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Synthesis of Ibuprofen using Nano - Preyssler as a Green and Environmentally Friendly Catalyst

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Abstract: ***The term "green sustainable chemistry" refers to the application of chemical engineering to create products and processes that are safer for Earth's biomes. To create effective pharmaceuticals without negatively impacting the environment, "green chemistry" employs efficient synthetic methods that are also kind to the planet. The environmental impact of developing new medicines is reduced, and the optimization process is sped up thanks to this. As catalysts, HPAs can improve the economy and the environment in a number of ways. We look at the many different types of reactions where heteropolyacid catalysts can be used as acids. SPNPs*** ***($H_{14}[NaP_5W_{30}O_{110}])/SiO_2$) are a very effective, cheap, and environmentally benign catalyst. The method is straightforward to implement and produces great yields with minimal effort. Both hydrolytic and thermal stability can be seen in SPNPs ($H_{14}[NaP_5W_{30}O_{110}])/SiO_2$). The anion created by Preyssler is safe and can be used multiple times.***

Keywords: Ibuprofen, Nano-Preyssler, Green, Environmentally Friendly Catalyst, and Synthesis

1. INTRODUCTION

For chemists everywhere, "green chemistry" [1] is the central idea at their disposal in the fight against environmental contamination. In today's industrialised culture, progress comes first in most fields, regardless of how it may affect people's health or the state of the planet. Every entity should adopt practises that do not compromise the quality of life for future generations. [2] Therefore, one should cross over to sustainability using green chemistry concepts as a stepping stone. At its core, green chemistry is concerned with designing synthetic procedures and products for maximum efficiency, making use of renewable raw materials, and doing away with or drastically minimising the usage of poisonous and/or hazardous chemicals and solvents. [3]

Achieving the goals of green chemistry requires a synthetic chemist to aim for a number of desirable characteristics, including atom economy, high product yield and selectivity, environmental friendliness, compatibility, cost effectiveness, experimental simplicity, etc. [4] The development of environmentally friendly catalysts is an important task encountered by chemists, and catalysis is a cornerstone of "green chemistry." Thus, a sustainable and "green" catalyst should have qualities such as minimal preparation cost, high activity, exceptional selectivity, high stability, quick recovery, and recyclability. In heterogeneous catalysis, the

catalyst and the reactants are in separate phases. [5] In most cases, the catalyst is a solid, while the reactants are gases or liquids. Heterogeneous catalysts have received a lot of attention in recent years because of the positive effects they can have on the economy and the environment. Flavanones are a type of polyphenolic compound that is produced naturally and may be found in a wide variety of plant foods; they make synthetic processes clean, safe, and high-yielding. Berries, tea, coffee, and even chocolate all contain flavanones. They can be obtained from a variety of plant-based diets and can be found in foods from all over the plant world.[6] They are plant pigments found in many foods and drinks, including fruits, vegetables, and beverages like tea, red wine, and coffee.

Plant pigments are found in both plants and berries. Antibacterial properties, cytotoxic powers, anti-inflammatory traits, and anticancer activities are just some of the purported biological effects of flavanone. Particular flavanones with A- or B-ring hydroxyl groups have been investigated as possible antioxidant drugs in this context. [7] You can find these flavanones on either the A or B ring. These flavanones can be found on either the A ring or the B ring. It is currently accepted that the flavanone's ability to scavenge free radicals is due in large part to the hydroxyl group's ability to provide hydrogen, thereby initiating a redox reaction. Flavanones are able to scavenge free radicals because of this process. This partnership is what allows flavanones to function so effectively as antioxidants. Flavanones' special qualities come from their ability to do this. [8]

Ibuprofen is chemically known as (2 RS)-1 [4-(2-methyl propyl)-phenyl] propionic acid (BP. 2004). Ibuprofen, first released in 1969 as an improvement over Aspirin, is a propionic acid derivative. Although less prevalent than with aspirin or indomethacin, stomach pain, nausea, and vomiting are still the most frequently reported adverse reactions. [9] If you need an NSAID, chances are you'll get ibuprofen as your doctor's first recommendation. It inhibits COX-1 and COX-2 without preference for COX-2. [10] Even though its anti-inflammatory effects may be less potent than those of other NSAIDs, it plays a crucial role as an analgesic and fever reducer. These results are a result of its ability to inhibit cyclooxygenases, enzymes essential in the production of prostaglandins. Prostaglandins are involved in the development of pain, inflammation, and fever. [11]

2. MATERIALS AND METHODS

Chemicals.

The compounds were purchased in their original form from Merck (Darmstadt, Germany). All solvents used in this study were obtained legally.

Instruments.

The uncorrected melting point data were obtained using the Electrothermal IA 9100 digital melting point instrument. Yields were determined using a 6890 GC machine from Agilent (Denver, CO, USA) equipped with a Hp-5 capillary. The nominal dimensions are 30 by 530 by 1.5 millimetres. KBr pellets were put through a Shimadzu model impact 400D FT-IR spectrophotometer to get the IR readings. Tetramethylsilane (TMS) was employed as an internal standard in Bruker AC-300F 400 MHz spectrometer recordings of 1 H NMR investigations performed in CDCl3. It was taken into consideration that the optical rotation was measured using a Bellingham Stanly polarimeter.

Catalyst Combination Process.
Silica-supported Preyssler nanoparticles (SPNPs) are synthesised using a method described in the literature. To do this, a solution of sodium bis(2- ethylhexyl) sulphosuccinate in cyclohexane was mixed with a solution of Preyssler acid in a fixed quantity of water (0.2 M). The chosen molar ratios of water to surfactant were 3, 5, and 7. As a further step, tetraethoxysilane was added to the microemulsion. The Preyssler acid/SiO2 nanostructure dispersions were centrifuged (1500 rpm) after being combined for 8, 12, 18, 25, and 30 hours at room temperature, and then the particles were washed with acetone four times and dried in a vacuum oven. The optimal ratio of water to surfactant was 3:1, while the optimal time duration was 30 hours.

Ethyl Lactate Synthesis
Vacuum distillation was used to remove water from 10 mL of lactic acid, and the acid was then refluxed with ethanol (12 mL), ($H_{14}[NaP_5W_{30}O_{110}]$)/$SiO_2$) (SPNPs) (0.05 g), and pyridine (0.1 mL) for 3 hours to produce Silica-Supported Preyssler Nanoparticles (SPNPs) (20 mL). TLC was employed to monitor the progress of the reaction. After the reaction was finished, the liquid was let to settle to room temperature and solidified in less than an hour. Filtration was used to remove the catalyst from the reaction mixture, and solvent evaporation and subsequent recrystallization yielded an unrefined product.

Ethyl-2-(methylsulphonyloxy)propanoate Synthesis.
The reaction mixture consisted of 1 gramme of ethyl lactate (8.47 mmol), 1.77 millilitres of triethylamine (12.71 millimol), and 15 millilitres of dry pyridine at room temperature (RT). The resulting mixture was heated to 0 degrees Celsius and swirled for 1 hour before being cooled to room temperature and agitated for another 2 hours. Following TLC confirmation of reaction completion, the final product was diluted with ethyl acetate. Hydrogen peroxide was used to wash the organic layer, anhydrous sodium sulphate was used to dry it, and a reduction in pressure was used to concentrate the chemical. Ethyl-2-(methylsulphonyloxy) propanoate was refined using column chromatography over silica gel (100-200 mesh) in hexane as the eluent to get rid of impurities.

Ethyl-2-(tosyloxy)propanoate Synthesis
At 0 degrees Celsius, 1 gramme (8.47 mmol) of ethyl lactate was dissolved in 15 mL of dry pyridine, and then TsCl (1.77 g) was added in increments until 9.32 mmol (moles) were obtained. After 1 hour of stirring at 0 degrees Celsius, the mixture was stirred for another 2 hours at room temperature. Once TLC showed that the reaction was complete, C2H5OAc was added to dilute the mixture. The organic layer was washed with hydrogen peroxide, dried with anhydrous sodium sulphate, and concentrated by decreasing the pressure. Column chromatography using silica gel (100-200 mesh) as the stationary phase and hexane as the eluent was used to purify the crude component, yielding the final, pure product. Total of four 2-(tosyloxy)ethylpropanoates.

Ethyl-2-(4-isobutylphenyl) propanoate Synthesis.
We combined 15 millilitres of pyridine, 2.73 grammes of isobutylbenzene (20.41 millimoles), and 0.05 milligrammes of (H_{14} $[NaP_5W_{30}O_{110}]$)/SiO2 nanoparticles at room temperature (SPNPs). Ethyl-2-(methylsulphonyloxy) propanoate, which was at room temperature, was added to the cold solution. After 8 hours of reflux at 80 degrees Celsius, this was cooled to room temperature. After chilling the reaction mixture to 0 degrees Celsius and quenching it

with diluted hydrochloric acid, ethyl acetate was utilised as an extractant. The organic layer was dried over anhydrous Na_2SO_4 to concentrate it at low pressure. The crude chemical was purified using column chromatography over silica gel with hexane as the eluent, yielding the pure product.

Synthesis of Ibuprofen.

It all started with dissolving 1 gramme (4.27 millimoles) of ethyl-2-(isobutylphenyl) propanoate in 6 mL of CH_3OH, followed by adding 479 milligrammes (8.55 millimoles) of KOH (8.55 millimoles) in 5 mL of H2O. Four hours were spent stirring the resultant solution at room temperature. The methanol was evaporated out under vacuum, and then the organic substance was extracted using ethyl acetate. After being washed with water, dried over anhydrous Na_2SO_4, and concentrated, the final product was the required chemical.

3. RESULT

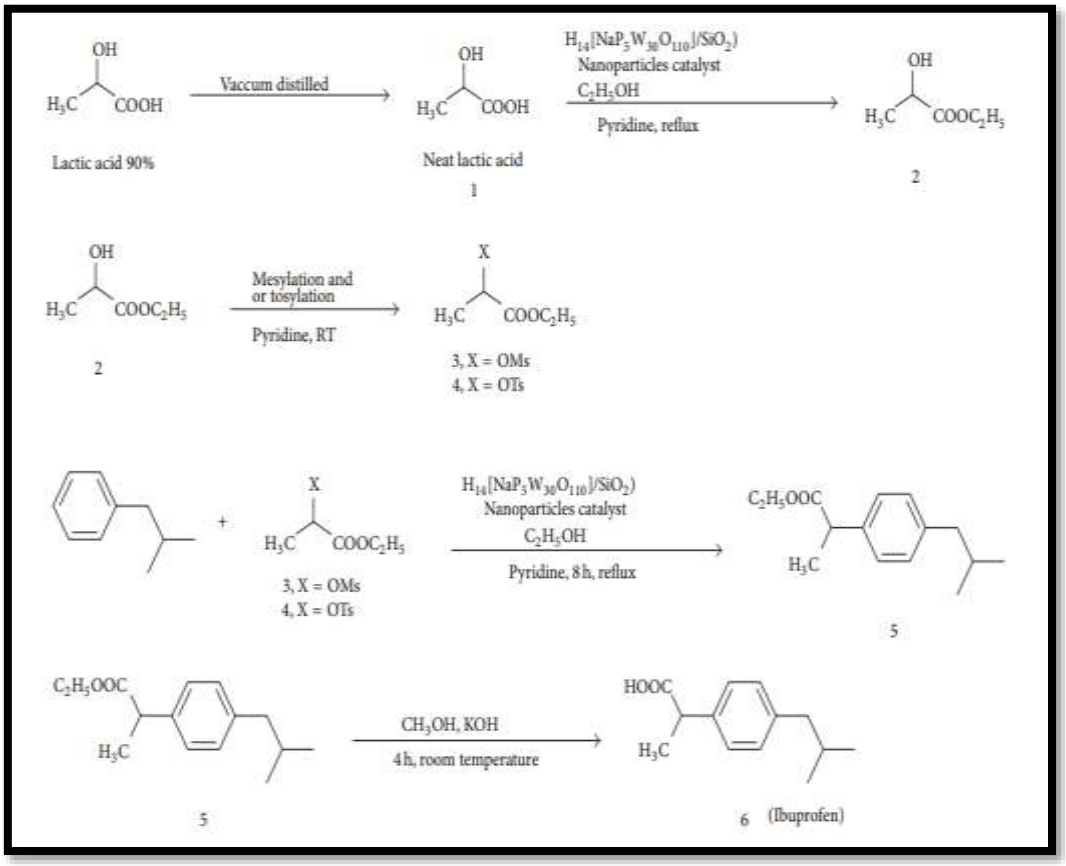

Fig. 1: Preyssler nanoparticle-supported silica gel for ibuprofen synthesis

Silica-supported Preyssler nanoparticles (H_{14} $[NaP_5W_{30}O_{110}]/SiO_2$) (SPNPs) were employed as catalysts for Friedel-Crafts alkylation. The method was carried out using mesylate and tosylate of ethyl lactate, both of which are derivatives of lactic acid.

Table 1. Synthesis of Ibuprofen

Entry	Catalyst	Yield
1	$H_{14}[NaP_5W_{30}O_{110}]/SiO_2$, (SPNPs)	96
2	$H_{14}[NaP_5W_{30}O_{110}$	92
3	$H_{14}[NaP_5W_{30}O_{110}]/SiO_2$	81
4	$H_3[PW_{12}O_{40}]/SiO_2$ (50%)	66
5	$H_{14}[NaP_5W_{29}MoO_{110}]$	89
6	$H_3[PMo_{12}O_{40}]$	63
7	$H_3[PW_{12}O_{40}]$	73
8	$H_4[SiW_{12}O_{40}]$	63
9	$H_4[SiMo_{12}O_{40}]$	51
10	$H_6[P_2W_{18}O_{62}]$	87
11	H_2SO_4	60
12	Free	10
13	*p*-TSA	64
14	Zeolite	69

We improved the yields of Ibuprofen ethyl ester synthesis using silica-supported Preyssler nanoparticles ($H_{14}[NaP_5W_{30}O_{110}]/SiO_2$] (SPNPs) and other acid catalysts.

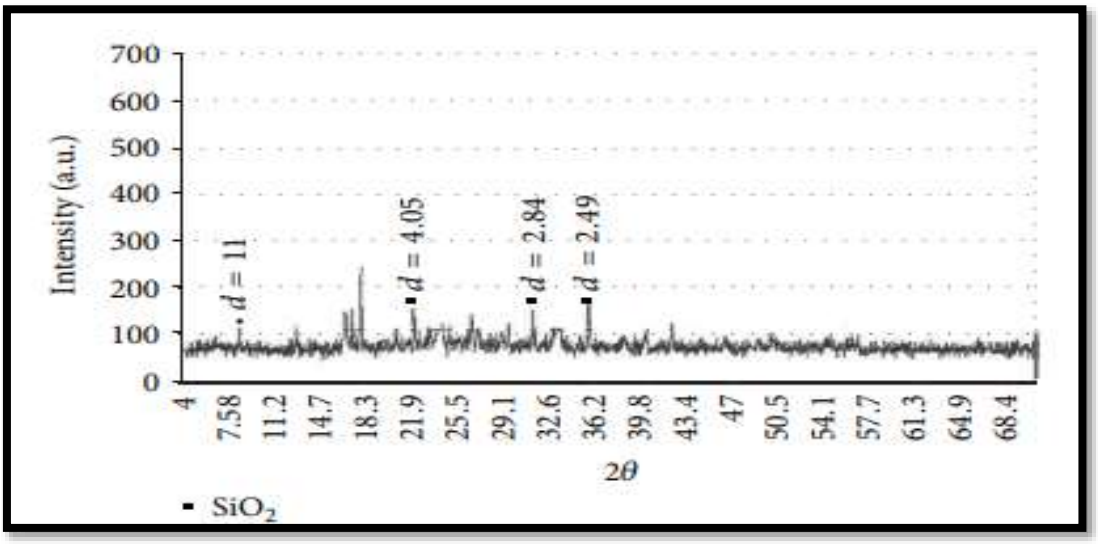

Fig 2. Pattern of X-ray diffraction (XRD)

In Figure 2, we can see the powder X-ray diffraction (XRD) patterns of the synthesised samples. SiO_2 atomic structure may be inferred from the spheres' unique patterns.

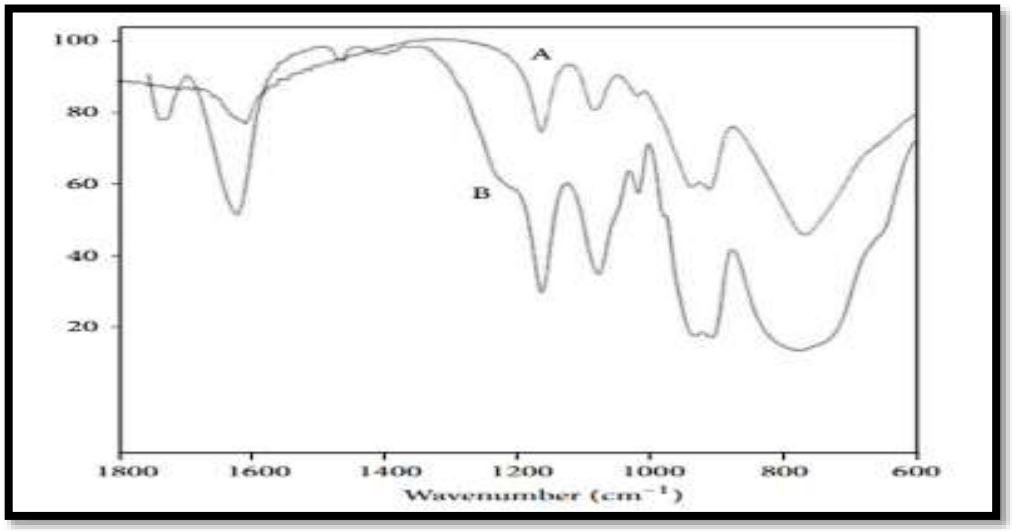

Fig 3. The bulk IR spectrum (A) and nano IR spectrum (B) of Preyssler heteropolyacid

Other synthetic materials have also been seen to exhibit similar diffraction patterns. Infrared spectroscopy was utilised to characterise the heteropolyacid (H_{14} [$NaP_5W_{30}O_{110}$]) on SiO_2 nanoparticles (SPNPs).

4. DISCUSSIONS

Compared to other heteropoly acids like Keggin and the usual approach using H2SO4, the findings demonstrate that the Silica-Supported Preyssler Nanoparticles (H_{14} [$NaP_5W_{30}O_{110}$]/SiO_2) (SPNPs) catalyst exhibits greater activity and performance in the synthesis of Ibuprofen. Its hydrolytic stability (pH 0-12) is essential for catalytic activities, and [12] it is superior to that of other heteropoly acids. Evidence from these reactions reveals that the (H_{14} [$NaP_5W_{30}O_{110}$]/SiO_2) (SPNPs) nano catalyst surpasses Keggin heteropoly acids in terms of reaction efficiency. [13] The likely culprit is the increase in surface area. When the particle size of nanomaterials decreases, the relative number of surface atoms increases, leading to enhanced catalytic activity. When taking into account reaction time, yield, and recycleability, silica-supported Preyssler nanoparticles (SPNPs), (SPNPs), (H_{14} [$NaP_5W_{30}O_{110}$]/SiO_2), were shown to be the best catalyst. Preyssler nanostructures supported by silica were made using a microemulsion [14]. The form of nanoparticles may also be altered by other synthetic ways of their production [15]. As was shown before, this is due to the fact that metastable states are capable of undergoing spontaneous modifications under equilibrium response circumstances.

5. CONCLUSIONS

In this paper, we present a simple, green, and cheap approach for synthesising ibuprofen using silica-supported Preyssler nanoparticles (H_{14} [$NaP_5W_{30}O_{110}$]/SiO_2) as a catalyst. The process is detailed in the following sections. The product may be worked up quickly and easily with this method, which also has a number of other benefits, such as high yields, simple operation, and a clear technique. These nanoparticles, specifically Silica-Supported Preyssler Nanoparticles (H_{14} [$NaP_5W_{30}O_{110}$]/SiO_2) have a number of benefits, including increased hydrolytic and thermal stability (SPNPs). Additional benefits can be gained through

the use of these nanoparticles. Among the many reasons why Preyssler's anion is so important is that it can be used repeatedly without causing harm. We think this method might be useful in the field of organic synthesis.

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