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A Novel and Facile one-pot Green Laboratory Synthesis of Aspirin without using Acetic Anhydride

Malik Sarika and Ratnani Sonia*

Ramjas College, North Avenue, University Marg, University of Delhi, Delhi-110007
sonia.ratnani@ramjas.du.ac.in

ABSTRACT

This methodology deals with the synthesis of aspirin through the reaction of salicylic acid with acetic acid in presence of traces of concentrated sulphuric acid. Acetic acid is working as an acetylating reagent in presence of concentrated sulphuric acid. This method embraces a safe and green synthesis due to absence of conventional hazardous acetic anhydride as acetylating agent. This experiment caters to the needs of undergraduate laboratory experiments with novel green method. This method improves the quality of laboratory work of students as they learn the impact of hazardous chemicals on the environment.

KEYWORDS; Organic Synthesis, Drugs, Pharmaceutical, Green Chemistry, Aspirin

***Corresponding author**

Sonia Ratnani

Chemistry Department, Ramjas College, North Avenue, University Marg,
University of Delhi, Delhi-110007
Email; sonia.ratnani@ramjas.du.ac.in

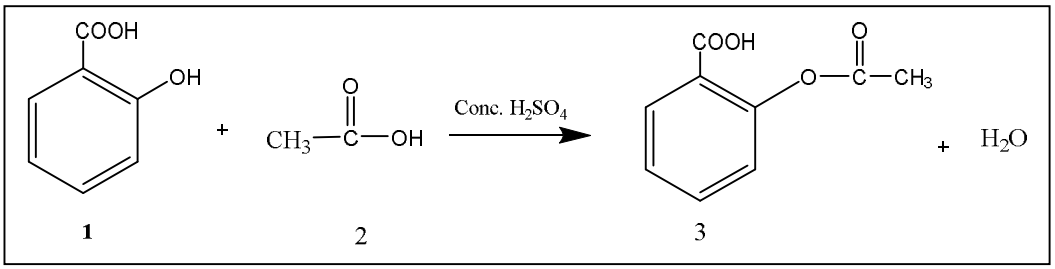
INTRODUCTION

Acetylsalicyclic acid referred to as Aspirin belongs to class of non-steroidal drugs (NSAD). The drug is widely used as an analgesic (painkiller), anti-pyretic (fever reducer), anti-inflammatory and anti-platelet agent depending on its dosage. It prevents inflammation and platelet aggregation by inhibiting irreversibly the cyclo-oxy genase enzyme (1 and 2 isoenzyme). This is because the enzyme is accountable for converting arachidonic acid to prostaglandin (mediator of inflammation) and prostaglandin is the precursor of thromboxane A2, which is a potent platelet aggregator. Therefore by inhibiting COX enzymes inflammation reduces.[1] The synthesis and studies of aspirin [2-5] is a common undergraduate laboratory experiment adopted by undergraduate curriculum.

Our environment is affected by actions of human in countless ways, many of which are detrimental in making the planet inhabitable. Future generation of chemists and innovators should aim at developing new chemical process that not only meet the demands of the mankind but also protect the environment. One of the solutions is to implement principles of green chemistry in methodology. Synthetic methodologies should be designed to use and generate substances that possess little or no toxicity to human health and the environment.

RESULTS AND DISCUSSION

This methodology deals with the synthesis of aspirin **3** in accordance with the curriculum adopted by undergraduate science students through the reaction of salicylic acid **1** with acetic acid **2** in presence of traces of concentrated sulphuric acid as depicted in scheme-1. The formation of the aspirin can be envisaged as shown in scheme 2. The reaction may presumably be proceeding through the protonation of acetic acid followed by the initial formation of the intermediate **4** which undergoes intramolecular proton transfer-elimination to give the aspirin **3**.



Scheme-1

Conventional methods of synthesis

As practiced over the year's synthesis of aspirin in undergraduate laboratory is conducted by following general routes:

a) Esterification of Salicylic acid using acetyl chloride using pyridine

b) Acetylation of Salicylic acid using acetic anhydride in presence of sulphuric acid and phosphoric acid.

Limitations of conventional method

The conventional methods involve acetyl chloride which is an irritant and corrosive. Cutaneous exposure results in skin burns while vapour causes extreme irritation of eyes and mucous membrane. Intoxication of pyridine may lead to dizziness, headache, and lack of coordination, nausea, salivation and loss of appetite. High concentration of acetic anhydride cause severe lung damage with short of breath. Acetic anhydride is banned nowadays as it is a precursor for Di-acetyl morphine (Heroin) Figure-1.[6] It is a toxic, irritating and lachrymatory substance.Comparative study of (Green) this method with conventional method is given in Table-1

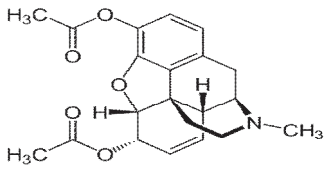
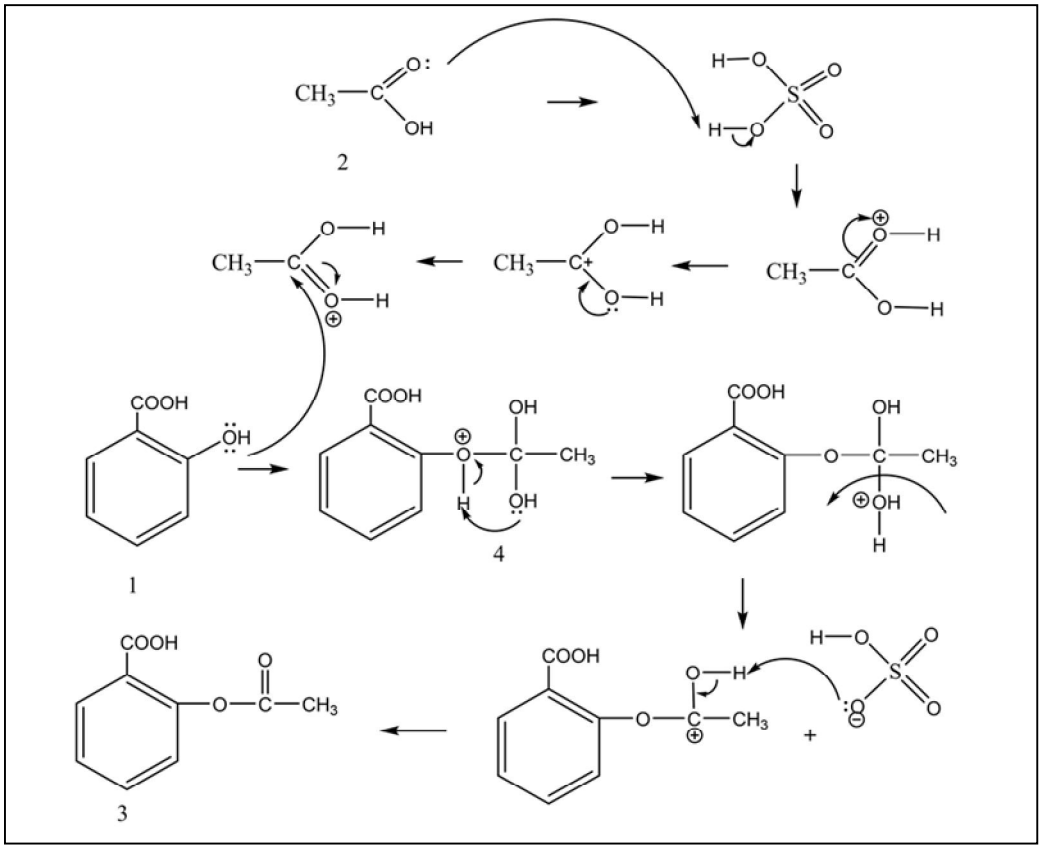


Figure-1



Scheme-2

EXPERIMENTAL

In a 100 mL Erlenmeyer flask approximately 2 g of Salicylic acid (white crystalline powder), was weighed. The exact weight taken was recorded to calculate the approximate yield. Minimum amount of glacial acetic was added drop wise with continuous swirling of conical flask to make a clear solution. Few (3-4) drops of sulphuric acid were added to the conical flask. The contents of the conical flask were warmed on a water bath maintained at a temperature of 50-70°C. The flask was then left undisturbed for about ten to fifteen minutes followed by cooling in ice bath for ten minutes. Appearance of white product indicated completion of the reaction. The white product was filtered using suction pump and was dried in a desiccator. The yield of the crude product was recorded.

RECRYSTALLIZATION

The crude aspirin was recrystallized by using hot ethanol, since acetic acid is very soluble in water. The percent yield of the crude product was determined and found 95%.

CHARACTERIZATION

The purity of the product was analyzed and characterized by its melting point, TLC and spectroscopic technique IR and NMR reported earlier.[7-17]

Table 1: "Comparative study of green method and conventional method"

S. No.	Feature	Green method	Conventional method
1.	**Cost effective**	Economical No heating, cheap and easily available reagents	Costly Heating/ Refluxing required at times, expensive reagents used e.g. Zinc, Acetyl Chloride, Acetic Anhydride (Not readily available i.e. banned)
2.	**Safe**	Non Hazardous Use of Acetic acid as acetylating agent	Hazardous Use of Acetyl Chloride and Pyridine or Acetic Anhydride as acetylating reagents
3.	**Atom Economy**	No byproduct/ Less waste	By products/Waste generated Zinc Acetate, Hydrogen Chloride (gaseousform)
4.	**Work-up**	Easy and Fast	Time Consuming

5.	**Yield**	92-95%	85-88%

CONCLUSIONS

In summary a simple, efficient, and green method has been developed for the synthesis of Aspirin through reactions of salicylic acid with acetic acid in presence of traces of concentrated sulfuric acid. Hence acetic acid is playing the role of acetylating reagent.

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