PREPARATION OF 2-AMINOETHYLSULFONIC ACID

Galuh Widiyarti[*)], Muhammad Hanafi, Siti Isnijah, L. Broto Sugeng Kardono, Ermawan, Ngadiman, and Andini Sundowo

Research Center for Chemistry (RCChem), LIPI, PUSPIPTEK Serpong, Tangerang , Banten, Indonesia

[*)]*E-mail: galuh_w01@yahoo.com*

Abstract

Preparation process of 2-aminoethylsulfonic acid (taurine) from ethanolamine, sulfuric acid and sodium sulfite has been studied. The process involves two steps of reactions, the first was esterification of ethanolamine (H_2N-CH_2-CH_2-OH) with sulfuric acid to produce the intermediate product of 2-aminoethyl ester (H_2N-CH_2-CH_2-OSO_3H) which then was extended to the second step by sulfonation with sodium sulfite to produce 2-aminoethylsulfonic acid (H_2N-CH_2-CH_2-SO_3H). These two process conditions were observed by varying mole ratio of reactants, temperature and time period of reactions. Taurine product was qualitatively analyzed using ^{1}H-NMR and LC-MS. Physical-chemical analysis were done by observing its melting point and determining its water, chloride and sulfate contents. Its melting point, water content, and sulfate content were 290^{o}C, 0.303%, and 3 ppm, respectively, while its chloride content was undetected. After purification, the yield of process was 25.57%.

Keywords: 2-aminoethylsulfonic acid, esterification, sulfonation, ^{1}H-NMR, LC-MS

1. Introduction

Most of the pharmaceutical industries in Indonesia depend on imported supply of their raw materials and their manufacturing were mainly on process of formulation. Long-term economic crisis affected the industries and effort to develop supply on industrial chemicals locally especially for pharmaceutical industries should be encouraged. Research on this area is really needed.

One of the imported materials is 2-aminoethylsulfonic acid (taurine) which is as amino acid composed of protein which is useful in metabolism process. It is also needed as a nutrition for brain in growth period, to stimulate a better condition of heart and eye [1]. Taurine deficiencies causes the disease related with the weakness of brain such as epilepsy, growth retardation and also gives negative effect on retina such as cardiomyopathy and retinal degeneration [2]. Reported other function of taurine is as an antihemolitic, antioxidant, cancer inhibitor, cardiac and hypocholesterolemic [3]. Besides as a pharmaceutical raw material, it is able to be used as intermediate surfactant [4]. Taurine is used as an energy supply in functional drinks which are available in Indonesia. Demand on taurine in Indonesia reached 4.500 tons/year and was supplied completely by import.

Taurine is derived from amino acid which has a simple molecular structure. Many procedures to prepare of 2-aminoethylsulfonic acid (taurine) mostly consist of two steps of reaction. Ethylene chloride (Cl-CH_2-CH_2-Cl) reacts with sodium sulfite to produce 2-chloroethylsulfonic acid (Cl-CH_2-CH_2-SO_3H) after refluxing for 72 hours and then it is reacted with ammonia to produce 75% of taurine. Reaction of ethanolamine and tionylchoride produces 2-chloroethylamine (80%) and then sodium bisulfite is added to produce taurine (40%) [5]. Taurine can also be prepared by ethanolamine and diethyl carbonate to produce 2-oxazolidone, then sodium hydrogen sulfite is added to produce 85% of taurine [6-11]. From the three procedures mentioned above, the second produces low yield while the first and third procedures involve starting materials which are difficult to obtain and carcinogenic. More over, the reaction takes long time, at high temperature and is in gas phase. If ethylene chloride and sodium chloride are used the reaction is difficult to be controlled to produce 2-chloroethyl sulfonic acid (Cl-CH_2-CH_2-SO_3H) and purification is also difficult. If thionyl chloride is used, this material is difficult to obtain and carcinogenic.

Based on literature study, we are conducting a research work to prepare 2-aminoethylsulfonic acid (taurine) in a laboratory scale. Technical grade raw materials of ethanolamine, sulfuric acid and sodium sulfite were

used. Better yield was expected to be obtained and production cost would be lower.

The aim of this research was to obtain the optimum condition of laboratory scale process for the preparation of 2-aminoethylsulfonic acid (taurine).

Materials and Equipments. Chemicals used in this study were technical grade of ethanolamine, sulfuric acid and sodium sulfite. Chemicals used for qualitative analysis was pro analysis grade from E. Merck or Aldrich.

The equipment used for preparation of 2-aminoethylsulfonic acid (taurine) consisted of three neck glass reactor, funnel, condenser, thermometer and hotplate.

2. Experiment

Preparation of 2-aminoethylsulfonic acid (taurine) was conducted in two step reactions. First, the esterification of ethanolamine with sulfuric acid followed by sulfonation as the second reaction. The two reactions were conducted under varying mole ratio of reactants, temperature and time period of reaction. Esterification of ethanolamine was exothermic reaction and cooling of reactor was needed to control the temperature. Mole ratio of reactants between ethanolamine and sulfuric acid was varied: 1:1 up to 1:1.7, time period of reaction 3-8 hours. The addition of sulfuric acid was done carefully and stirred in 500 rpm. The intermediate product of 2-aminoethyl ester was produced and washed by using ethanol to remove the excess of sulfuric acid. Then, it was filtered and dried. The reaction was studied by observing periodically the change of acidity and temperature of reaction mixture. The reaction of sulfonation was conducted at 60-100^{o}C with the mole ratio of reactants between the 2-aminoethyl ester and sodium sulfite was 1:1 up to 1:1.7. The time period of reaction was 3-8 hours. The reaction mixture was sampled periodically and analyzed qualitatively with Nuclear Magnetic Resonance (^{1}H-NMR). The purification of product was done by washing with methanol and hydrochloric acid and followed by recrystallization.

Molecular weigh of product was analyzed by using LC-MS. Physical-chemical properties of product was determined by observing its melting point and analysis of water, sulfate and chloride content.

3. Results and Discussion

It was showed that each mole ratio has same pattern that after 5 hours reaction there were no change in acidity and also no increase in temperature. Figure l shows that during the addition of sulfuric acid, there was decreasing of acidity from pH 13 to pH 4. The temperature was also changed. After 1.5 hours from starting reaction the temperature increased from 21 to 60^{o}C, followed by decreasing temperature to 28^{o}C. After 5 hours reaction, there were no changing of acidity as well as temperature of reaction mixture. It indicated that after 5 hours the reaction condition was optimum.

By using time period of 5 hours the reaction conversion for each mole ratio was observed. Mole ratio of reactants between ethanolamine and sulfuric acid 1:1.5 was the optimum condition as indicated in Figure 2.

It is showed that the conversion of esterification using mole ratio 1:1.5 and time period of 5 hours was 81.33% and there was no increasing of conversion for higher fraction of sulfuric acid. It could be concluded that mole ratio of ethanolamine and sulfuric acid 1:1.5 was the optimum mole ratio for esterification reaction.

The second reaction, sulfonation of 2-aminoethyl ester with sodium sulfite was sampled every hour for each mole ratio of reactant as well as temperature reaction. It were analyzed with ^{1}H-NMR. ^{1}H-NMR spectrum showed that 2-aminoethylsulfonic acid (taurine) has

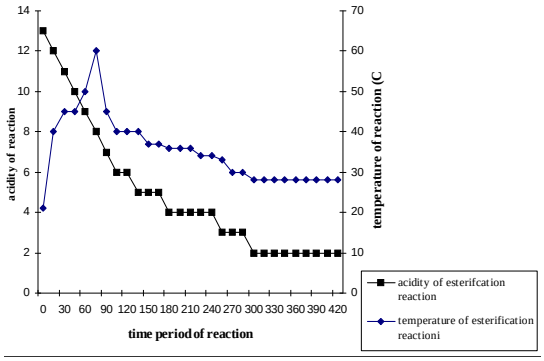

Figure 1. The Acidity and Temperature of Esterification Reaction of Intermediate Product of 2-Aminoethyl Ester

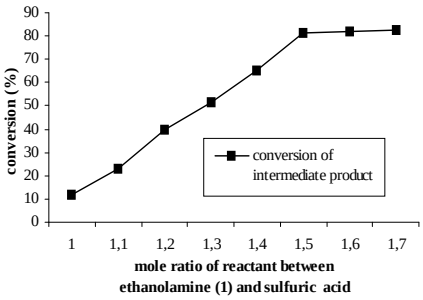

Figure 2. The Conversion of Esterification Reaction of Intermediate Product of 2-Aminoethyl Ester

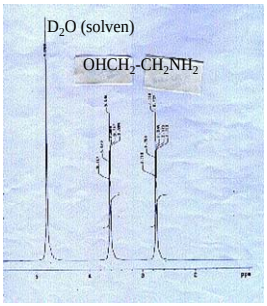

Figure 3. ^{1}H-NMR Spectrum of Ethanolamine

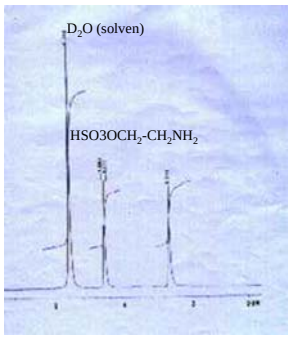

Figure 4. ^{1}H-NMR Spectrum of Intermediate Product of 2-aminoethyl ester

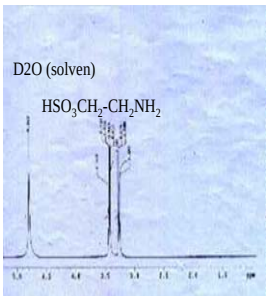

Figure 5. ^{1}H-NMR spectrum of 2-aminoethyl sulfonic acid product.

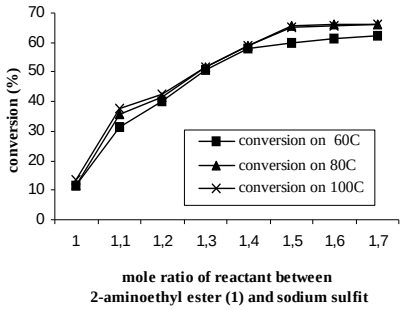

Figure 6. Second reaction optimization, sulfonation reaction at 60 – 100°C

been produced in 5 hours reaction which was indicated by methylene ($HOCH_2$) and (NH_2CH_2) peaks at 3.443 ppm and 3.283 ppm, respectively (Fig. 5). The peak was changed, the peak of reactant ethanolamine ($HOCH_2$) was at 3.608 ppm and (NH_2CH_2) was at 2.729 ppm (Fig. 3), and an intermediate product ($HOCH_2$) was at 4.283 ppm and (NH_2CH_2) was at 3.343 ppm (Fig. 4). It can be noted that the time period of 5 hours was sufficient for the second reaction.

The conversion of second reaction for each mole ratio of reactant at 60-100°C temperature with time period of 5 hours were determined and the results shown in Figure 6.

It is noted that the optimum condition of the sulfonation reaction of the intermediate 2-aminoethyl ester with sodium sulfite to produce 2-aminoethylsulfonic acid (taurine) was at 80°C, time period of 5 hours and mole ratio of reactant 1:1.5. After evaporation of reaction mixture and followed by crystallization, crude taurine was produced. The conversion of the sulfonation reaction was 65.51%. By using higher temperature (100°C) and higher fraction of sodium sulfite (1:1.6 and 1:1.7) there was no significant increasing of yield. It could be concluded that the optimum condition of sulfonation was at 80°C. After product purification by washing with hydrochloric acid and methanol and followed by recrystallization, total yield was 25.57%. In laboratory scale, the lost of processing was considered high.

^{1}H-NMR spectrum of the reactant, intermediate product and taurine product showed that conversion of first and second reactions were 100%, its mean that all of reactant was converted to each product. Figure 4 for ^{1}H-NMR spectrum of intermediate product from the first reaction showed that the peak was a 2-aminoethyl ester's peak, its mean that all of ethanolamine converted to 2-aminoethyl ester as an intermediate product. It is the same for the second reaction, that 2-aminoethyl ester was converted to taurine as the main product, which was shown in figure 5. The result for weight of product estimation indicated that conversion for first reaction was only 81.33%, and for second reaction was only 65.51%, it means that overall reaction gave a relatively high loss for each product. This result is probably due to the formation of byproduct ethyleneimine and polymerization of intermediate product if pH and temperature of the reaction mixture was more than 7 and 100°C. It is caused by ineffectiveness of purification and crystallization of intermediate product, and ineffectiveness of purification of taurine product in which product was washed using HCl and methanol and recrystallization which has an effect for the conversion of pure taurine, it was only about 25.57%.

Analysis of the intermediate product and purified taurine by using LC-MS showed the molecular weigh of 141.0299 and 125.0326 respectively. In literature the molecular weight of the intermediate product of 2-aminoethyl ester and taurine were 141.1414 and 125.1422. Physical-chemical analysis showed that the melting point of the intermediate product was 75^{o}C, while water and sulfate content were 1.58% and 7.02%, respectively. Due to high sulfate intent in intermediate product, purification of the intermediate product was necessary by washing with ethanol. Purification of taurine was done by washing with hydrochloric acid and methanol followed by recrystallization. Purified product has melting point of 290^{o}C with water and sulfate content of 0.303% and 3.3 ppm respectively. Chloride was not detected in final product. In this observation heavy metal contents have not been analyzed.

4. Conclusion

2-aminoethylsulfonic acid (taurine) as one of the pharmaceutical industrial materials can be prepared from technical grade of ethanolamine, sulfuric acid and sodium sulfite as raw materials with 2 steps of reaction, *i.e* esterification and sulfonation reactions. The optimum condition of reaction for esterification were at mole ratio of reactants between ethanolamine and sulfuric acid 1:1.5, and time period of 5 hours. While the optimum condition of sulfonation were at 80^{o}C, mole ratio of reactants between 2-aminoethyl ester and sodium sulfite 1:1.5, and time period of 5 hours. In these conditions it could be produced taurine with the conversion of 65.51% and total yield after purification was 25.57%. The melting point of prepared 2-aminoethyl sulfonic acid (taurine) is 290^{o}C with water and sulfate contents of 0.303% and 3.3 ppm, respectively.

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