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Research article

Synthesis & characterization of 4- hydroxyacetanilide starting from acetanilide

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ABSTRACT

This research deal with the new way of synthesizing paracetamol because traditional method is not suitable in general conditions and acetic anhydride is not readily available in the present scenario. In the first step the acetanilide was nitrated with nitric acid in the presesnce of sulphuric acid to form p-Nitroacetanilide, and then it was reduced to p-Amino derivative, then it was converted to diazonium salt. In the final step the diazonium salt was treated with 10% NaOH solution. Final compound was washed with water and recrystallized from ethanol. Products were characterized by melting point and FTIR. This method gives 80% yield.

Keywords: Crude, Characterization, FTIR, Gliflozins,.

INTRODUCTION

Acetaminophen or more prominently known as paracetamol is a well known non steroidal anti- inflammatory drug (NSAID) used all over the world. It is widely used in mild to moderate pain, headache and as antipyretic. Its property of reducing the pain was exposed nearly 100 years ago when its acetanilide, which is having almost same structure as paracetamol was removed as a pain killing remedy due to its toxic effect. It is the most valuable drug in the treatment of pain, inflammation and pyrexia in every group of patients even in the patients having osteoarthritis. Studies shows that paracetamol causes asthma, eczema and allergic rhinitis in children, which is due to the glutathione depletion in the lungs and causing inflammation of airway and bronchoconstriction [1].

MATERIAL AND METHODS

Instrument

Brukar FT-IR spectrometer was used for taking IR spectra of the compounds by making KBr discs. Melting points were determined by electrically heated melting point apparatus.

Hydrochloric acid, absolute alcohol, dipotassium carbonate, sodium nitrite, nitric acid, zinc, diethyl ether and sodium hydroxide were purchased from Qualigens chemicals pvt. Ltd. and crude paracetamol was purchased from Alkem pharmaceuticals pvt ltd [2].

p-Nitroacetanilide (2): Acetanilide (3g, 22.2 mol.) and 5 ml of glacial acetic acid were taken in a 50 ml Erlenmeyer flask and then 5 ml of sulphuric acid was poured and acetanilide was dissolved, the whole mixture was placed in an ice-salt bath and the temperature was maintained between 0-5oC. Meanwhile a solution of conc. Nitric acid (2 ml) and conc. Sulphuric acid (1.3 ml) was prepared and cooled to 0-5oC The latter solution was added to the former solution of acetanilide dropwise with a caution that the temperature should not exceed 10oC. Then the mixture was allowed to stand for half an hour at room temperature. The mixture was poured on 15 g of ice and crude compound was precipitated and then filtered. Then it was washed three times with cold water and recrystallized with ethanol. The product was yellow solid (1.75 g, 55%; melting point 214- 216oC) [3].

p-Aminoacetanilide (3): p-Nitroacetanilide (1g) was taken in a round bottom flask and dissolved in 20 ml ethanol. Conc HCl (2.5 ml) was added with stirring. Powdered zinc was added to the mixture and then it was removed from ice bath and then warmed for 10 minutes on a water bath until all solid dissolved. Sodium hydroxide (24%, 6M) was added. The mixture was separated by extraction with an alkaloidal compound and small addition of potassium carbonate A water soluble compounds were removed and organic layer was evaporated under vaccum. Crude brown solid was obtained (0.70g, 70%). Diazonium salt: p-Aminoacetanilide was diazotized with sodium nitrite and HCl at a

temperature below 5oC.

Paracetamol (5): A solution of 25% sodium hydroxide was prepared and cooled to 10oC. Then it was added to diazonium salt in an Erlenmeyer flask and a reddish white precipitate was obtained. It was filtered and washed with cold water and recrystallized from ethanol to give reddish white crystals (70%, 165-167oC) [4, 5].

RESULT AND DISCUSSION

IR spectra of acetanilide was matched with standard spectra of acetanilide provided in the literature with peaks at: 3250-3115 cm-1 (2o amide, N-H stretching); 2019-1705 cm-1 (monosubstituted benzene); 1650 cm-1 (C=O stretching for ketone); multiple peaks were observed in the region of 1500 cm-1 (C=C aromatic stretching, C-N stretching of amide); bending peaks were obtained at 750 cm-1 (N-H bending, monosubstituted benzene).

p- Nitroacetanlide: It was prepared from acetanilide by nitration in the presence of conc. Nitric acid, sulphuric acid and glacial acetic acid at a temperature below 5oC. IR spectra of the compound was found to be similar with an additional peaks between the region of 1550-1350 cm-1(asymmetric N=O stretching), which shows that nitro group was successfully attached. A bending was also observed at 855 cm-1, which shows benzene was para substituted.

p-a minoacetanilide: It was prepared by addition of 6M NaOH to the above compound in the presence of zinc & hydrochloric acid. It was characterized by the removal of peaks at 1550- 1350 cm-1. Some more peaks were observed at 3450 cm-1(primary N-H stretching); 1310 cm- 1(C-N aromatic stretching); bending peak of N- H group was observed at 845 cm-1. Bending peaks showing para substitution were obserbed at 855 cm-1.

Diazonium salt was prepared by diazotization reaction of p-aminoacetanilide with sodium nitrite and hydrochloric acid at a temperature below 5oC. IR spectra were shown the absence of stretching peaks of primary N-H stretching. All other peaks were same as the previous spectra.

Paracetamol was prepared by warming the diazonium salt with 10% NaOH. The IR spectra confirmed the presence of phenol with a peak between the regions of 36500-3629 cm^{-1}(O-H stretching). The melting point of paracetamol was found to be 170 ^oC with a percentage yield of 70% [6].

CONCLUSION

Above research shows that paracetamol can also be prepared by diazotization reaction with a good percentage yield and purity, this method rules out the necessity of acetic anhydride.

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