# Synthesis and structural analysis of the drug Aspirin using Jmol interface

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## 1. Introduction

Aspirin (acetylsalicylic acid) is a synthetic organic drug derived from salicylic acid. Salicylic acid is a natural product found in the bark of the willow tree and was used by the ancient Greeks and Native Americans to treat fever and pain. However, salicylic acid is bitter and irritates the stomach.

A German chemist named Felix Hoffman was the first to synthesize aspirin in 1897. Hoffman's father had severe arthritis but could not tolerate salicylic acid he was taking for pain relief. The name given for Hoffman's new compound was A-spirin. Apparently this comes from acetylation (A-), together with Spirin, part of the name for Meadow-sweet (Spiraea ulmaria), a plant rich in salicylates.

Friedrich Bayer, the employer of Hoffman, patented the name and began marketing the product in 1899. It was a huge success and sales grew rapidly. Bayer's company set up by himself, is generally reckoned to have been the first pharmaceutical company and the production of aspirin is generally accepted to have laid the foundation of the modern pharmaceutical industry.

In this work the drug aspirin, was synthesised in the real time lab. the yield of the drug was determined. The 3D structure of the reactant and products were drawn in the Jmol interface. The structural features of the reactants and products were analysed with simulated $^{1}$HNMR obtained from JSPEC view of Jmol.

## 2. Objectives:

- To synthesis the drug Aspirin in real time lab
- To demonstrate the mechanism of formation of the drug Aspirin
- To create 3D structure of the reactants and products in Jmol interface
- To analyse the structures of the reactants and products with simulated $^{1}$HNMR obtained from JSPEC view of Jmol.

## 3. EXPERIMENTAL PROCEDURES AND METHODS

**Apparatus required:**

- Round Bottom flask
- Water bath
- 250 ml beaker with glass rod
- Buchner funnel
- 250 ml of conical flask
- Weight machine
- Filter papers
- Watch glass

**Chemicals required:**

- Sulphuric acid - 4 to 5 drops
- Acetic anhydride - 4 ml
- Salicylic acid - 3 gm

**Procedure:**

- About 3 g of salicylic acid was weighted and taken in a 250 ml conical flask
- Around 4 ml of acetic anhydride and 4 to 5 drops of con. sulphuric acid was added into the conical flask
- The above mixture in the conical flask was mixed thoroughly and heated over a water bath up to 60° C for about 10 minutes
- Then the mixture was cooled over the ice bath
- 25 ml of ice water was added inside the conical flask to decompose the excess acetic anhydride
- As the solution was cooled over the ice bath, the crystals of Aspirin forms gradually

## 4. The process of synthesis of Aspirin

**Step 1:** Heating the mixture over a water bath

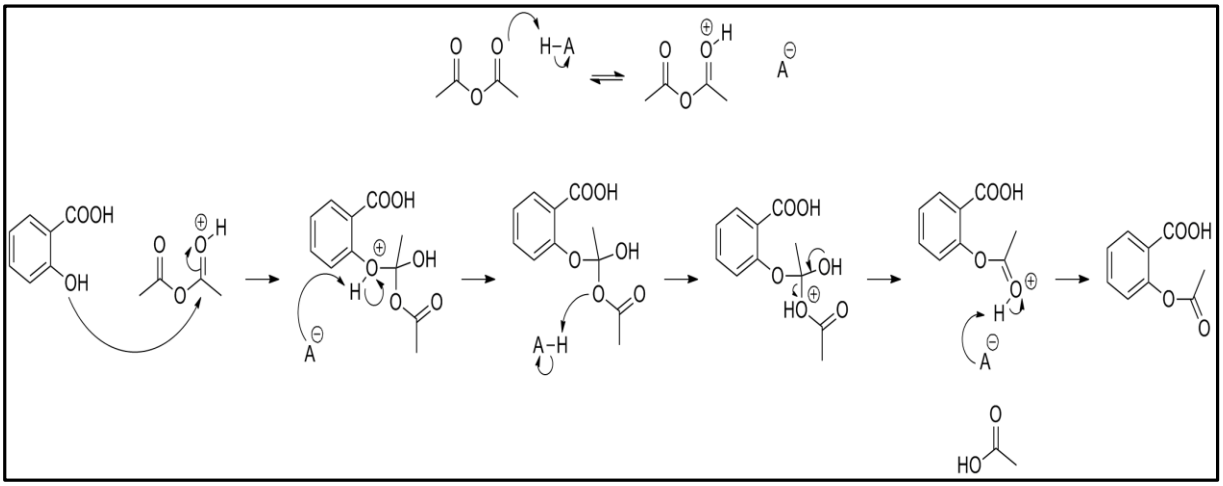
**Step 2:** Cooling the mixture over ice bath

**Step 3:** Addition of ice water into the mixture

**Step 4:** Filtrating the Aspirin crystal from the solution


**Step 5:** The end product Aspirin formed after drying

## 5. Mechanism of Aspirin formation

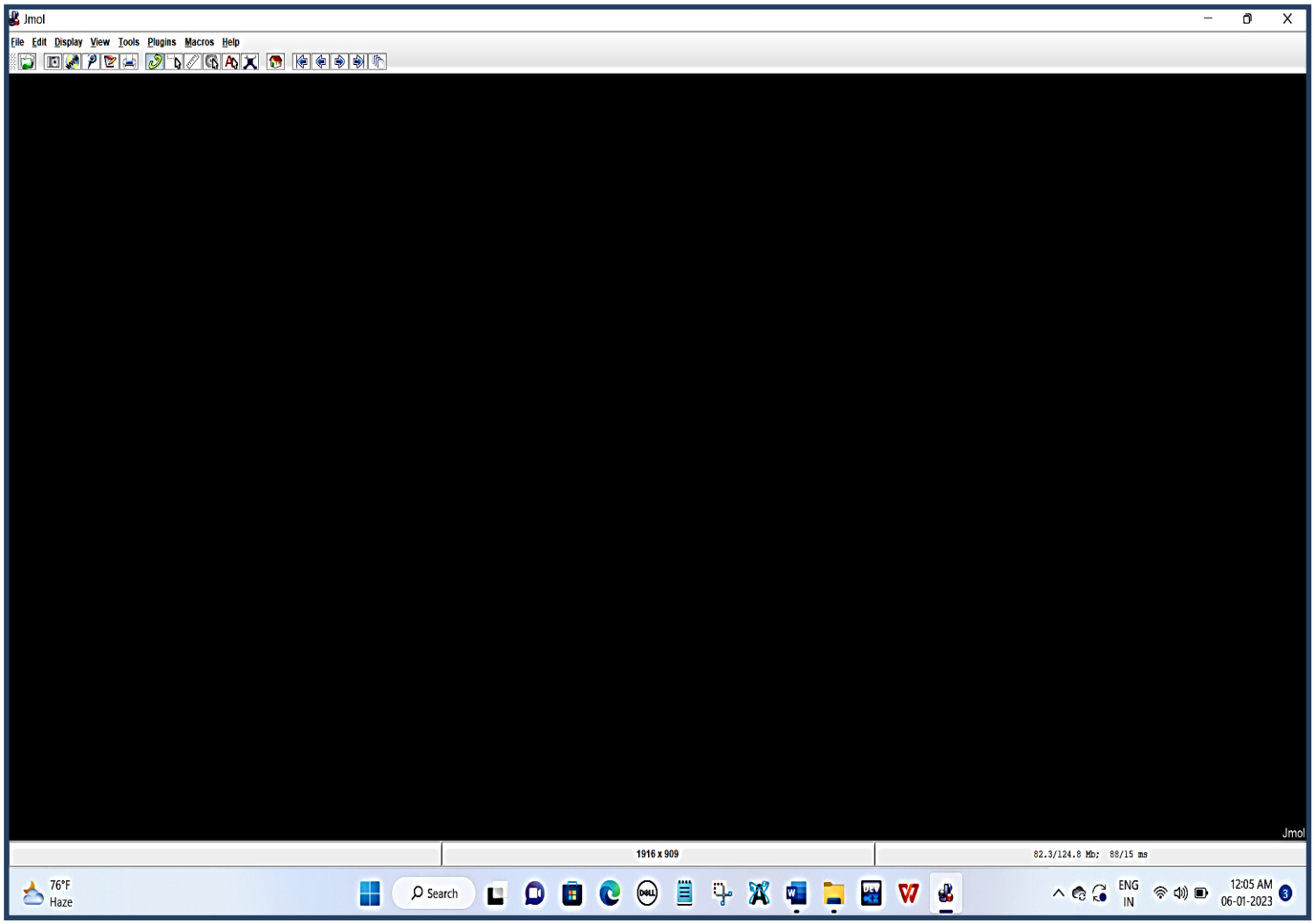


## 6. INSTALLATION OF Jmol

- Jmol is an open-source Java viewer for chemical structures and biomolecules in 3D
- It is free and open source software, written in Java, it runs on Windows, Mac OS X, Linux and Unix systems.

**Procedure for installation of Jmol**

- First install Jmol in your desktop or in your pc.
- If you need any help about Jmol you can refer to this link :www.jmol.sourceforge.net
- At first we installed Jmol in our pc.
- At first it looks like this




**About the compound**

| | |
|---|---|
| Compound name: | ASPIRIN |
| Chemical formula: | $C_9H_8O_4$ |
| Molar mass: | 180.158 g·mol$^{-1}$ |
| Melting point | 135°C |
| Boiling point | 140 °C |

### 6.1. Procedure for creating 3D structure of ASPIRN in Jmol

**Step 1:** Open Jmol in your desktop or in your pc

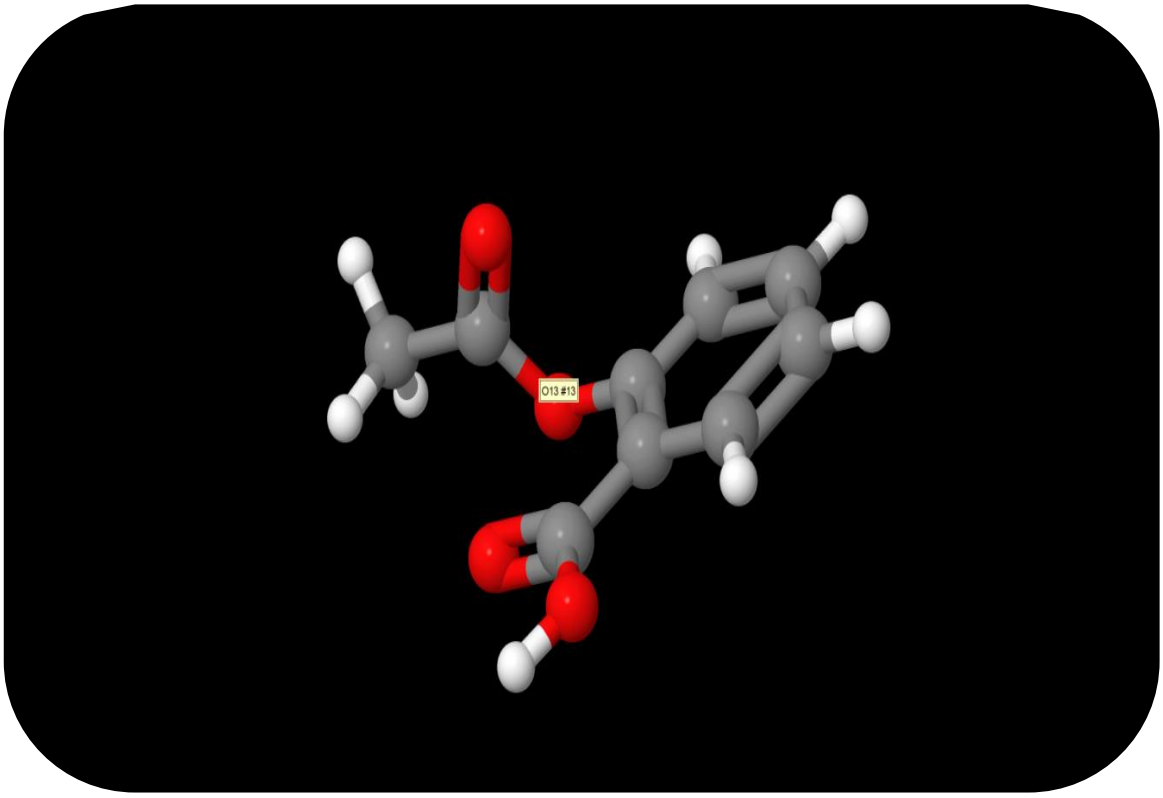
**Step 2**: Go to file and then click **'Get MOL'**

**Step 3:** A dialogue box opens with the provision to type the name of the molecule

**Step 4:** Type the name of the molecule as "ASPIRIN" and click enter

**Step 5:** The 3D structure of ASPIRIN was imported from the database

**3D STRUCTURE OF ASPIRIN CREATED IN Jmol**



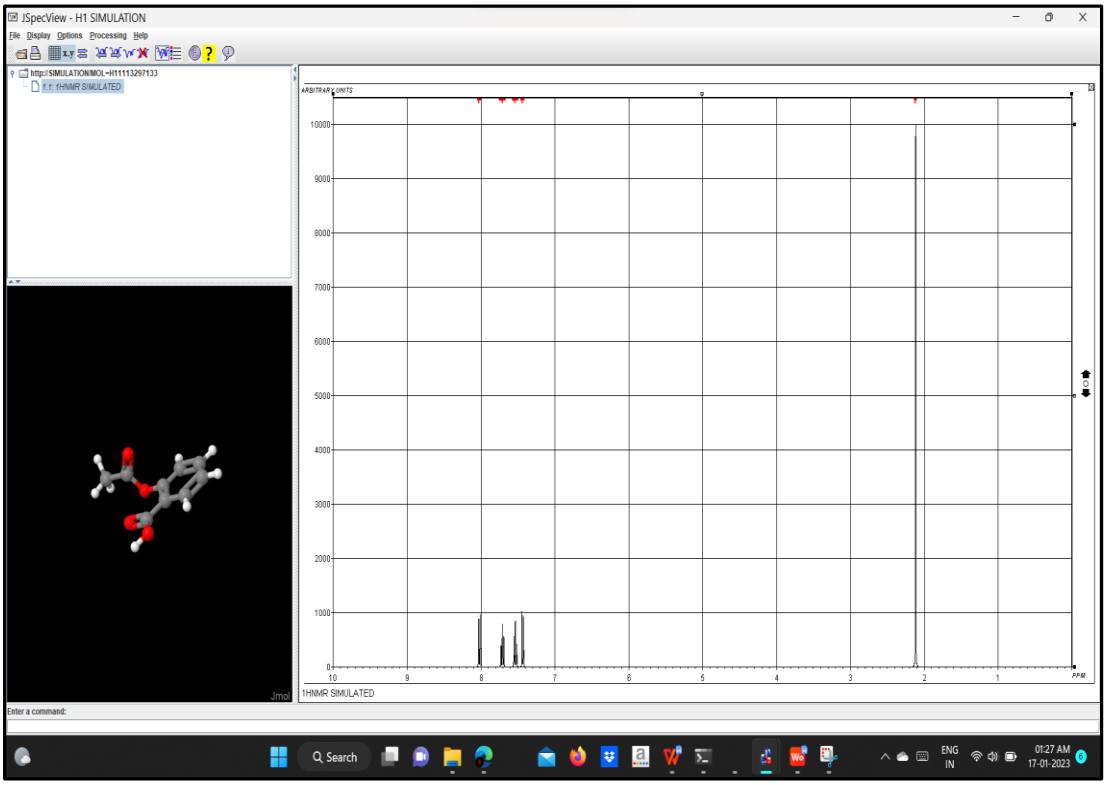

**6.2. Procedure for obtaining simulated $^{1}$HNMR of Aspirin in JSPEC view of Jmol**

**Step 1:** Open the Jmol interface window with the 3D structure of Aspirin

**Step 2:** In the menu bar go to "Tool" menu click the spectra inside that choose $^{1}$HNMR

**Step 3:** New JSPEC view dialogue box opens with simulated $^{1}$HNMR spectra of Aspirin

## SIMULATED $^{1}$HNMR SPECTRA OF ASPIRIN IN JSPEC VIEW OF Jmol




**About the compound:**

| | |
|---|---|
| Compound name: | ACETIC ANHYDRIDE |
| Chemical formula: | $C_4H_6O_3$ |
| Molar mass: | 102.09g/mol |
| Melting point | -73.1 °C |
| Boiling point | 139.5 °C |

### 6.3. Procedure for creating 3D structure of Acetic anhydride in Jmol

**Step 1:** Open Jmol in your desktop or in your pc

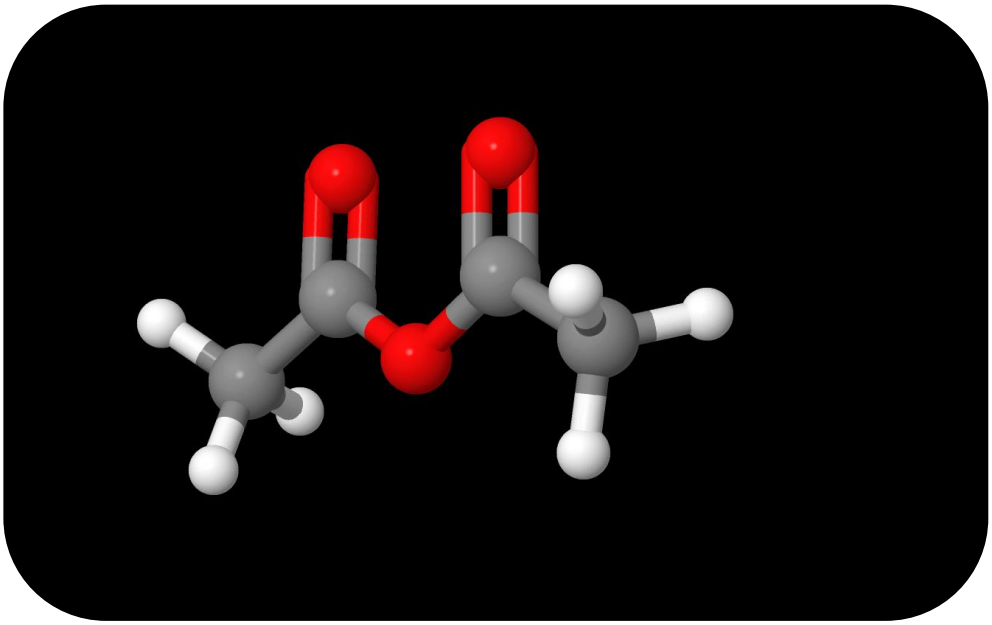
**Step 2:** Go to file and then click **'Get MOL'**

**Step 3:** A dialogue box opens with the provision to type the molecule

**Step 4:** Type the name of the molecule as "acetic anhydride" and click enter

**Step 5:** The 3D structure of acetic anhydride acid was imported from the database

**3D STRUCTURE OF ACETIC ANHYDRIDE IN Jmol**



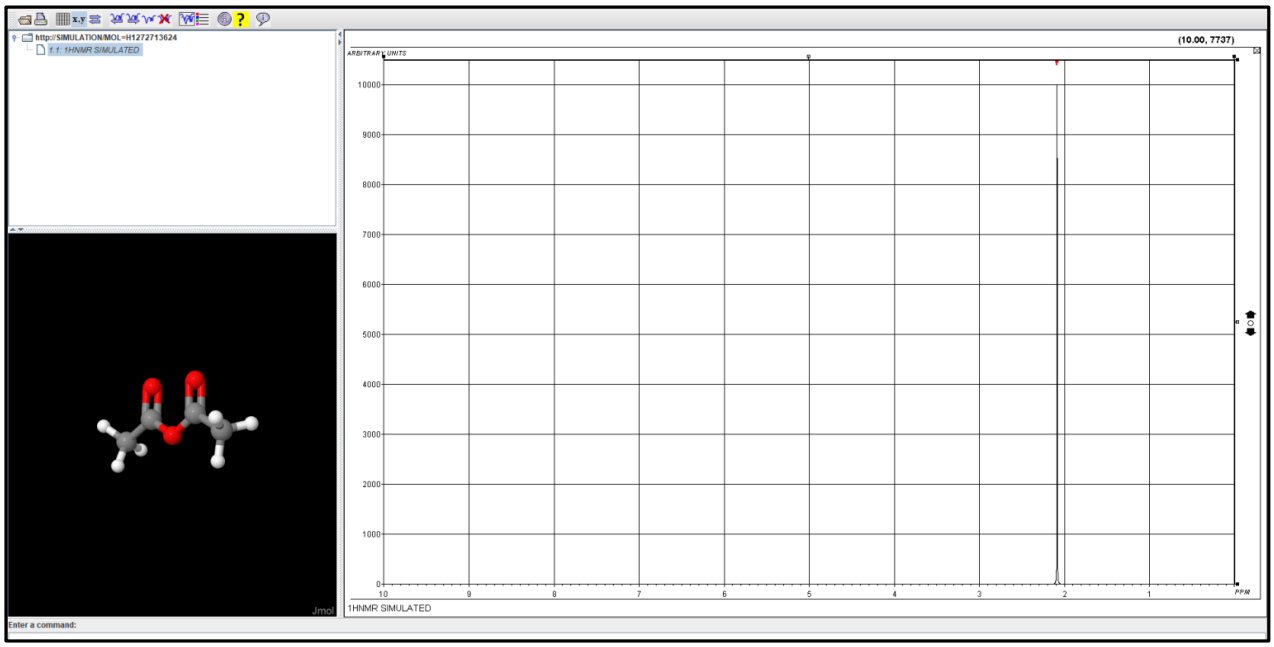
## 6.4.Procedure for obtaining simulated $^{1}$HNMR of Acetic anhydride in JSPEC view of Jmol

**Step 1:** Open the Jmol interface window with the 3D structure of acetic anhydride acid

**Step 2:** In the menu bar go to "tool" menu click the spectra inside that choose $^{1}$HNMR

**Step 3:** New JSPEC view dialogue box opens with simulated $^{1}$HNMR spectra of acetic anhydride

**SIMULATED $^{1}$HNMR OF ACETIC ANHYDRIDE IN JSPEC VIEW OF Jmol**



**About the compound:**

| | |
|---|---|
| Compound name: | Salicylic acid |
| Chemical formula: | $C_7H_6O_3$ |
| Molar mass: | 138.121 $g \cdot mol^{-1}$ |
| Melting point | 158.6 °C |
| Boiling point | 211°C |

### 6.5. Procedure for creating 3D structure of Salicylic acid in Jmol

**Step 1:** Open Jmol in your desktop or in your pc

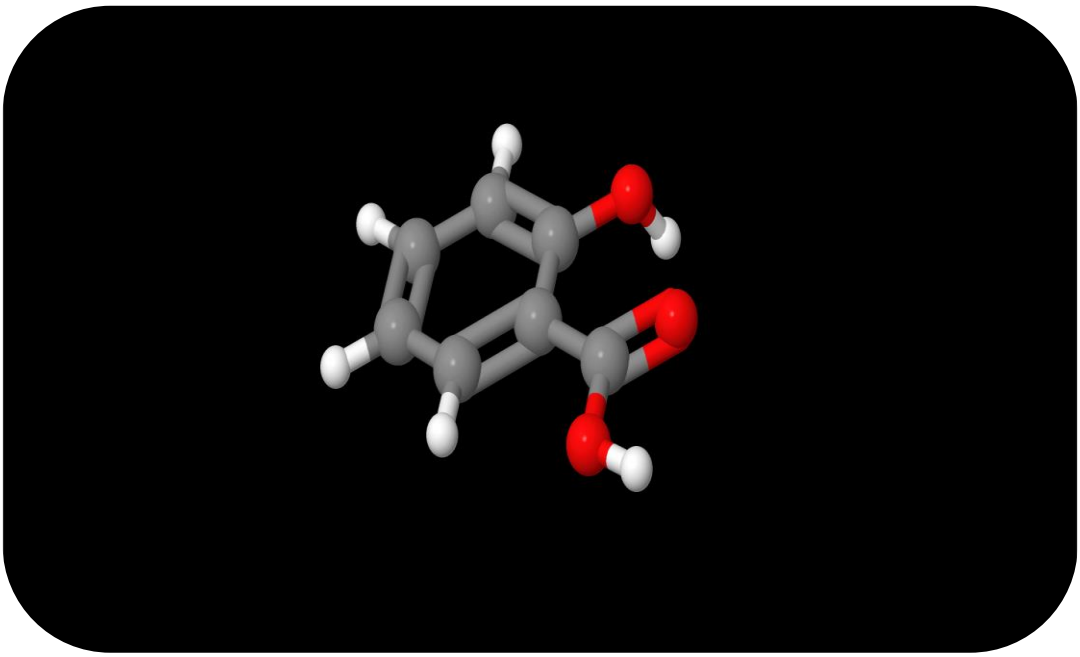
**Step 2:** Go to file and then click **'Get MOL'**

**Step 3:** A dialogue box opens with the provision to type the molecule

**Step 4:** Type the name of the molecule as "Salicylic acid" and click enter

**Step 5:** The 3D structure of Salicylic acid was imported from the database

**3D STRUCTURE OF SALICYLIC ACID CREATED IN Jmol**



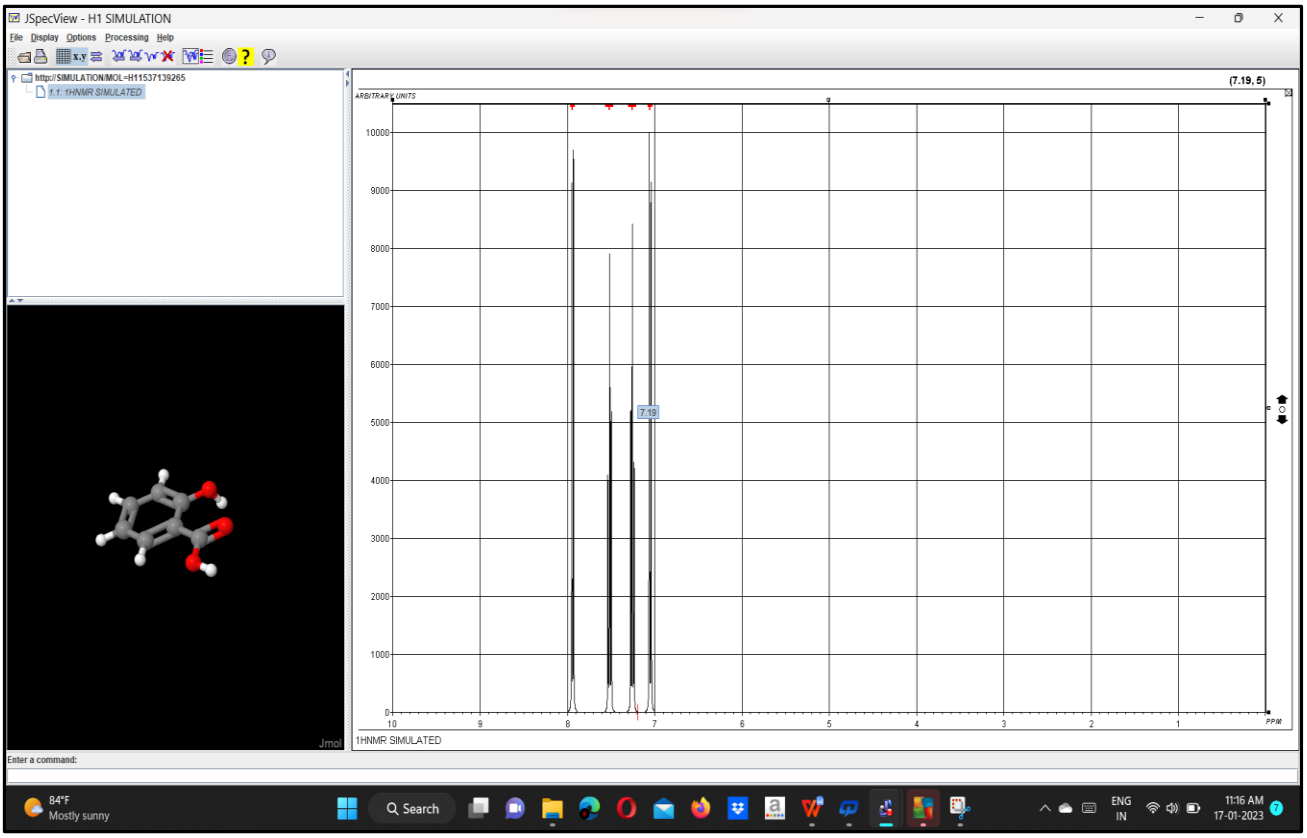
### 6.6. Procedure for obtaining simulated $^{1}$HNMR of salicylic acid in JSPEC view of Jmol

**Step 1:** Open the Jmol interface window with the 3D structure of Salicylic acid

**Step 2:** In the menu bar go to "tool" menu click the spectra inside that choose $^{1}$HNMR

**Step 3:** New JSPEC view dialogue box opens with simulated $^{1}$HNMR spectra of Salicylic acid

**SIMULATED $^{1}$HNMR OF SALICYLIC ACID IN JSPEC VIEW OF Jmol**




**About the compound:**

| | |
|---|---|
| Compound name: | Acetic Acid |
| Chemical formula: | $CH_3COOH$ |
| Molar mass: | 60.052 g·mol$^{-1}$ |
| Melting point | 16 to 17 °C |
| Boiling point | 118 to 119 °C |

### 6.7. Procedure for creating 3D structure of acetic acid in Jmol

**Step 1:** Open Jmol in your desktop or in your pc

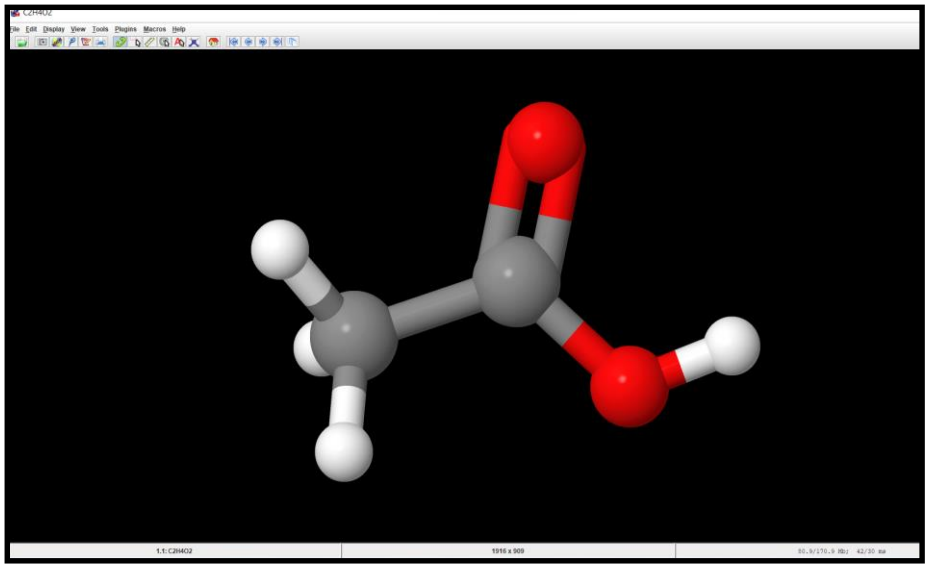
**Step 2:** Go to file and then click **'Get MOL'**

**Step 3:** A dialogue box opens with the provision to type the molecule

**Step 4:** Type the name of the molecule as "acetic acid" and click enter

**Step 5:** The 3D structure of acetic acid was imported from the database

**3D STRUCTURE OF ACETIC ACID IN Jmol**



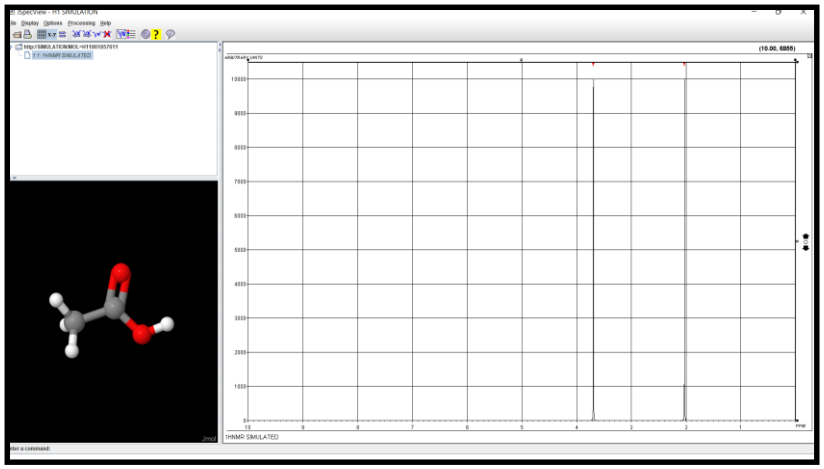
### 6.8. Procedure for obtaining $^{1}$HNMR of acetic acid in JSPEC view of Jmol

**Step 1:** Open the Jmol interface window with the 3D structure of acetic acid

**Step 2:** In the menu bar go to "tool" menu click the spectra inside that choose **$^{1}$HNMR**

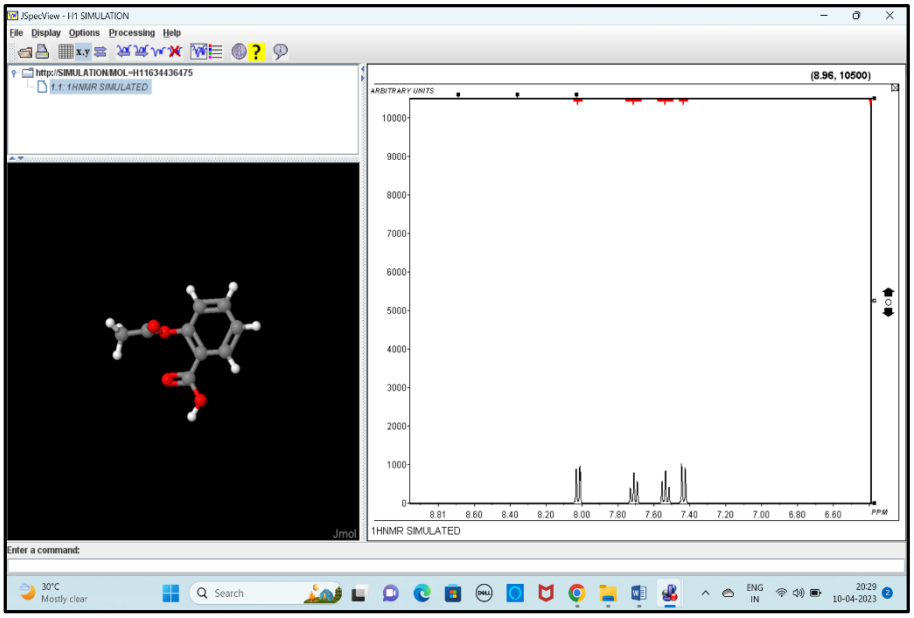
**Step 3:** New JSPEC view dialogue box opens with simulated **$^{1}$HNMR** spectra of acetic acid

**SIMULATED $^{1}$HNMR SPECTRA OF ACETIC ACID IN JSPEC VIEW OF Jmol**

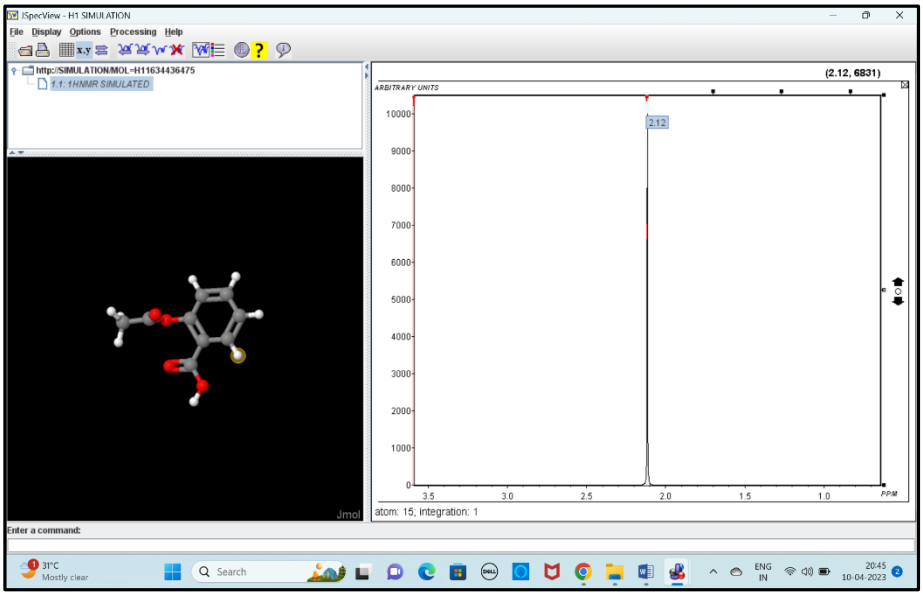


## 7. Result and Discussion

### 7.1. Interpretation of simulated $^{1}$HNMR spectra of aspirin (Product) molecule obtained from JSPEC view of Jmol

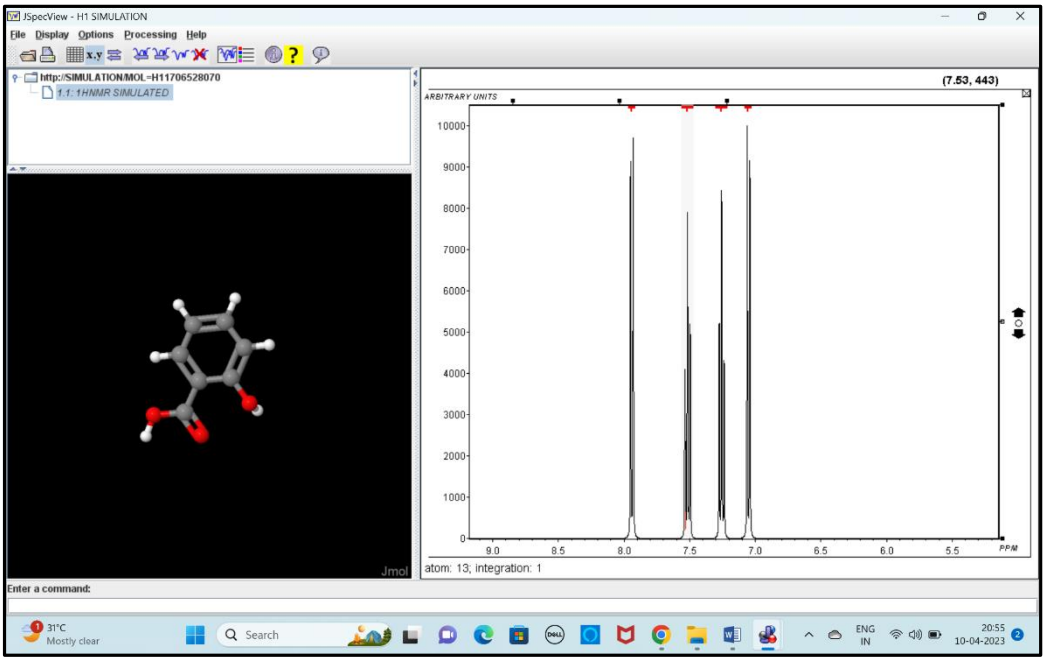



- The protons of the aromatic ring appear as series of multiplets from 7.4 to 8 PPM.
- The proton ortho to the acetoxy group appears at 7.42 PPM
- The proton meta to the acetoxy group appears at 7.73 PPM
- The proton para to the acetoxy group appears at 7.54 PPM
- The proton ortho to carboxylic group appears at 8.02 PPM



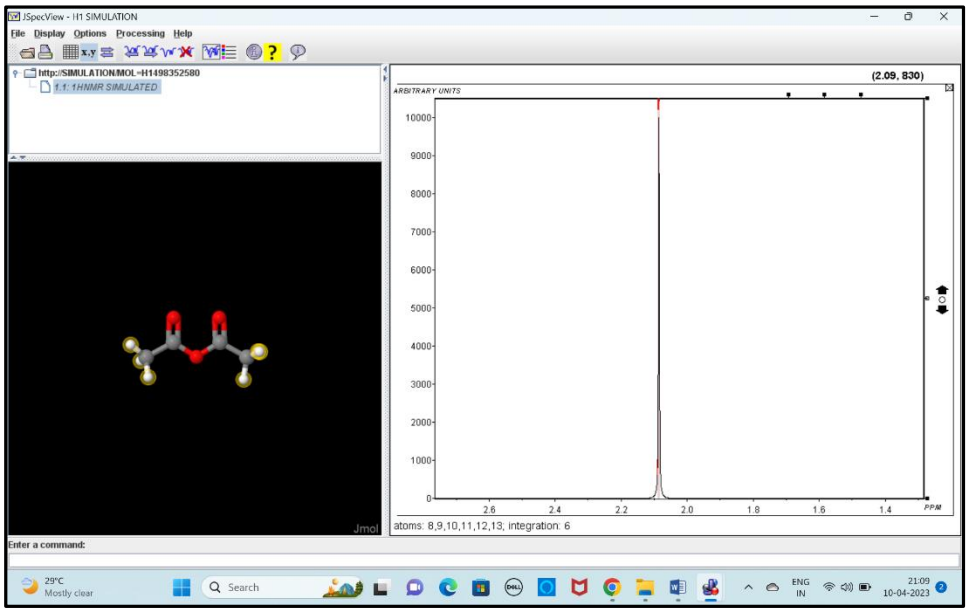

- The methyl group proton appears as a singlet at 2.12 PPM, due to inductive deshielding of acetyl group on the oxygen side of the carboxy group.

## 7.2. Interpretation of simulated 1HNMR of salicylic acid (Reactant) molecule obtained from JSPEC view of Jmol




- The protons of the aromatic ring appear as series of multiplets from 7.4 to 8 PPM.
- The above multiplets were similar to that of the multiplets appeared in the aspirin molecule.

## 7.3. Interpretation of simulated 1HNMR of acetic anhydride (Reactant) molecule obtained from JSPEC view of Jmol




- A singlet peak appears for all the protons at 2.02 PPM

- During the formation of Aspirin, the acetic anhydride molecule was hydrolysed into acetic acid molecules. (Addition of cold water)
- The –OH group in the salicylic acid molecule was replaced with the acetyl group of the acetic acid molecule

## 8. Conclusion

Synthesis of Aspirin occurs via the process of esterification. Acetic anhydride is used as it is cheap and forms a by-product, acetic acid which is not corrosive and can be recovered. All addition of chemicals to aspirin is done in the fume hood.