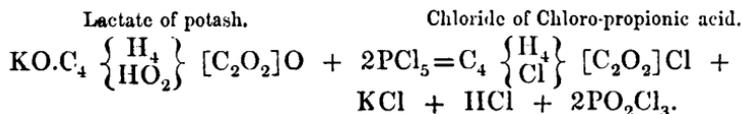
Hydrated oxide of lead is taken up in considerable quantity by a hot aqueous solution of taurine, the clear filtered liquid becoming only slightly turbid on cooling. On exposure to the air, it deposits a considerable quantity of carbonate of lead. An aqueous solution of taurine does not decompose carbonate of lead, even at the boiling heat.

These results show that taurine is by no means an indifferent body, as it has hitherto been considered, but rather a weak acid, the acid properties of the primary compound, ethyl-sulphuric acid, being weakened in it by the substitution of amidogen for hydrogen, to nearly the same extent as, in trichloraniline, the basic properties of aniline are weakened by the introduction of chlorine.

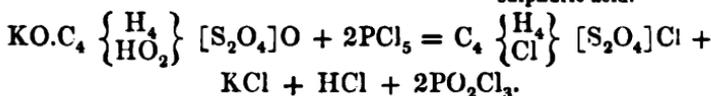
The consideration of taurine as amido-ethyl-sulphuric acid, is further supported by its formation from isethionic acid by a process analogous to that of alanine from lactic acid.

CHLORIDE OF CHLORETHYL-SULPHURIC ACID, AND CHLORETHYL-SULPHURIC ACID.

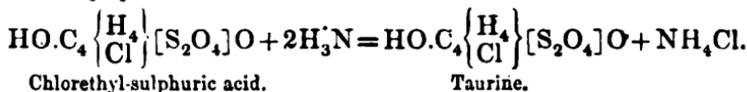
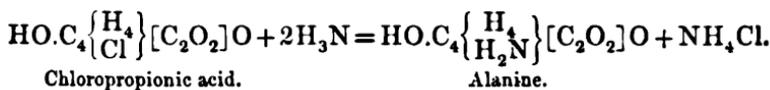
If isethionic acid be really constituted similarly to lactic acid, as above suggested, it may be expected to exhibit, under the influence of pentachloride of phosphorus, a transformation similar to that of lactic acid, yielding in fact the chloride of chlorethyl-sulphuric acid thus:—



Isethionate of potash.

Chloride of Chlorethyl-
sulphuric acid.

It may further be expected that the chlorethyl-sulphuric acid, resulting from the action of water on this chloride, will be converted, by appropriate treatment with ammonia, into taurine, just as the analogously constituted compound, chloropropionic acid, is thereby converted into alanine:



These expectations have been completely fulfilled by the results of the following experiments:—

To prepare chloride of chlorethyl-sulphuric acid, 60 grammes (1 at.) of finely pulverized isethionate of potash, dried at 100° C., were introduced, together with 150 grms. (2 ats.) of pulverulent pentachloride of phosphorus, into a capacious tubulated retort, the two substances being mixed together as completely as possible with a bent glass rod. The mixture, after a while, begins to get warm and to liquefy, and at length boils, with copious evolution of hydrochloric acid fumes, a large quantity of oxychloride of phosphorus distilling over at the same time into the receiver. If, after this violent action is over, the retort be gently heated, nearly pure oxychloride of phosphorus distils over at first; afterwards, when the heat is raised, a much heavier, mobile, oily liquid, having a strong pungent odour, passes over in somewhat considerable quantity. This liquid consists mainly of the chloride of chlorethyl-sulphuric acid, while in the retort there ultimately remains a dry, blackish, saline mass.

The chloride of chlorethyl-sulphuric acid, which boils at about 200° C., may be easily and completely separated from the oxychloride of phosphorus by fractional distillation; nevertheless, I have not succeeded in preparing this compound quite pure, apparently because a quantity of chloride of isethionic acid $\text{C}_4 \left\{ \begin{array}{l} \text{H}_4 \\ \text{HO}_2 \end{array} \right\} [\text{S}_2\text{O}_4]\text{Cl}$, is formed at the same time, which

chloride boils at nearly the same temperature as the chloride of chlorethyl-sulphuric acid. A precisely similar observation was made by myself and Dr. Lautemann with regard to the distillation of salicylic acid, or salicylate of soda, with pentachloride of phosphorus, the chloride of salicylic acid thereby produced being always more or less accompanied by chloride of salicylic acid.

The distillate which passes over in the rectification of the crude product at 200° C.—at which the boiling temperature remains to a certain degree stationary—is a nearly colourless, heavy liquid, which fumes in the air, does not mix with water, and has an intense and very persistent odour, strongly recalling that of volatile oil of mustard. Analysis gave the following numbers:

0.626 gm. burnt with oxide of copper gave 0.346 gm. carbonic acid and 0.150 gm. water, corresponding to 15.0 p. c. carbon and 2.6 p. c. hydrogen.

0.5055 gm. passed in the state of vapour over red-hot lime gave 0.7825 gm. chloride of silver = 38.3 p. c. chlorine.

0.604 gm. passed over red-hot carbonate of soda, which was finally heated in a stream of oxygen, yielded 0.905 gm. sulphate of baryta, corresponding to 20.8 p. c. sulphur.

The formula $C_4 \left\{ \begin{matrix} H_4 \\ Cl \end{matrix} \right\} [S_2O_4]Cl$ requires

	Calculated.		Found.
C_4	24	14.7	15.0
H_4	4	2.5	2.6
S_2	32	19.6	20.5
O_4	32	19.6	„
Cl_2	71	43.6	38.3
	<hr/>	<hr/>	
	163	100.0	

The somewhat too large amounts of carbon and sulphur shown by the analysis, on the one hand, and the great deficiency of chlorine on the other (a product obtained in another preparation yielded 39.2 p. c. chlorine), corroborate the supposition that the compound analysed contained a small quantity of chloride of isethionic acid.

Chloride of chlorethyl-sulphuric acid is but very slowly decomposed by water at ordinary temperatures. A drop of it covered with a large quantity of water did not disappear completely in

the course of a week. Heated with water to 100° C. in a hermetically sealed tube, it dissolves somewhat readily, yielding hydrochloric and chlorethyl-sulphuric acid, and losing its odour at the same time. It dissolves easily in potash, with great evolution of heat; also in aqueous ammonia, with abundant formation of sal-ammoniac. Taurine is not produced in this last reaction, but probably the amide of amido-ethyl-sulphuric acid.

The solution of chloride of chlorethyl-sulphuric acid in absolute alcohol, even after being heated in a hermetically sealed tube to 100° C., does not yield any chlorethyl-sulphate of ethyl on addition of water.

If the strongly acid solution obtained by heating the chloride of chlorethyl-sulphuric acid with water in sealed tubes for several days be completely freed from admixed hydrochloric acid, by evaporation, first over the open fire, afterwards over the water-bath, a thickish acid liquid is obtained, consisting chiefly of chlorethyl-sulphuric acid. This acid forms crystallizable salts with oxide of lead, oxide of silver, and other bases. For the preparation of the pure acid, I have used the silver-salt, which crystallizes easily and in beautiful forms.

The solution of the crude acid diluted with a moderate quantity of water dissolves carbonate of silver with effervescence. After it has been treated, for a while with a slight excess of the carbonate of silver, without heating, but with frequent agitation, the clear filtered saline solution, which is very sensitive to the action of light, and still more to that of heat, is evaporated nearly to dryness in vacuo over sulphuric acid, being at the same time protected from the light. The crystalline mass separated from the mother-liquor, and washed with a little cold water, is well comminuted and re-dissolved in the smallest possible quantity of cold water, and on again leaving the filtered solution to evaporate in vacuo, the pure chlorethyl-sulphate of silver crystallizes out in large transparent rhombic prisms, the mother-liquor yielding an additional quantity on further concentration. Analysis gave the following numbers:

1.256 grm. of the silver-salt burnt with oxide of copper yielded 0.440 grm. carbonic acid and 0.182 grm. water = 9.5 p. c. carbon and 1.6 p. c. hydrogen.

1.015 grm. ignited with carbonate of soda in a stream of

oxygen, yielded 0.987 grm. sulphate of baryta = 13.3 p. c. sulphur.

1.257 grm. precipitated with hydrochloric acid, yielded 0.703 chloride of silver = 43.1 p.c. silver.

The formula $\text{AgO.C}_4 \left\{ \begin{matrix} \text{H}_4 \\ \text{Cl} \end{matrix} \right\} [\text{S}_2\text{O}_4]\text{O}$ requires

	Calculated.		Found.
C_4	24.0	9.5	9.5
H_4	4.0	1.6	1.6
Cl	35.5	14.1	—
S_2	32.0	12.7	13.3
O_6	48.0	19.1	—
Ag	108.0	43.0	43.1
	<hr/>	<hr/>	
	251.5	100.0	

The aqueous solution of this salt is rapidly decomposed by heat, especially at the boiling temperature, with separation of chloride of silver, isethionic acid being doubtless reproduced; but the decomposition is never complete, even after the heating has been continued for several days.

The aqueous solution of chlorethyl-sulphuric acid obtained by precipitating the silver-salt with sulphuretted hydrogen, has a strong acid reaction, and sustains a boiling heat without alteration. When concentrated by evaporation, finally in vacuo over oil of vitriol, it crystallizes in long colourless prisms, which are highly deliquescent, and melt at a moderate heat.

The salts of chlorethyl-sulphuric acid are easily, and to all appearance completely, decomposed by boiling with free alkali, yielding a metallic chloride and probably an isethionate. Carbonate of potash produces the same decomposition at the boiling heat.

Attempts to replace the chlorine of chlorethyl-sulphuric acid by hydrogen have, to a certain extent, given negative results. The free aqueous acid boiled with zinc, gives off a large quantity of hydrogen, without forming a trace of hydrochloric acid. Addition of sulphuric acid increases the evolution of gas, but even in this case the hydrogen does not remove any chlorine from the acid. Neither is any decomposition produced in the acid solution by the hydrogen evolved by a powerful voltaic current with two anal-

gamated zinc plates as the electrodes. The replacement of the chlorine by hydrogen is, however, easily effected by the electrolysis of a weak alkaline solution of an alkaline chlorethyl-sulphate, or by treating the soda-salt in the cold with sodium-amalgam.

In this respect, chlorethyl-sulphuric acid exhibits considerable resemblance to the homologous compound, chlormethyl-sulphuric acid, which I obtained in 1845 from trichlormethyl-sulphuric acid, and to which I then gave the name of chlorelayl-hyposulphuric acid.*

TAURINE

It has already been observed that chlorethyl-sulphuric acid is converted into taurine by the action of ammonia. The transformation is easily effected as follows: Dry chlorethyl-sulphate of silver is sealed up in a strong glass tube, with a large excess of the strongest aqueous ammonia,† and the clear saline solution which is immediately formed on agitation is heated to 100° C. for several hours. The liquid remains unclouded, but, if subsequently evaporated over the water-bath, deposits a considerable quantity of chloride of silver. The dry residue dissolves in water, with the exception of the chloride of silver; the solution still retains a very small quantity of silver, which is best removed by adding a drop of hydrochloric acid immediately after the residue is dissolved.

The clear, slightly acid filtrate is evaporated to a small bulk, and mixed with strong alcohol, which precipitates a considerable quantity of taurine. The crystalline precipitate thus formed always contains, besides taurine, a variable quantity of another substance, which, when the whole is recrystallized from water, mixes with the beautiful crystals of taurine, in small white, opaque, crystalline nodules; this substance also gives off ammonia when boiled with potash-ley. I think it probable that this compound is the amide

of taurine, $C_4 \left\{ \begin{array}{l} H_4 \\ H_2N \end{array} \right\} \left\{ \begin{array}{l} S_2O_4 \\ H_2 \end{array} \right\} N$, mixed perhaps with the amide

of isethionic acid $C_4 \left\{ \begin{array}{l} H_4 \\ HO_2 \end{array} \right\} \left\{ \begin{array}{l} S_2O_4 \\ H_2 \end{array} \right\} N$.

* Ann. Ch. Pharm. liv, 168, ff.

† With alcoholic ammonia, the product obtained is not taurine, but another crystalline compound, not yet investigated.

To remove this adventitious substance, the impure taurine precipitated by alcohol was boiled with potash-ley (in another preparation the same treatment was immediately applied to the crude solution of taurine filtered from the chloride of silver after addition of hydrochloric acid) till the odour of ammonia was no longer perceptible, and the highly concentrated alkaline solution was then mixed with about twenty times its volume of absolute alcohol, which, as already remarked, does not precipitate taurine from its alkaline solutions. The clear filtrate, diluted with water, evaporated, slightly acidulated with hydrochloric acid, and again evaporated to a small bulk, yields, on addition of a large quantity of strong alcohol, a copious crystalline precipitate of taurine, contaminated only with a small quantity of chloride of potassium. A better method of precipitating the taurine from its alkaline alcoholic solution might perhaps be to pass carbonic acid into it. By recrystallization from water, it is ultimately obtained in large hard crystals, and perfectly pure.

I have subsequently found that the crude chlorethyl-sulphuric acid obtained by treating the chloride of chlorethyl-sulphuric acid with water, may be used, instead of the silver-salt, for the preparation of taurine. The liquid, after being freed by evaporation from admixed hydrochloric acid, is to be neutralized with ammonia, and the ammonia-salt evaporated to dryness, and heated for some time to 100° C., in a hermetically sealed tube, with excess of saturated aqueous ammonia. The resulting solution is then to be treated in the manner above described, excepting that the larger quantity of sal-ammoniac which it contains must be removed by boiling with hydrated oxide of lead.

Taurine prepared by either of these processes agrees in every respect with that which is obtained from ox-bile, as I have convinced myself by comparative experiments. Analysis gave the following numbers:

0.3855 grm. taurine burnt with oxide of copper in a tube containing chromate of lead and metallic copper at its open end, finally in a stream of oxygen, gave 0.2715 grm. carbonic acid and 0.199 water = 19.3 p. c. carbon and 5.7 p. c. hydrogen.

0.3955 grm. ignited with carbonate of soda in a stream of oxygen, yielded 0.743 grm. sulphate of baryta = 25.8 p. c. of sulphur.

The formula $\text{HO.C}_4 \left\{ \begin{array}{c} \text{H}_4 \\ \text{H}_2\text{N} \end{array} \right\} [\text{S}_2\text{O}_4]\text{O}$ requires

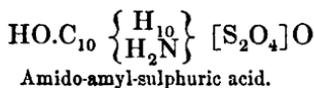
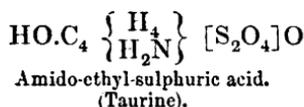
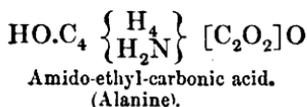
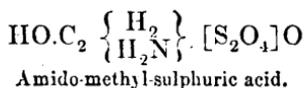
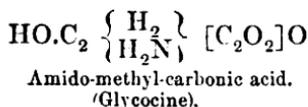
	Calculated.		Found.
C ₄	24	19·2	19·3
H ₇	7	5·6	5·7
N	14	11·2	—
S ₂	32	25·6	25·8
O ₆	48	38·4	—
	125	100·0	

Glycocine, $\text{C}_4\text{H}_5\text{NO}_4$, and taurine, $\text{C}_4\text{H}_7\text{NS}_2\text{O}_6$, which exist in bile, together with cholalic acid—doubtless in the same state of combination as glycocine and benzoic acid in the hippuric acid of urine—appear like heterogeneous compounds, when regarded merely according to their empirical formulæ; nevertheless, they are nearly related to one another, as shown by the simple mode of formation of taurine just described.

If glycocine be regarded as amido-acetic acid, that is, as carbonic acid in which one of the extra-radical oxygen-atoms is replaced by amido-methyl, then taurine must be regarded as an analogous derivative of sulphuric acid, excepting that one of the extra-radical oxygen-atoms is replaced by amido-ethyl instead of by amido-methyl, as shown by the following formulæ:



Since it is known that, besides glycocine, many similarly constituted homologous derivatives of the fatty acids—especially leucine (amido-propionic acid)—are widely diffused in the animal body, the observation that the functions of taurine in the bile-compounds, is precisely similar to that of glycocine, lends some degree of probability to the supposition that the animal body contains, besides taurine, other similarly constituted homologous derivatives of sulphuric acid, especially amido-methyl-sulphuric acid, the direct analogue of glycocine, and amido-amyl-sulphuric acid, analogous to leucine, both of which compounds perhaps enter into the composition of many animal substances rich in sulphur, such as horn, hair, &c.



I regard it as by no means a thankless problem to search for these and other compounds homologous and analogous to taurine in the animal body, and especially in the secretions which are peculiarly rich in sulphur. From the above-described mode of formation of taurine, we might also expect that the artificial preparation of these other compounds would not be difficult. I am at present engaged with the attempt to convert chlormethyl-sulphuric acid—a compound very closely resembling chlorethyl-sulphuric acid—by the action of ammonia, into amido-methyl-sulphuric acid, an acid which may be expected to exhibit considerable resemblance to taurine.
