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Electrochemical Synthesis of 5-Aminosalicylic Acid from 5-Nitrosalicylic Acid in Alkaline Media

Mohammad Bagher Pasha Zanousi[1*], Mohammad Saber Tehrani[2], Ardeshir Kermani[3], and Jilla Khalighie[4]

[1]Chemistry Department, Noshahr and Chalous Branch, Islamic Azad University, Chalous , Iran
[2]Chemistry Department, Science and Research Campus, Islamic Azad University,Tehran , Iran
[3]Faculty of Chemistry, Amir Kabir University,Tehran , Iran
[4]Iranian Research Organization for Science and Technology

ABSTRACT

5-Aminosalicylic acid (5-ASA) is currently prepared by electrochemical reduction of 5-nitrosalicylic acid (5-NSA) in acidic media. In this work, electrolytic reduction of 5-NSA in alkaline media is presented. Reaction conditions and parameters such as anode and cathode electrodes, electrolyte type, reaction time, temperature, current, and the pH for isolation of product are investigated. The yield of the reaction was 90.9%, and the melting point was 280 °C with decomposition. The UV-Vis and FT-IR spectra of the product was in good agreement with the standard material. The elemental analysis of the product was almost the same as the standard.

Keywords: 5-aminosalicylic acid, 5-nitrosalicylic acid, electrochemical synthesis, elemental analysis, reduction.

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* .Corresponding author : pashazanousi@ yahoo.com

INTRODUCTION

5-ASA, known as Mesalazine is used for treatment of Ulcerative Colitis [1,2]. This compound with the molecular weight of 153.13 and the empirical formula of C_7 H_7 N O_3 contains C, 54.9%, H, 4.61%, N, 9.15%, and O, 31.34%, or 90.2% of salicylic acid.

The molecular structure of 5-ASA is shown in Fig. 1.These white to pink crystals melt and decompose at 280°C [3]. It is slightly soluble in cold water and ethanol, but is more soluble in hot water. It is also soluble in HCl.

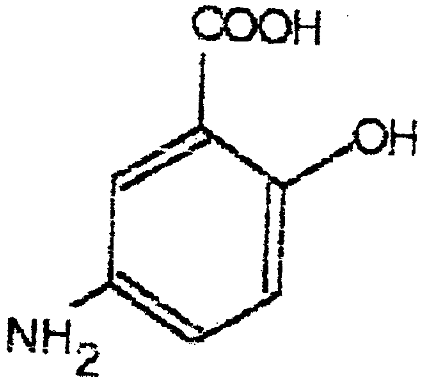


Fig 1. Molecular structure of 5-ASA

5-ASA could be produced by different methods, among them, chemical reduction of 5-NSA [4,5], nitration and reduction of salicylic acid [6,7,8], Kolbe Method [9],direct amination of salicylic acid [10,11,12,13],and sulfanilic acid method [14].

The main problem in electrochemical reduction of aromatic nitro compounds in acidic media specially at elevated temperature is the occurrence of the Bamberger rearrangement in the reaction intermediate [15,16,17]. In other words, in acidic environment aromatic compounds are subjected to nucleophilic attack. The attacking groups or molecules are those present in the reaction media such as water. Hence, in such environment, there are side reactions and the product is different from the expected one. Meanwhile, the yield of the reaction is so low, because the electrolytic reduction is not selective [18].

Accordingly, electrolytic reduction in alkaline media was proposed for the present work. The advantages of alkaline media in the present case are, elimination of acidic media difficulties, and corrosion, lower applied potential needed for the electrolytic cell, easier isolation and recovery of the product, and use of much lower temperatures. The electrolytic cell used for the reduction of the nitro compound in alkaline media was as follow ;

Ni| 5M NaOH |CH OH,1M NaOH,5-NSA | Cu

Anodic and cathodic chambers were separated by means of a semipermeable membrane to prevent direct mixing of the solutions. Factors such as the reaction time, current, temperature, type of electrode used as cathode, pH for isolation of the product, and the reaction mixture were optimized. The reaction yield under the optimized conditions was 90.9%. The reaction time depends on the reactant concentration, current density, electrode surface, and the current efficiency for reduction. The reaction temperature was far below 60°C, because elevated temperatures result undesirable side reactions or decomposition of nitro compound or the amine. If the reactant was insoluble or slightly soluble in aqueous solution, an organic solvent miscible with water is added to the catholyte . The organic solvent should be inert and dissolve the nitro compound. It is also advisable to prevent air contact with the reaction mixture which causes further oxidation of the amine. Hence, use of nitrogen environment is recommended.

EXPERIMENTAL

An Interspect Model 200-X , FT-IR spectrometer, a Shimadzu Model UV 210-PC, UV-Vis spectrometer, a Horiba F-12 pH meter equipped with a combined glass electrode, and a Phillips Model PE-1507 power supply unit were used for measurements. Copper foil (99.9 % pure), nickel foil (99.9 % pure), graphite and iron electrodes, cathodic membrane and nitrogen gas obtained from domestic firms. Hydrochloric acid, sodium metabisulfite, sodium hydroxide, potassium hydroxide, sodium carbonate, potassium carbonate, and methanol were analytical grade, obtained from

E. Merck. Double distilled deionized water used throughout the experiments.

In order to perform and optimizing the reaction parameters, the electrochemical cell was set up as follow; the anode chamber contained Ni foil as electrode and 25 mL of 5 M sodium hydroxide as anolyte. The cathode chamber contained Cu foil as electrode, 1.0 g of 5-NSA, 20 mL of 1M sodium hydroxide and 5 mL of methanol as catholyte.

RESULTS AND DISCUSSION

OPTIMIZATION OF TIME, TEMPERATURE, AND CURRENT

To optimize each parameter, all the other factors were kept unchanged except the one under investigation. The cell was the same as mentioned above. The results were compared by percentage of the recovery of the product. The best results were obtained in 180 min., at 25° up to 60° C, while the current adjusted to 300mA.

CHOICE OF ELECTROLYTE AND ELECTRODE

Three different electrodes namely; copper, graphite, and iron were tested as cathode. It was revealed that the best yield was obtained with the copper electrode. To choose the best catholyte, 25 mL of 5 M of an electrolyte used as anolyte, and 20 mL of 1M of the same electrolyte plus 5mL of methanol and 1g of the reactant as the catholyte. It was indicated that the best result could be obtained with 1M sodium hydroxide and methanol. It must be mentioned that the tested electrolytes were sodium and potassium hydroxides, and sodium and potassium carbonates.

OPTIMIZATION OF pH FOR ISOLATION OF THE PRODUCT

When reaction was completed, the reaction mixture in the cathode chamber transferred to a beaker. The pH of the mixture was adjusted to 1, 2, 3, 3.5, and 4 using 1M of hydrochloric acid. The best result obtained at pH=3.5 and it was chosen as the optimum pH for isolation of the product. The mixture was then heated and filtered while it was still hot. Then 2g of sodium metabisulfite dissolved in 100mL of water was added and left to crystallize. Then the crystalline product collected on filter paper. The product was again dissolved in hot water, some active charcoal was added and filtered. The filtrate was left to be crystallized. The melting point, UV-Vis and FT-IR spectra of the product were taken and compared with those of the standard material. All the results were found to be in good agreement with the standards.

CONCLUSION

According to the obtained results, it is possible to prepare 5-ASA by electrolytic reduction of 5-NSA in alkaline medium. The optimized conditions for the reaction are; copper as cathode and nickel as anode electrodes, 25 mL of 5M sodium hydroxide in anodic chamber, 20 mL of 1M sodium hydroxide plus 5mL of methanol and 1g of 5-NSA in cathodic chamber. The optimised parameters are listed in Table 1.

Table 1. Optimized conditions and parameters for electrochemical synthesis of 5-amino salicylic acid.

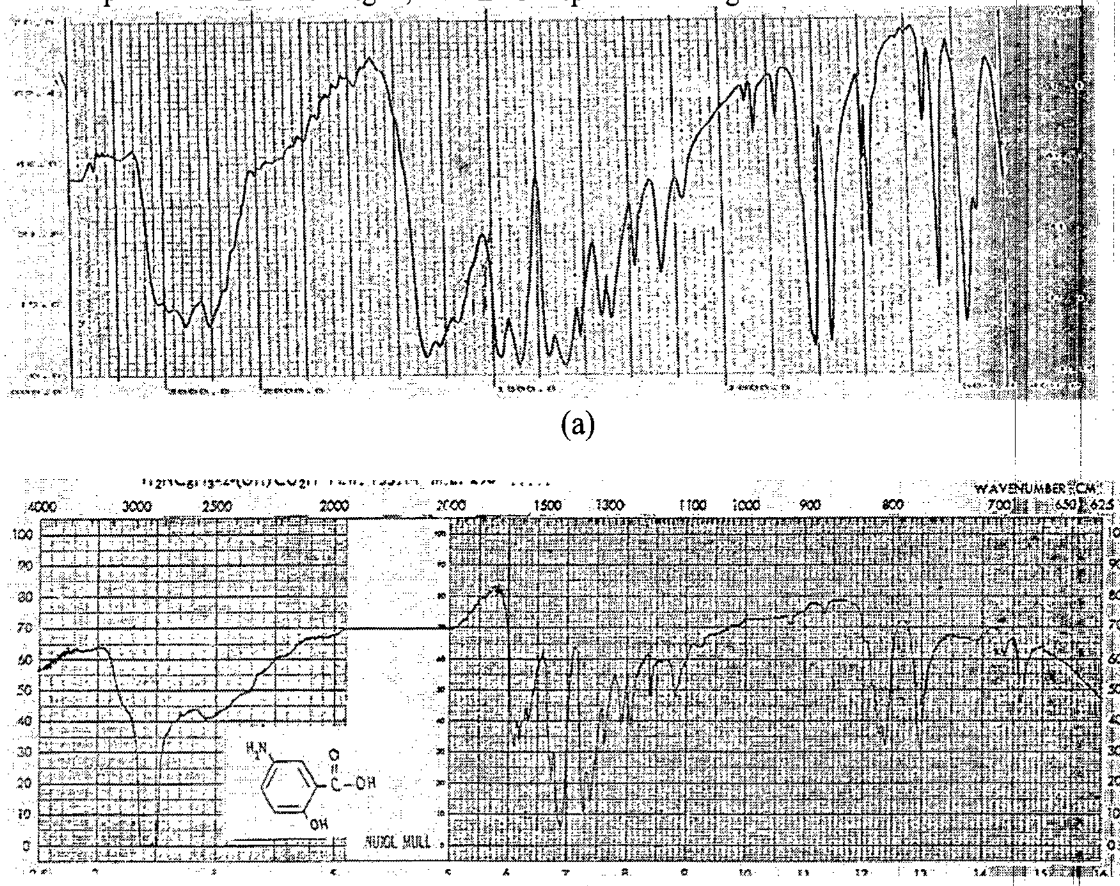
Parameter	Chosen (Optimized)
Anode Electrode	Nickel Foil
Cathode Electrode	Copper Foil
Anolyte	25mL of 5M NaOH
Catholyte	20mL of 1M NaOH +5mL of Methanole
Reaction Time Required	180 min.
Temperature	25° C
Current	300 mA
pH for Isolation	3.5
Weight of Reactant	1.0 g
Yield	90.9%
Melting Point	280° C (d)

obtained product was in good agreement with the standard. The results are compared in Table 2.

Table 2. Comparison of the elemental analysis of the obtained product and the standard material.

Sample	C%	H%	O%	N%
Product	54.90	4.60	31.30	9.20
Standard	54.90	4.61	31.34	9.15

The IR spectrum of the product shows exactly the same peaks as the standard material. The position of the peaks due to –COOH, -OH, and –NH_2 groups in both spectra are the same [19,20]. The IR spectra are shown in Fig. 1, and the UV spectrum in Fig 2.



(a)

(b)

Fig 1. The IR spectra of the prepared 5-ASA and its standard material.(a-prepared ASA and b-standard ASA).

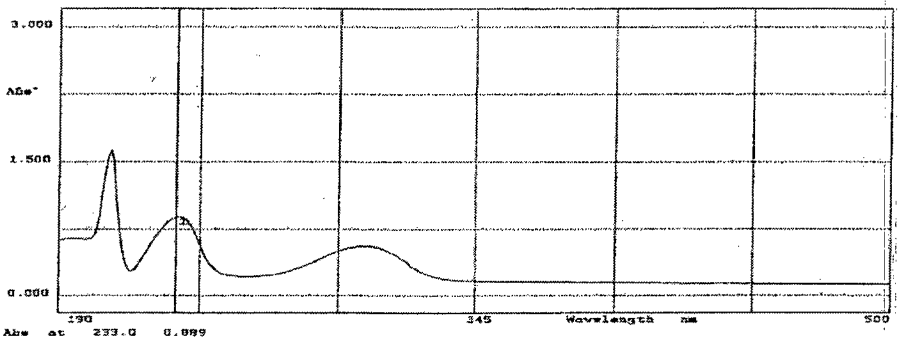


Fig 2. The UV spectrum of the prepared 5-ASA

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