Journal of Molecular Catalysis A: Chemical 317 (2010) 41–45

Contents lists available at ScienceDirect

Journal of Molecular Catalysis A: Chemical

journal homepage: www.elsevier.com/locate/molcata

Solvent free synthesis of acetyl salicylic acid over nano-crystalline sulfated zirconia solid acid catalyst

Beena Tyagi **,[1], Manish Kumar Mishra [1], Raksh Vir Jasra *

Discipline of Inorganic Materials & Catalysis, Central Salt & Marine Chemicals Research Institute (CSMCRI), Council of Scientific and Industrial Research (CSIR), GB Marg, Bhavnagar-364 002, Gujarat, India

ARTICLE INFO

Article history:
Received 6 June 2009
Received in revised form 8 October 2009
Accepted 20 October 2009
Available online 30 October 2009

Keywords:
Acetyl salicylic acid
Aspirin
Solid acid catalysts
Sulfated zirconia

ABSTRACT

Acetyl salicylic acid, commonly known as Aspirin or Ecotrin, has been synthesized by an eco-friendly route using solid acid catalysts namely nano-crystalline sulfated zirconia, sulfated titania, zeolite H-beta, H-Y, H-ZSM-5 and acid treated K-10 clay. Among all the solid acid catalysts studied, nano-crystalline sulfated zirconia showed highest catalytic activity and was found to be efficient in minimal amount to obtain excellent yield (95 wt%) of acetyl salicylic acid crystals. Thermally regenerated catalyst showed similar yield as obtained with the fresh catalyst.

1. Introduction

Solid acids have emerged as potential alternate catalysts to the conventional liquid acids [1,2] due to their non-hazardous nature, requirements in catalytic amounts, enhanced selectivity and easier post-reaction work-up. The ease of separation without resulting into problem of waste disposal and option of re-use of the solid acid catalysts render the processes employing solid acid catalysts as green processes. Among the various solid acid catalysts, sulfated zirconia is a potential catalyst for the isomerization of *n*-butane at ambient temperature [3] and has been extensively studied for the isomerization of *n*-alkanes, cycloalkanes and alkenes [4–7]. It has also been used for various acid catalyzed reactions such as alkylation, acylation, esterification, etherification, nitration, and oligomerization [8,9]. Besides sulfated zirconia, zeolites and acid treated clays are well known catalysts for acid catalyzed reactions. For example, we have reported excellent catalytic activity and selectivity for the desired product by using these solid acid catalysts for various industrially important organic transformations, such as isomerization of terpenes [10–13] and coumarin synthesis by Pechmann reaction [14,15] using sulfated zirconia; nitration of o-xylene [16] and acylation of toluene [17] using zeolites; and isomerization of α-pinene [18] using acid treated clay. In the present study, we extended our focus to synthesize acetyl salicylic acid (ASA) using these solid acid catalysts via O-acetylation of salicylic acid with acetic anhydride.

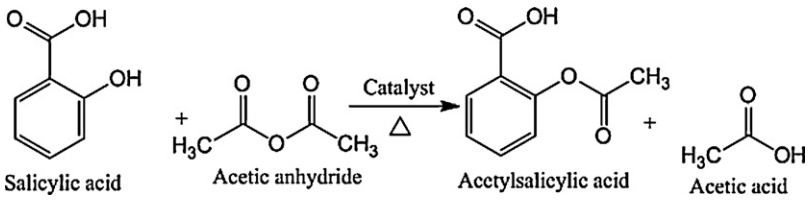
Acetyl salicylic acid, commonly known by its trade name, Aspirin, is an effective non-steroidal analgesic, antipyretic and anti-inflammatory drug and is one of the most widely used medicines around the world. The use of aspirin extends beyond pain relief by inhibiting the production of prostaglandins chemicals responsible for inflammations to life saver by reducing the risk of heart stroke as it prevents the aggregation of platelets. Today more than 10 million kilograms of aspirin is annually produced world-wide and is the most successful product for drug industry that generates largest revenues for pharmaceutical companies.

Commercially, salicylic acid synthesized by Kolbe-Schmidt reaction [19] is acetylated with acetic anhydride in presence of an acid catalyst [20] mainly H_2SO_4 [21] and H_3PO_4 [22] at 80–90 °C. Pure acetyl salicylic acid is obtained after crystallization of cooled reaction mixture. The use of H_2SO_4 and H_3PO_4 is not desirable as these are corrosive, hazardous, not separable, not re-usable resulting to the problem of spent acid disposal. A brown liquid impurity also appears during re-crystallization of acetyl salicylic acid from water, usually in trace amount but sometimes in large quantity also, which is to be removed by filtering the hot aqueous solution and thus making process tedious and results into acetyl salicylic acid crystals of low purity.

Very few studies have been reported to synthesize acetyl salicylic acid to replace conventional H_2SO_4 [23–25]. Acetyl

* Corresponding author. Present address: R & D Centre, Reliance Industries Limited, Vadodara Manufacturing Division, Vadodara-391346, Gujarat, India. Tel.: +91 265 6603935; fax: +91 265 6693934.
** Corresponding author.
E-mail addresses: btyagi@csmcri.org (B. Tyagi), rakshvir.jasra@ril.com (R.V. Jasra).
[1] Tel.: +91 278 567760; fax: +91 278 566970.

1381-1169/$ – see front matter © 2009 Elsevier B.V. All rights reserved.
doi:10.1016/j.molcata.2009.10.019



Scheme 1. Synthesis of acetyl salicylic acid by O-acetylation of salicylic acid with acetic anhydride over solid acid catalyst.

chloride-pyridine has been used [23,24] as the acetylating agent at lower temperature with 33% yield of acetyl salicylic acid. Peng and Song [25] reported water soluble 12-tungustophosphoric acid as a catalyst at room temperature with 57–71% yield of acetyl salicylic acid accompanied with the formation of a gummy polymeric by-product, which needs to be removed and thereby leading to an extra step in the process. Microwave assisted synthesis of acetyl salicylic acid from salicylic acid and acetic anhydride using H_3PO_4 [26–28] and other acidic as well as basic catalysts namely H_2SO_4, $AlCl_3$, $MgBr_2{\cdot}OEt_2$, $CaCO_3$, NaOAc, NEt_3 and dimethylaminopyridine [29] is also reported. Besides being corrosive in nature, use of acid catalyst resulted into unwanted polymeric side-products. Use of base catalysts necessitates post reaction the neutralization of reaction mixture.

In the present study, we report the synthesis of acetyl salicylic acid by the O-acetylation of salicylic acid with acetic anhydride using nano-crystalline sulfated zirconia (Scheme 1). For comparison, other solid acid catalysts namely, sulfated titania, zeolite H-beta, H-Y, H-ZSM-5 and acid treated K-10 clay were also studied. The significance of the study lies in the solvent free economical synthesis of acetyl salicylic acid of high purity crystals in excellent yield (65–95 wt%) and the re-usability of the solid acid catalyst after separation followed by thermal activation. To the best of our knowledge, it is the first report [30] of the solvent free green catalytic synthesis of acetyl salicylic acid using a solid acid catalyst.

2. Experimental

2.1. Materials

Salicylic acid and acetic anhydride were supplied by M/S Loba Chemie, India and S.D. Fine Chem. Ltd., India, respectively. Na-forms of zeolites were procured from Zeocat, Switzerland and acid treated K-10 clay was from Sigma–Aldrich, USA.

2.2. Catalyst synthesis

Nano-crystalline sulfated zirconia has been prepared by one step sol–gel technique [12]. A typical synthesis involves the addition of concentrated sulfuric acid (1.02 ml) to zirconium *n*-propoxide precursor (30 wt%) followed by the hydrolysis with water (water:Zr-P molar ratio 4:1). After 3 h aging at room temperature, the resulting gel was dried at 110 °C for 12 h followed by calcination at 600 °C for 2 h. Sulfated titania was also prepared using the similar methodology. Zeolite H-beta, H-Y, H-ZSM-5 have been prepared by ammonium cation exchanged of the respective Na-forms followed by thermal decomposition [17].

2.3. Catalyst characterization

The crystallinity of all the catalysts and the crystalline phases of calcined sulfated zirconia and titania was determined by X-ray powder diffractometer (Philips X'pert) using CuK_α radiation ($\lambda = 1.54056$ Å). The sample was scanned in 2θ range of 10–80° at a scanning rate of $0.04^\circ\ s^{-1}$. Crystallite size of tetragonal phase of zirconia and anatase phase of titania was determined from their characteristic peak, i.e., at $2\theta = 30.18$ (1 1 1) and 25.30 (1 0 1) for zirconia and titania, respectively by using Scherrer formula [31] as below:

$$\text{Crystallite size} = \frac{K\lambda}{W\cos\theta}$$

where, K, shape factor = 0.9, $W = W_b - W_s$; W_b is the broadened profile width of experimental sample and W_s is the standard profile width of reference silicon sample.

FT-IR spectra of the catalysts were recorded by FT-IR spectrophotometer (PerkinElmer, GX, USA) in the range of 400–4000 cm^{-1} with a resolution of 4 cm^{-1} as KBr pellets.

Specific surface area, pore volume and pore size distribution of all the catalysts were determined from N_2 adsorption-desorption isotherms at −196 °C (ASAP 2010, Micromeritics, USA). Surface area and pore size were calculated by using BET equation and BJH method, respectively [32]. The samples were degassed under vacuum (1×10^{-3} mmHg) at 120 °C for 4 h, prior to adsorption measurement to evacuate the physisorbed moisture.

The bulk sulfur (wt%) retained in sulfated zirconia and titania samples after calcination at 600 °C was analyzed by elemental analyzer (PerkinElmer 2400, Sr II, USA).

2.4. Synthesis of acetyl salicylic acid

O-acetylation of salicylic acid with acetic anhydride was conducted in a batch reactor (20 ml) in presence of solid acid catalyst. Salicylic acid (1 g) and acetic anhydride (3 g) and catalyst (0.1 g, pre-activated at 450 °C for 2 h except K-10, which was pre-activated at 120 °C for 2 h) were taken in a 20 ml reaction tube of reaction station (Radleys Discovery Technologies, UK) equipped with a magnetic stirrer. The mixture was heated at different temperatures in the range of 90–120 °C for reaction times ranging from 30 to 240 min. The reaction mixture was cooled and filtered to separate the catalyst. Unreacted acetic anhydride was hydrolyzed to acetic acid by adding water (10 ml) and the product acetyl salicylic acid was obtained from this solution by the slow evaporation of water at room temperature. The fast recovery of the product was also obtained by adding dichloromethane to the solution, which was separated from the aqueous layer and acetyl salicylic acid was obtained by evaporating the dichloromethane. However, from green synthesis view, we have used the first method without adding dichloromethane throughout this studies. The yield of acetyl salicylic acid was calculated as below:

$$\text{Yield (wt\%)} = \frac{\text{obtained wt. of product}}{\text{theoretical wt. of product}} \times 100$$

The crude yield of acetyl salicylic acid obtained was 92–95%. The crude crystals of acetyl salicylic acid were re-crystallized with ethanol–water mixture and characterized by melting point, DSC and TG-DTA (Mettler Toledo Star^e SW 7.01), FT-IR (PerkinElmer GX, USA), and ^{1}H NMR-spectroscopy (Bruker Avance-II 500).