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Taurine

George William Schnabel
Union College - Schenectady, NY

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TAURINE

by

George William Schnabel

A thesis presented to the Department of Chemistry of
Union College in partial fulfillment of the requirements for
the degree of Bachelor of Science.

By George William Schnabel

Approved by H. F. Herbrandson

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INTRODUCTION

This thesis is a primary investigation into a new synthesis of taurine. The sulfite of ethylene glycol is reacted with ammonium hydroxide to produce taurine. This method of synthesis was suggested by Dr. Harry Herbrandson.

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HISTORICAL

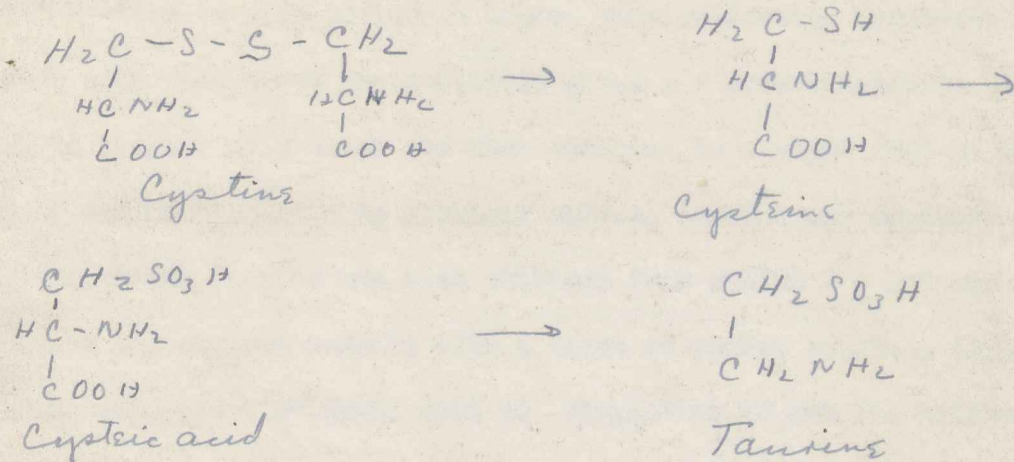
The discovery of taurine is credited to Leopold Gmelin (1). In an investigation into various constituents of ox bile (2) a nitrogen-containing weakly acidic substance which is soluble in water but almost insoluble in alcohol was isolated. It was not until a later date that the sulfur in the compound was noted (3).

Taurine or 2-aminoethane-1-sulfonic acid is present in the bile salts as the amide of cholic acid (4). The function of the bile in digestion is well known (4). Bile production is essential for normal digestion of fats and the absorption of fatty acids. Its function in digestion is that of emulsifying fats and activating pancreatic lipase. The absorption of fat-soluble substances, ^{such} as carotene, vitamins A, D and K is dependent upon the bile salts. Aside from digestion the bile acts as an antiputrefying agent *in* the small intestine and also is mildly cathartic.

Taurine is found as a natural product in many other places. It is found in the brain (5), in lungs, flesh extracts of oxen, shark blood; in the liver, spleen, and kidney of the ray; in muscles, oysters, and molluscs (6). It has also been separated from ox bile (2) (7). The best natural source is said to be the large muscle of the abalone (8). Seventy-four kilograms will give 362 grams of taurine.

Taurine is probably produced in the animal body from waste sulfur-containing materials as they pass through the liver (9). Cystine is probably the precursor of taurine in the liver, but the intermediate compound (apparently not cysteric acid) has not been identified. Taurine is related

to the amino acids cystine and cysteine by the following in vitro reactions (9);



Friedmann (10) converted cystine to taurine with fair yields (59%).

In a paper on the oxidation of sulfhydryl compounds by hydrogen peroxide cysteine is converted to taurine with 40% yields (11). Then White and Fishman (12) modified a preparation by Friedmann (10) and obtained taurine from cysteic acid. None of these methods is very practical.

Taurine's synthesis need not be confined to naturally occurring substances but may be approached from other synthetic materials. Kolbe (13) converted isethionic acid to 2-chloro-ethylsulfonyl chloride, hydrolyzed this product to 2-chloro-ethylsulfonic acid and obtained taurine from this by this action of aqueous ammonia. Gabriel prepared it from ethylene imine and sulfur dioxide (14) and also by the oxidation of 2-mercaptothiazoline with bromine water (15). Augies (16) reports a quite complex preparation by the sulfonation of acetaldehyde with chlorosulfonic acid followed by the formation first of the aldehyde ammonia, then of the imido compound and finally by reduction to the amino compound. Reyehlen (17) discovered a synthesis which, in turn, received improvements by Cortese (18), then Bessaigne (19). He obtained taurine from bromo-ethylamine and ammonium sulfite. Taurine was prepared in considerable quantity from the sodium salt of taurocholate (20). In Organic Syntheses (21) a 44-51% conversion to taurine

is outlined. The product is obtained by reacting ethylene bromide with sodium sulfite to give sodium 2-bromo-ethylsulfonate. Treatment of this product with phosphorus pentachloride gives 2-bromoethylsulfonyl chloride which is treated with water and then ammonia. In a paper (22) on the addition of sodium bisulfite to alkylene oxides, taurine was obtained from ethylene oxide. Taurine was also obtained from sodium 2-hydroxy-ethylsulfonate and aqueous ammonia with a trace of sodium sulfite. (23). Wertheim (24) added sulfuric acid to vinylamine to get it. Goldberg (25) synthesized taurine by adding sulfuric acid to ethylene hydroxy amine and then adding sodium sulfite. Heath and Piggott (26) reduced 2-nitroethanesulfonic acid with Raney nickel to give a 65% conversion.

Schick (27) has presented the best synthesis. Ethylene chloride is sulfonated with sodium sulfite and then aminated with ammonia. He reports a ninety per cent conversion.

Taurine is reported to decompose at $300-305^{\circ}$ (17) and $327-328^{\circ}$ (12). In a paper (28) on the titration curves of taurine and cysteic acid, taurine is reported to have:

$$K_a = 1.8 \times 10^{-9}$$
$$K_b = 3.0 \times 10^{-13}$$

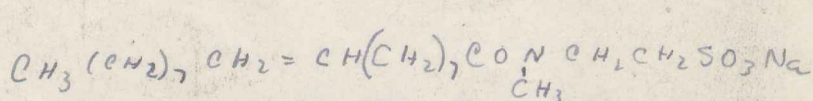
The heat-capacity and entropies have also been calculated (29).

The zwitter-ion hypothesis is qualitatively applicable to taurine and the results of a paper by Carr and Shutt (30) indicate that the whole of the ampholyte is converted to the zwitter-ion form only over an extremely narrow range of p H (about 2.4 to 2.6).

It has been demonstrated that taurine will slightly increase respiration (31), lower blood sugar (32). It has no effect on liver-fat deposition (33) and blood pressure (32).

Taurine as a component in some, ~~as~~ wetting, cleansing, dispersing, and bleaching agents, ^{It} has commercial potentialities. Amides derived from the combination of taurine and its N-alkyl derivatives with high-molecular-weight, fatty, or sulfonic acids such as ~~de~~ or octadecane-sulfonic are of value as wetting, cleansing and dispersing agents (46), (47). Of compounds of this type is one marketed as Igepon T, which

has the structure:



This is a neutral salt with good detergent properties which is stable in both acidic and alkaline solutions (47). The N-chloro compounds,



Because it was necessary to prepare the sulfite of ethylene glycol used in the reaction under consideration in this thesis, a literature search was conducted to find a suitable method for the preparation of the sulfite.

Organic sulfites are prepared by the action of thionyl chloride on various hydroxy compounds. According to the literature, the reaction appears to be general for primary and secondary alcohols, phenol, and polyhydroxy compounds in which the hydroxyl groups are adjacent.

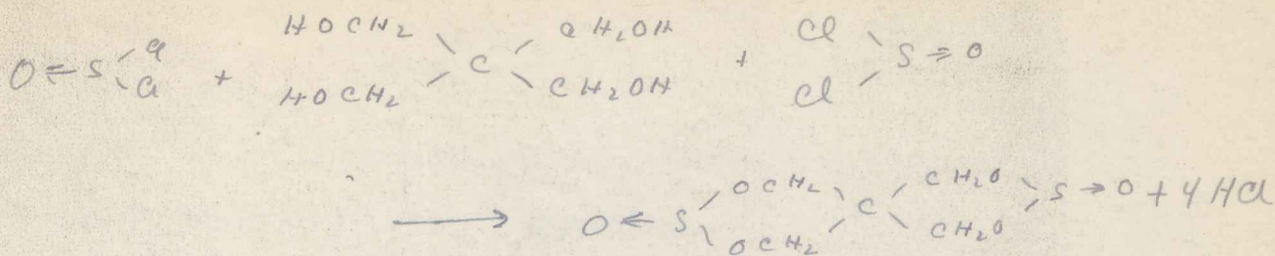
Majima (34) in a paper on the action of thionyl chloride upon polyhydroxy alcohols demonstrates:



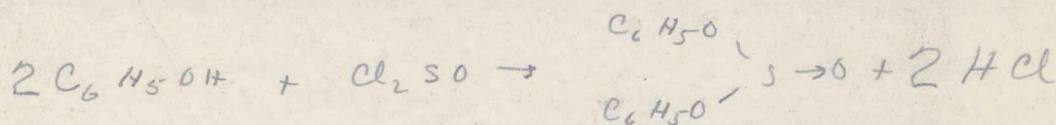
Richter (35) reports in an article about the aromatic esters of sulfurous acid:



Orthner (36) reporting on acetone compounds of pentaerythritol shows:

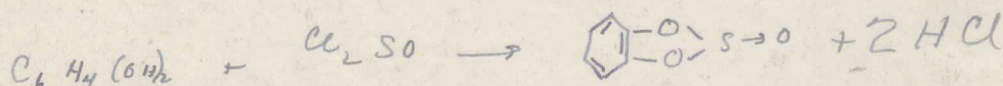


Richter (35) in his report shows:

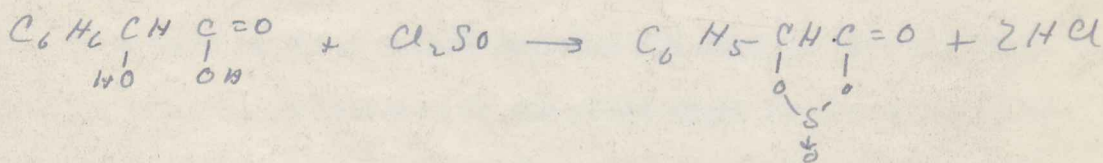


Green (37) in an article on aromatic thionyl and chlorothionyl

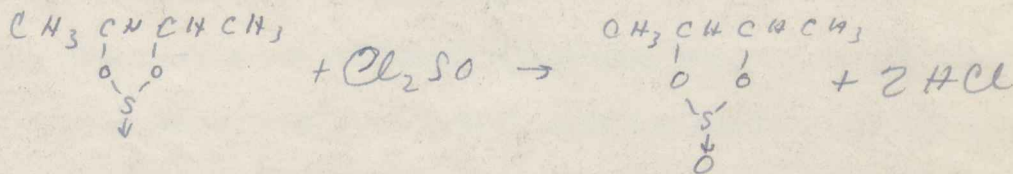
Derivatives gives:



On the paper on the action of thionyl chloride on phenyl-glycolic acid, Garre and Liebermann (38) demonstrate:



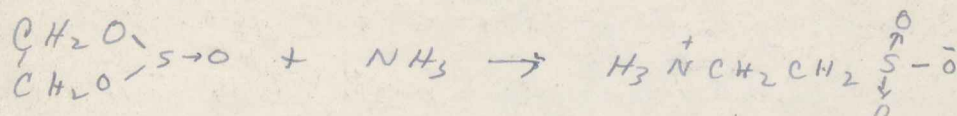
Denivelle reports in an article on 2,3-Butanediol and its esters:



Various sulfito preparations are reported by: Voss and Flanke (40), Barkenbus and Owen (41), Gerrard (42), Bert (43), and Suter and Gerhart (44).

DISCUSSION

This thesis has demonstrated that taurine may be obtained by reacting ethylene sulfite with ammonia. The equation for this reaction may be written:



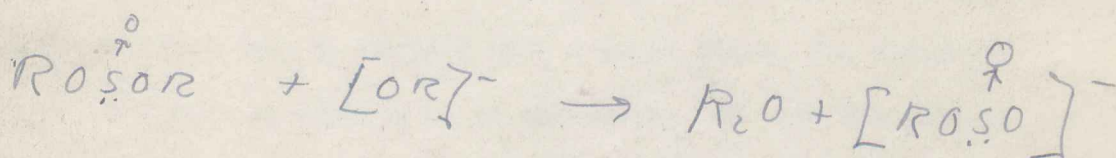
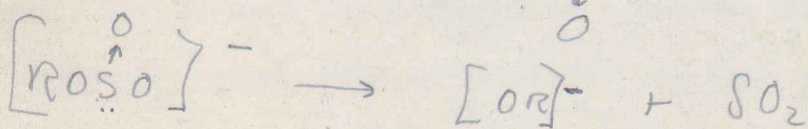
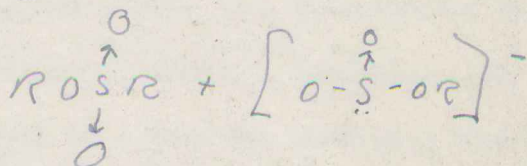
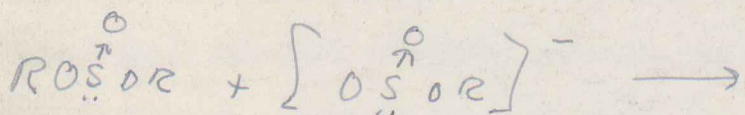
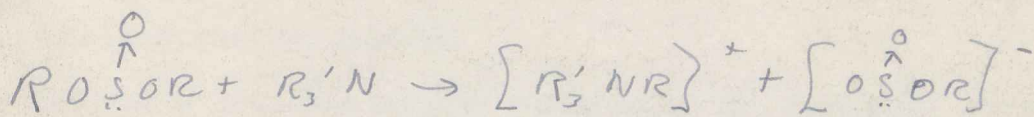
RUN NUMBER	TEMP. OF RX. (°C)	% YIELD	M.P. (UNCORR.)	QUAL. TEST
1	10-20	12.5	345-65°	+
2	7	13.0	345-60°	+
3	20	9.6	345-65°	+
4	40	19.5	345-55°	+

The yields by this reaction varied from 9.6 per cent to 19.5 per cent. From the data in table I, an increase in the yield might be accomplished by raising the reaction temperature. Conducting the reaction with anhydrous ammonia might contribute to higher yields.

The decomposition point was found higher than reported in the literature because an aluminum block was used to take the readings and the thermometer was uncorrected. The blue color obtained from the phenol-calcium hypochlorite mixture was considered evidence of the presence of taurine (27).

The mechanism of this reaction has not been worked out. However a possible solution to this may be the mechanism suggested by Bissinger, Kung, and Hamilton (50) when they observed an ether and sulfur dioxide as by-

products to a similar rearrangement of alkyl sulfites to alkane sulfonate esters. The postulated rearrangement is:



EXPERIMENTAL

Preparation of ethylene sulfite:

Ethylene sulfite was prepared according to the procedure of Suter and Gehart (44). One mole of thionyl chloride was added dropwise over a half hour period to a mole of ethylene glycol in a three-necked flask fitted with a dropping funnel, mechanical stirrer, condenser, and thermometer, the condenser was connected to a trap for absorbing hydrogen chloride. The mixture while being agitated was kept at approximately 50° by first applying an ice bath and then, once the evolution of hydrogen chloride was started, by heating with a small flame. The dissolved hydrogen chloride ^{was} removed by an aspirator, and then the mixture was fractionated. This gave 92.6 grams boiling between 168-174° for an 86% yield of ethylene sulfite.

Carlson and Cretcher (45) report b.p. 86-88° (38 m m.). Majima (34) reports b.p. 64-66.5° (12 m m) and b.p. 169-172°.

Preparation of taurine:

Ten cc. (approximately 14 gm.) of ethylene sulfite was added dropwise with constant mixing to 100 cc. of concentrated ammonium hydroxide in a three neck flask fitted with a dropping funnel, mechanical stirrer, and a thermometer. The mixing reactants were brought up to 40° by a small flame. The mixture was maintained at that temperature and the mixture was cooled with an ice-bath when necessary. The temperature throughout the reaction was not allowed to vary more than one degree. The excess ammonia was then taken off under reduced pressure; the water was taken off by applying a flame and

reduced pressure. The water was removed until there was a thick white paste left. The vacuum was broken and the residue taken up in 10 cc of boiling water. Fifty cc. of absolute ethanol was added and the mixture was allowed to stand over night. By the following day a residue was formed which was filtered off and dried at a hundred degrees. The residue consisted of 3.09 grams of white material which was found to decompose as it melts at 345° to 355° (uncorr.). An aluminum block was used to take the melting points.

A qualitative method for determining the presence of taurine (27) was used. It consisted of adding a small amount of the product to twenty cc. of water in a flask containing 5 cc. of 1% phenol solution. This was mixed and ca. 0.1 gm. of calcium hypochlorite was added and shaken with the solution. The flask was immersed in a boiling water bath for approximately 3 min. then cooled. A deep blue color, indicative of the presence of taurine, appeared.

SUMMARY

The synthesis of taurine or 2 - aminoethane- 1 - sulfonic acid has been accomplished by the reaction of the sulfite of ethylene glycol with ammonia.

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