



NOTE

Synthesis of Mercaptoethylammonium Chloride in Alkaline Medium

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(Received: 11 May 2011;

Accepted: 24 February 2012)

AJC-11114

A new way synthesis of mercaptoethylammonium chloride is reported. Using NaOH replace HCl, the results present that the target product can be made in alkaline medium and the velocity of new way is much faster than the tradition one, which is hydrolyzed at high pressure. ¹H NMR and IR characterized the structure of the product.

Key Words: Alkali medium, Mercaptoethylammonium chloride, 2-Mercaptothiazoline, Synthesis.

With the nuclear crisis in Japan growing daily, mercaptoethylammonium chloride (systematic name: cysteamine HCl, 2-aminoethanethiol hydrochloride), as a radiation-protective agent has caused worldwide concern. It has received particular attention as an important medicine intermediate and biochemical reagent that plays a significant physiological function and has strong complexation ability. It is widely used in cosmetics¹, medicaments^{2,4}, animal fodder additives^{5,6}, a new thiol cationic surfactant⁷, biomaterials used in alkylation, biochip and biochemical drug making^{8,9}, biomolecules¹⁰ and multifunctional proteins.

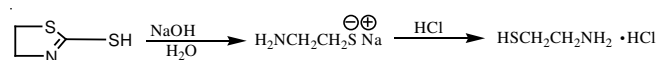
The traditional synthesis of mercaptoethylammonium chloride utilizes 2-mercaptothiazoline is opened in an HCl solution at high pressure and temperature¹¹. This method, however, requires a long production cycle. Typically, to synthesis 1 mol of mercaptoethylammonium chloride, a standard chemical synthetic procedure could take as long as 45 h. As well because an autoclave is necessary in the procedure, production costs and security problems cannot be ignored. In the work, alkali solution is employed in synthesis of Mercaptoethylammonium chloride.

All the reagents were used without any modification. During the experiments, distilled water was used. The experiment was conducted as follows: A mixture of 2-mercaptothiazoline and NaOH solution was stirred in a three-necked bottle and allowed to react for several hours. Hydrochloric acid was then added to the bottle until the pH was 3. The mixture was cooled, crystallized and filtered. The residue was swilled with absolute alcohol, after which the alcohol was set aside. Then, the filtrate was vacuum distilled and the solid was again swilled with

absolute alcohol. The alcohol was evaporated under reduced pressure, yielding a pale yellow solid. The solids were placed in a vacuum drying box and dried for 4 h at 60 °C.

The overlays of the NMR spectra obtained in D₂O are shown that the methylene resonances (the hydrion of α-C at 3.067 ppm and the hydrion of β-C at 2.697 ppm) can be used to determine the various species in solution. The IR spectrum of the product showed an absorption band at 3004 cm⁻¹ (NH₂), which superposed with the absorption band of the CH₂-CH₂ group and the absorption band of S-H at 2487 cm⁻¹.

In alkali medium, a large amount of OH⁻, which has stronger nucleophilicity than H⁺, is present. This is helpful for the ring opening reaction of 2-mercaptothiazoline. The acidity of mercaptans is much stronger than that of alcohol. After reaction of mercaptans with NaOH, a stable salt is produced. When 2-mercaptothiazoline is fixed in an alkali solution, the reaction system becomes a single phase one and the reaction proceeds rapidly. During the reaction process, some acidic gases are produced but these can be absorbed by the solution. The reaction balance thus moves forward and the process is shortened compared to other methods. The mechanism of the reaction is as follows:



Concentration of sodium hydroxide solution: Firstly, the reaction was carried out at different concentration of sodium hydroxide solution and it was found that the reclamation rate was improved with increasing concentration of sodium hydroxide solution. A maximum was reached when the

concentration of sodium hydroxide solution was 30 % (Fig. 1). Under this condition, the influences of 2-mercaptothiazoline hydrolyzed in alkali medium were investigated and the result was showed that the new method has four keys *i.e.*, concentration of sodium hydroxide solution, reaction time, the mole ratio of 2-mercaptothiazoline to sodium hydroxide and product purity.

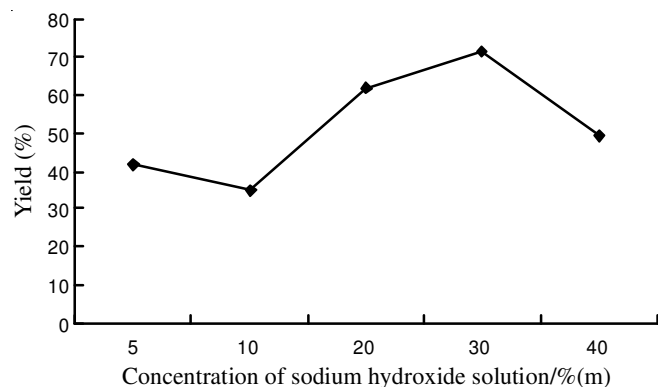


Fig. 1. Effect of concentration of sodium hydroxide on yield

Reaction time: Fig. 2 shows the trend of reclamation rate. And the rate increases as the reaction time increases. A maximum is reached at 3 h, after which the rate decreased. The amido lost in alkali medium, which reduces the yield. Cross linking of SH-, which forms insoluble substances, also decreases the rate and eliminates the reaction liquids.

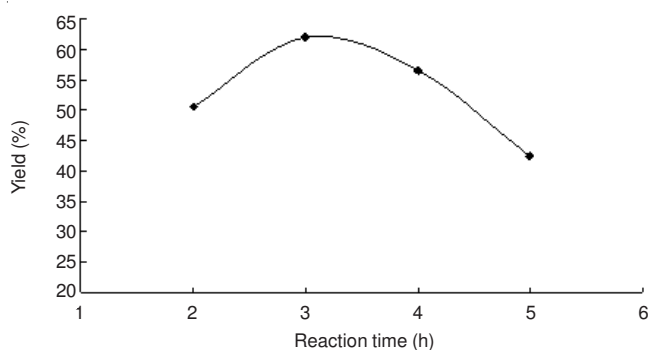
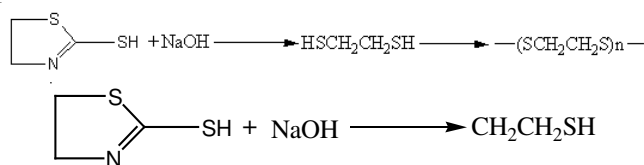


Fig. 2. Effect of reaction time on yield

Mole ratio of 2-mercaptothiazoline to sodium hydroxide:

As Fig. 3 shows the mole rate of 2-mercaptothiazoline to hydroxide increases with increasing mole rate, the maximum was at 1:7 and then sharply declining thereafter. If acidic gases, such as H₂S or CO₂, are formed after hydrolysis and cannot be absorbed completely, the reaction cannot proceed to completion and the rate decreases. The addition of one mole rate of NaOH completely absorbs acidic gases formed, thus increasing the rate and pushing the reaction toward completion. When the mole ratio is over 7:1, redundant OH⁻ appears in the reaction

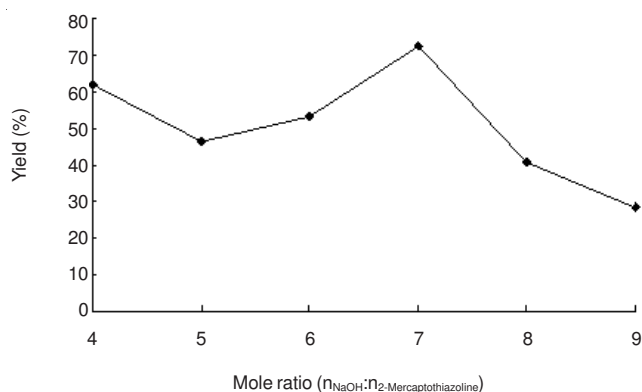


Fig. 3. Effect of sodium hydroxide on the mole rate of 2-mercaptothiazoline

system. This can attack the carbenium groups attached to S, causing side reactions to occur and the yield to decrease. The optimum mole rate of 2-mercaptothiazoline to sodium hydroxide is 1:7.

Product purification: The use of HCl to adjust the pH of the product to 3 causes a large amount of NaCl to form. Sodium chloride and mercaptoethylammonium chloride both dissolve in water, so it is difficult to separate them completely. Because mercaptoethylammonium chloride has different dissolution characteristics compared to sodium chloride, ethanol was used as a separation reagent to separate the two. The procedures for this are as follows: The salt is hydrolyzed with HCl. After cooling, the liquid is extracted and the filtrate is separated by reduced pressure distillation. The solid obtained is washed with ethanol, after which reduced pressure distillation is again performed. A waxy white solid is obtained. The ethanol recovered could be regenerated for repeated use.

Conclusion

Present method has shorter process reduced (from 45 h to 3 h) and milder conditions than the tradition one. It can be applied into some similar ring-opening reactions of heterocyclic compound.

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