SYNTHESIS OF ACETAMIDE FROM INDIGENOUS SOURCES

Z. Iqbal*, I. Khokhar, F. Deba*, E. Haq*, and A. Waheed***

*PCSIR Labs. Complex, Ferozepur Road Lahore.
**Punjab University, Lahore, 54600-Pakistan.

ABSTRACT: Acetamide was synthesized by reacting acetic acid and four brands of commercially available urea fertilizers, kisan, sona, babbar sher, engro and pure urea. Reaction conditions were optimized. Maximum yield was obtained by the reaction of equimolar acetic acid and urea samples for 4.5 hours and distilling at 190-225°C. In each set of experiments all reaction conditions were same except the reflux time. Yields obtained by using pure urea Kisan, Sona, Babbar sher and Engro urea were 89.7%, 61.6%, 63.3%, 66.8 % and 68.9% respectively. The optimum yields of the reactions were obtained. FT-IR and GLC were used for the identification and confirmation of the acetamide.

Keywords: *Acetamide, Amonia, Synthesis, Organic*

INTRODUCTION

Acetamide is an amide of acetic acid having a formula C_2H_5NO, commercially known as lipamide and schercomide (Michael and Irene, 1986). It is a neutral molecule, its acidic and basic properties being so weak that they are not manifested in water solution (Kirk and Othemer, 2002). Owing to its polarity and high dielectric constant, it acts as solvent for organic and inorganic compounds and forms many stable solvates (Jander and Winkler, 1958; Kimiko and Kenichi, 1980). Its neutral and amphoteric characteristics make it valuable as a anti-acid in the lacquer, explosives and in cosmetic industries (Isaac and Kerridge, 1988). It has been widely used as a soldering flux ingredient, as a dye solvent and in urea molding compounds (Eweka and Kerridge, 1999). Its hygroscopic properties are the reason for its use as a plasticizer in leather, cloth and various other films and coatings and as a humectant for paper (Dagang and Zhang, 2006). Other uses involve activator in bleaching liquors, as a wetting agent and penetration accelerator in dyeing, as a special food for promoting mold growth and as a raw material in organic synthesis. It is used in synthesis of many important drugs; ampicillin, cephaclor, cephalexin, cephradine, sulphacetamide, acetamidine hydrochloride and methyle amine (Maryadele *et al,* 2006). Acetamide was prepared by various ways Cheronis in 1957 prepared it from ester and ammonia, followed by the heating of ammonium acetate at 100-200°C (Cheronis, 1963). It was also prepared by the heating of acetonitrile with hot hydrochloric acid (Cheronis et al., 1965). Heating of ammonia and acetic acid also produces acetamide and this study was conducted by Cheronis and Ma (1964). It can be prepared by the dehydration of ammonium acetate (Ullmann, 2003). Acetamide and its derivatives were prepared and their anticonvulsant and antimicrobial activities were studied by Ozkanli *et al.* (1994). Acetamide has been used for the synthesis of heterocyclic compounds. (Walid and Pervaiz, 2002, Carolyn *et al.*, 2005). Its halogenated derivatives were also synthesized.(Ranjit *et al.*, 2006, Kzuhara *et al.*, 2004 and Savinkina *et al.*, 2007). It is also used in the preparation of bioactive compounds (Vasoya *et al.*, 2005) . Its hydrolysis behaviour was studied by Berg *et al.*, 2002 and Ikchoon *et al.*, 2004). Its bond lengths and strengths were studied by Matthias and Martin (2001) and Rui *et al.* (2008). Acetamide structure has been completely reviewed through spectroscopic techniques by Thomas et al.(1997). In the present studies we have prepared acetamide from the locally available urea fertilizers and acetic acid.

MATERIALS AND METHODS

The commercial grade samples of urea fertilizers (Kisan, Sona, Babbar sher and Engro) and acetic acid were purchased from the local market. Pure urea of 99.99% purity (E. Merk) was purchased from local chemical supplier.

One hundred gram urea (1.66 moles) and 100 gram acetic acid (1.66 moles) were charged into a three-necked round bottom flask. Condenser and thermometer were adjusted and temperature was raised gently. When the urea melted then the temperature was raised rapidly by controlling the thermostat of heating mantle. Heavy white fumes

of ammonium carbamate (NH_2COONH_4) along with ammonia and acetic acid started coming off. The temperature 190°C was attained in 2.0 hours. Material refluxes at this temperature (190°C) and it was maintained for thirty minutes to ensure the completion of reaction. The material was allowed to cool in the flask and then distillation was carried out. Fraction collected from 195- 225 °C, was cooled and crystals were re-crystallized by using hot methanol and diethyl ether. It was then dried in hot air oven at 60°C; yield was calculated and then stored in an airtight container.

All experiments were performed by using the same procedure except reflux time that varied from 2.0-4.5 hours. In each case reaction was performed, product was weighed and yield was calculated. Product was identified first by melting point, mixed melting point and then by using copper sulphate, phenol-hypochlorite test. Infrared spectroscopy of all the samples was performed and results were compared with the standard sample. It was observed that all samples show almost same kind of peak pattern. Three main areas were observed which were 3500 to 3100cm^{-1}, 1670-1640 cm^{-1} and 1640-1550 cm^{-1} respectively. pure acetamide also show these peaks and these comparable to each other. Then assay was performed by gas liquid chromatography.

Analysis of the acetamide

Copper sulphate test: Fifty milligram of sample was added to 2 ml of 20% NaOH solution in a test tube. A filter paper was placed over the top of the tube and crushed down around the tube. Two drops of 10% copper sulphate solution were dropped over the filter paper. Test tube was heated with a small flame for one minute. A ring of blue color was formed indicating the presence of acetamide.

Phenol- Hypochlorite test: One milliliter of 4% aquous solution was mixed with 1 ml of aquous sodium hypochlorite solution. Few crystals of the sample were dropped in to the test tube and then gently warmed. Blue color was developed indicating the presence of acetamide.

Spectroscopic analysis: Thermo Nicolt FT-IR 200 (USA) was used for the analysis of acetamide. A disc of acetamide with KBr (Potassium Bromide) was prepared and absorptions by the various functional groups were recorded. It was compared with the IR spectrum of standard sample. Spectrum of each sample was taken by the same procedure and data was recorded for comparison.

Chromatographic analysis: Shimadzu C-R4A, Chromatopac, GC fitted with flame ionizer detector and data processor was used for the analysis of acetamide. A PEG capillary column (25m * 0.2mm i.d.) was operated with temperature programming from 150 to 300 °C. The injection and detector temperatures were maintained at 300 °C and 290°C respectively. Helium at the flow rate of 60 ml/ min and at split ratio of 1:50 was used as carrier gas. Identification and confirmation of acetamide was based on the retention time as compared to the retention time of the standard acetamide under the similar conditions.

RESULTS AND DISCUSSION

Four varieties of urea fertilizers and acetic acid were used without purification for the synthesis of acetamide. It was observed that reaction time imparts a dominant role in the yield of acetamide and maximum yields pure urea 89.7%, kisan urea 61.6%, sona urea 63.3%, babbar sher urea 66.8 % and engro urea 68.9%, respectively. Formation of ammonia from urea and carbon dioxide from acetic acid take place quickly and they escape through the condenser. This condition reduces the reactants in the flask considerably and so the product. On the other hand when we heat reactants slowly and reflux then product was obtained with good yield. Reflux was started at 116°C (boiling point of acetic acid). After that temperature was raised to 150°C within thirty minutes. At that stage ammonium carbamate was formed and more heating converts ammonium carbamate into acetamide. When we heat the reaction mixture vigorously loss of intermediate ammonium carbamate also takes place. That is why in the experiments where reaction time was two hours the yield was low because of the liberation of ammonia, carbon dioxide, acetic acid and ammonium carbamate. Temperature 190°C was attained by using air condenser and then it was maintained for thirty minutes. This temperature indicates the completion of reaction and thirty minutes are required to remove water vapors trapped in the product.

In the next experiments the reflux time was increased keeping in mind that contact time and slow heating of reactants will increase the product. Besides these fertilizers samples parallel experiments were performed with pure urea under the similar conditions and in all the cases it was observed that the yield of acetamide was more than any other sample. It was because that urea fertilizers contain various concentrations of fillers, binders and other ingredients in their formulation

which lead to the formation of by products. while in the case of pure urea byproducts are not formed as it contains no impurity. Reflux and distillation of the product was carried out with air condenser. The distillation is the critical condition for this product. Acetamide was recrystallized by using hot methanol and diethyl ether. Product was identified by melting point (80.7 °C), mixed melting point (81.4 °C), copper sulphate, phenol-hypochlorite test (blue ring on filter paper), infrared spectroscopy and assay was performed through GLC (Snell and Ettre, 1969). The analysis of the product was performed on GLC by using SE-30 column, injection temperature was 230°C, detection temperature was 250°C and flow rate was 30ml / minute. Standard acetamide was taken from E.Merk. Peak area and peak height of the samples were same as that of standard.

CONCLUSIONS: Acetamide was successfully prepared from acetic acid and four brands of commercially available urea fertilizers. Reflux time and stirring parameters were studied. From these experiments it is concluded that yield of acetamide increases by stirring the reactants as compared to without stirring in each case. Another inference is that as we increase the reflux time the yield of product also increases. When we increase the reflux time liberation of ammonia is retarded and reaction of ammonia with acetic acid increases. Formation of ammonium carbamate and its liberation to air stops and its conversion to acetamide increases. The best yields are obtained at reflux time 4.5 hours and beyond that yield did not increase considerably. Out of these four brands and pure urea the yield is Engro urea > Babbar sher urea > Sona urea > Kisan urea while the yield of pure urea was greater in all the cases. (Fig.1-5).
It is concluded from the study that urea fertilizers can be utilized for the production of acetamide.

REFERENCES

Berg M.N., D.J. Repeta and J. Laroche. Dissolved organic nitrogen hydrolysis rates in Axenic Aureococcus anophagefferens. Appl. Environ. Microbiol., 68:401-404 (2002).

Carolyn E., L. E. Anderson, Overman and P.W. Marry. Asymmetric rearrangement of allylic trichloroacetamides. Org. Synth., 82:134 (2005).

Cheronis N.D. and J.B. Entrikin. Identification of organic compounds, Interscience puplishers, Inc, NewYork, pp: 534 (1963).

Cheronis N.D., J.B. Entrikin and E.M. Hordnett. Semi micro Qualitative organic analysis, 3rd Edition, Interscience publisher, Inc, New York, pp:117, 118, 459 (1965).

Cheronis N.D and T.S. Ma. Organic functional group analysis by micro and semi micro methods, Interscience publisher, Inc, New York, pp: 174 (1964).

Dagang L. and L. Zhang, Structure and properties of soy protein plastics plasticized with acetamide. Macromol. Mater.Eng., 291: 820-828 (2006).

Eweka, E. I. and D. H. Kerridge, Solution chemistry of molten amide- nitrte eutectics. Chem. Papers. 53 : 11-15 (1999).

Ikchoon, L., C.K. Kim and B. Lee. Studies on the acid hydrolysis. J. Phy. Org. Chem.,3: 397-403 (2004).

Isaac, I.Y. and D.H. Kerridge. Effect of acetamide on solubility of metals, J. Chem. Soc. 21:2201-2208 (1988).

Jander G. and G. Winkler. J.Inorg.Nucl.Chem., .2: 24-33 (1958).

Kimiko U. and O. Kenichi. Acetamide in polar solvents: hindered internal rotation and intermolecular interactions. Org.Mag. Reson., 15: 13-17 (1980).

Kirk and Othmer. Encycopedia of chemical technology. 1:45-49, (2002).

Kuzuhara S., H. Sato and E. Kasai. Effect of urea on PCDD/Fs formation through De Novo synthesis. Organohalogen Comp., 66 (2004).

Maryadele J.O., N. Patricia, C. B. Koch, K. J. Roma. Merck Index. Published by Merck Research Laboratories, White House Station USA., 9-10 (2006).

Matthias B. and Martin K. Hydrogen bond energetic: a simulation and statistical analysis of N-Methyl acetamide, water and human lysozyme. J. Phys. Chem., 105: 11000-11015 (2001).

Michael and A. Irene. The thesaurus of chemical products, Generic to Trade. 1:1 (1986).

Ozkanli F., S. Dalkara, U. Calis and A. Willke. Synthesis of some N-arylazole acetamide derivative and their anticonvulsant and antimicrobial activities. Arzneimittelforschung., 44(8): 920-924 (1994).

Ranjit V., N, Munasinghe and JohnE.T. Corrie. Optimised synthesis of 6-iodoacetamidotetramethylrhodamide. Arkivoc., 2:143-149 (2006).

Rui M.S., A.w. Robert and G. Labat. Hydrogen bond patterns in the congruent comlex 4-nitphenol acetamide. Acta Cryst., 64:306-308 (2008).

Savinkina, E. D., E. Al'bor, I. Bufavlev, Zamilatskov. Synthesis and structures of polyiodide acetmide complexs of transition metal. Russian J. of Inorg Chem., 52:1056-1062(2007).

Snell F. D. and L. Ettre. Encyclopedia of industrial chemical analysis, Inerscience publishers a division of John Willy & Sons. New York.8: 597-611 (1976).

Thomas D., T. Peter and C. Thomas. Synthesis of propiolamide and NMR studies of formamide, acetamide and propiolamide. Magnetic resonance in chem., 35: 571-576 (1997).

Ullmann's Encyclopedia of industrial chemistry. Sixteenth Edition, Germany, Vol. A-1, pp. 71-72, vol. 24 pp.348 (2003).

Vasoya S.L.,P.T. Chovatia. D.H. Purohit and H.S. Josh. Green chemistry approach to the synthesis of potentially bioactive aminobenzylated Mannich bases through acitive hydrogen compounds. J.Serb. Chem.Soc., 70:1163-1167 (2005).

Vogel A.I.Test book of practical organic chemistry, 3rd Edition, Longman Greem & Co., New York, pp: 401-403 (1956).

Walid M. Fathalla and Pavel Pazdera, Synthesis of heterocyclic skeletons by reaction of N-(2-Cyanophenyl)-benimidoyl chloride with thioacetamides. Molecules., 17:96-103 (2002).

Figure 1:

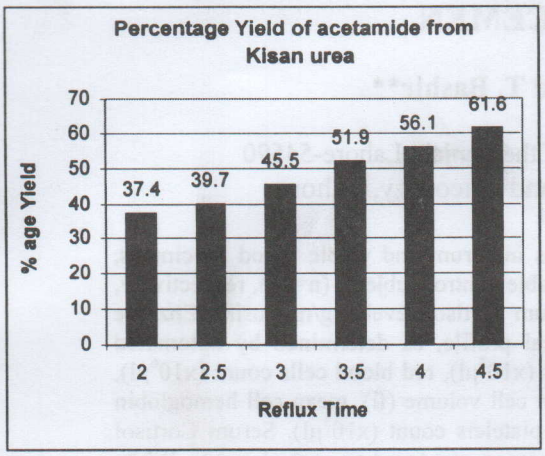

Figure 1:

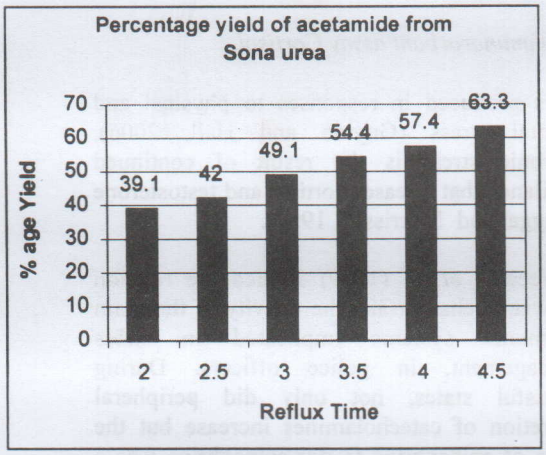

Figure 2:

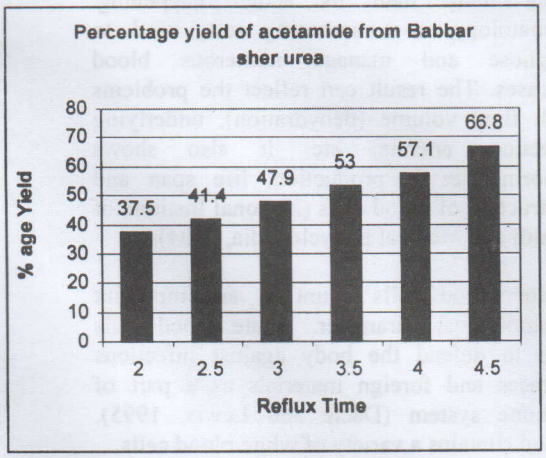

Figure 3:

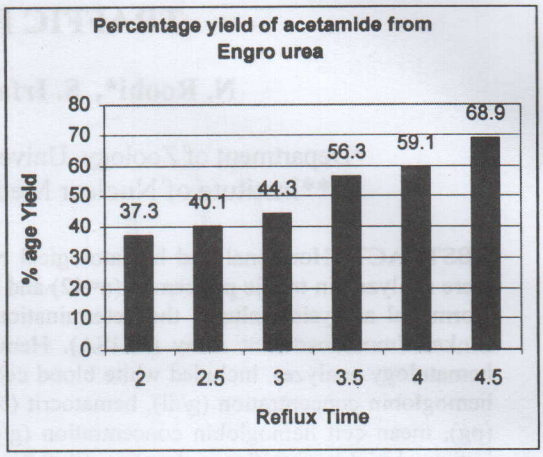

Figure 4: