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Green Synthesis of Acetyl Salicylic Acid by Using PT - Zeolites Catalysts

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ABSTRACT

O-acetylation of salicylic acid has been carried out under solvent-free conditions using protonated zeolites (Hβ, HZSM-5and HY) and these platinated forms (Pt-Hβ, Pt-HZSM-5& Pt-HY) as solid acid catalysts to synthesize acetyl salicylic acid. The process has simpler work up procedure and the catalyst has been successfully recovered and recycled. The zeolite catalysts have been characterized by different techniques like BET surface area measurement, total acidity by NH3-TPD/ n-butylamine back titration method and crystallinity by powder X-ray diffraction. O-acetylation using platinated zeolite catalysts under was found to be an efficient and environment friendly (green) process. Platinated zeolites were found to be much more effective, reusable, recyclable, and green catalysts for the synthesis of acetyl salicylic acid when compare to protonated zeolites.

Keywords: O-acetylation; protonated zeolites; platinated zeolites (Pt-Hβ, Pt-HZSM-5& Pt-HY)

Introduction:

Solid acids are an alternate to liquid catalysts[1,2] due to their non-toxic nature and enhanced selectivity. Now a day's transformations such as alkylation, esterification and isomerization are preferably conducted using this environmental friendly solid acids[3-5] especially in petroleum industry and for fine chemical synthesis[6-10].

Among solid acids, zeolites play a key role in the shift from homogeneous to heterogeneous catalytic process. Zeolites have been widely used in bulk chemical processes such as oil refining and they have advantage of higher surface area and well delivered uniform structure under environmentally benign conditions[11-19]. Zeolites are well known catalysts for acid catalyzed reactions such as isomerization of terpenes[20-23], coumarin synthesis by Pechmann reaction[24-25], nitration of *o*-xylene[26], acylation of toluene[27], etc.

Acetyl salicylic acid (Acetyl salicylic acid) is an analgesic (painkiller), an antipyretic (fever reducer) and an anti-inflammatory agent. Commercially acetyl salicylic acid is synthesized by Kolbe-Schmidt reaction [28] in which salicylic acid is acetylated with acetic anhydride in presence of an acid catalyst[29] mainly H_2SO_4[30] and H_3PO_4[31] at 80-90 ^{0}C. The use of H_2SO_4 and H_3PO_4 is not desirable as these are corrosive, hazardous not separable, not reusable resulting to the problem of spent acid disposable.

The present study deals with the synthesis of acetyl salicylic acid by o-acetylation of salicylic acid with acetic anhydride using zeolites and its modified forms as solid acid catalysts. Zeolites in their protonated and platinated forms were prepared and characterized for their physico-chemical properties before their use in *o*-acetylation reaction. Since, zeolite solid acid catalysts have shown good catalytic activity in some of the acid catalyzed reactions, the research work presented in this article was carried out with an expectation that this type of a solid acid would also be more effective in *o*-acetylation. Optimization of reaction conditions for *o*-acetylation reaction was studied by varying molar ratio of the reactants, reaction temperature, reaction time and weight of the catalyst. Activation and reusability of these solid acids was also taken up.

Experimental:

Chemicals:

Zeolites in their sodium form (Na-β, Na-Y & Na-ZSM5) were supplied by Sud Chemie India Private Limited, Baroda. Salicylic acid, acetic anhydride and chloro platinic acid (H_2PtCl_6) were supplied by M/S LOBA Chemie, India.

Preparation of solid acid catalysts:

Protonation of Na-zeolites by ion exchange method:

Sodium form of zeolites such as (Na-β, Na-Y & Na-ZSM5) zeolites were protonated by exchanging the Na^+ ions of the parent zeolite by H^+ ions (protonation).

Protonated zeolites (HZSM5, Hβ and HY) were prepared by ion exchange method. 5 gm of the Na-zeolites were immersed in 100 ml of 1*M* ammonium nitrate solution and stirred for overnight. The mixture was filtered, washed with deionized water, dried in hot air oven at 120 ^{0}C for 12 h and calcinated in a muffle furnace at 550 ^{0}C for 5 h.

Synthesis of platinated zeolites:

Pt-Hβ, Pt-HZSM5 and Pt-HY zeolites containing 0.75% of Pt were prepared by impregnation method in which a known weight of the zeolte (Hβ or HZSM5 or HY) was mixed with 1%H_2PtCl_6 and a few drops of deionized water. The resulting mixture was made into a paste, which was then dried in a hot air oven at 120 ^{0}C for 12 h, powered and calcinated in a muffle furnace at 550 ^{0}C for 5 h.

Characterization of solid acid catalysts:

Bruaner-Emmet-Teller (BET) surface area of zeolites was measured by NOVA 1000 Quanta chrome high-speed gas sorption analyzer instrument. The total acidity of zeolites was measured by NH_3-TPD and *n*-butyl amine back titration methods[32]. The powder X-ray diffraction (PXRD) patterns were recorded by X-ray powder diffract meter (Philips X'pert) using CuKα radiation (λ = 1.5418 A°) using graphite crystal monochromator.

Catalytic activity studies of zeolite solid acid catalysts in the synthesis of acetyl salicylic acid:

O-acetylation of salicylic acid with acetic anhydride was carried out in a 50 ml round bottomed (RB) flask fitted with a water cooled condenser. The reactions were carried out on a hot plate-magnetic stirrer in presence of zeolite solid acids. The reaction mixture (salicylic acid, acetic anhydride and catalyst) was heated at a particular temperature for a definite period of time. After a definite period of time, the hot reaction mixture was filtered to separate the catalyst. Ice cooled water was added to the reaction mixture to hydrolyze the unreacted acetic anhydride to acetic acid. The reaction mixture was then cooled to obtain a white solid of acetyl salicylic acid (acetyl salicylic acid). Thus obtained crude acetyl salicylic acid was filtered, washed with water, dried and re-crystallized with ethanol-water mixture.

The re-crystallized acetyl salicylic acid was characterized by melting point, LCMS and ^{1}HNMR spectroscopy.

Reusability of zeolite catalysts in the synthesis of acetyl salicylic acid:

To study the re-usability of the used zeolite (both protonated and

platinated forms) catalyst, the catalyst was filtered from the reaction mixture washed with acetone, dried at 120 °C for 5 h and calcined at 550 °C for 1 h. Thus reactivated catalyst was subjected to *o*-acetylation reaction of salicylic acid under same reaction conditions. The re-activation and re-usability of the used solid acid catalyst was repeated for 5 reaction cycles.

Results and discussion:

Characterization of zeolite catalyst:

Zeolite catalysts were characterized for their physico-chemical properties such as surface area, total acidity and crystallinity.

Surface area:

The values of surface area of zeolite catalysts obtained by BET method are given in Table 1. The values are comparable to the values mentioned in the literature[33].

The BET surface area of zeolites either in their sodium or protonated forms was found to be almost the same. The BET surface area of protonated zeolites was not much affected on loading platinum, but found to be slightly lower than their other forms.

Total acidity:

The total acidity of the zeolite catalysts used in the present investigation was determined by NH_3-TPD and *n*- butyl amine back titration methods (Table 1). Total acidity of Na zeolites was least active when compared to protonated & Pt –forms.

Table 1: Surface properties of zeolite catalysts used in the present study.

Sl. No.	Zeolite catalyst	BET Surface area (m^2/g)	Total acidity by NH_3-TPD (n-butyl amine back titration) (mmol/g)
1	Naβ(Si/Al=25)	685	0.22 (0.19)
2	NaY(Si/Al=5)	905	0.11 (0.10)
3	NaZSM5(Si/Al=30)	410	0.18 (0.20)
4	Hβ	590	1.11 (1.01)
5	HY	720	0.78 (0.79)
6	HZSM5	383	1.01 (0.95)
7	Pt-Hβ	565	1.28 (1.24)
8	Pt-HY	702	0.91 (0.88)
9	Pt-HZSM5	363	1.12 (1.10)

In case of zeolites the total acidity (measured by both the methods) was found to be in the order: Hβ > HZSM5> HY

Among the zeolites, Hβ & HZSM5 were found to have higher concentration of acid sites when compared to HY. The values of total acidity obtained by both NH_3-TPD as well as *n*-butyl amine back titration method are comparable to a reasonable extent.

However, upon loading of platinum on protonated zeolites the total acidity of Pt- zeolites was found to be slightly increased. It has been reported that the incorporation of Pt increases the total acidity of a solid acid by increasing the number of protonic (Brönsted) acid sites[34].

Crystallinity:

PXRD data was used to characterize crystalline phases of zeolite catalysts (Figure 1). The PXRD pattern of zeolite-β consists of both sharp (22.5^0) and a broad (7.5^0) peak indicating the presence of tetragonal and monoclinic symmetry. Characteristics peaks $2\theta = 22\text{-}25^0$ were observed for ZSM-5. The peak corresponding to $2\theta = 22.5^0$ is typically for β- zeolites.

The zeolite-Y framework shows tetrahedral sites. The PXRD pattern of Y & ZSM-5 zeolites were found to be in agreement with PXRD patterns reported in the literature[35]. No difference between the PXRD patterns of protonated zeolites and platinated zeolites was observed indicating that the platinum was only dispersed on the surface of zeolites support without much interaction. Since a very small amount of platinum is incorporated over zeolites, no reflection corresponds to Pt or any compound of Pt was observed.

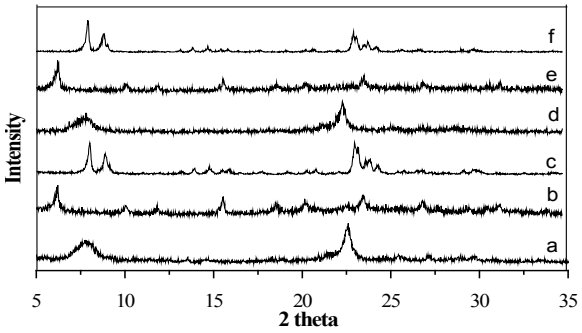
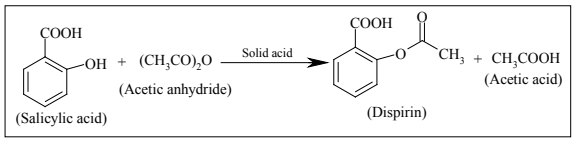


Figure 1. PXRD patterns of zeolite catalysts: (a) Hβ (b) HY (c) HZSM5 (d) Pt-Hβ (e) Pt-HY (f) Pt-HZSM5.

Catalytic activity studies of zeolites in the synthesis of acetyl salicylic acid

O-acetylation of salicylic acid (SA) with acetic anhydride (AA) over zeolite catalyst was carried out in liquid phase (Scheme 1). Acetyl salicylic acid obtained from the o-acetylation reaction was characterized by measuring its melting point, LCMS and 1H NMR spectroscopy.



Scheme 1. *O*-acetylation of salicylic acid with acetic anhydride over zeolites catalyst.

The data obtained by the measurements is given below.

- Melting point – 135 oC.
- LCMS method – (a) 10 mM NH4CO3; (b) ACN; flow rate 1 mL/min; Column X Bridge C8 - Purity of acetyl salicylic acid was 99.136 % with its mass in negative mode at 179.0.
- 1HNMR (400MHz: DMSO: TMS): δ7.9 (d, 1H, ArH), 7.6 (t, 1H, ArH), 7.3 (t, 1H, ArH), 7.2 (d, 1H, ArH), 2.2 (s, 3H, CH3), 13 (s 1H, –COOH); 2.5 (solvent). The 1HNMR peaks of acetyl salicylic acid were found to be similar to those reported in the literature.

In general all the zeolites (sodium, protonated and platinated forms) were found to be active in *o*-acetylation. However, when the reaction was carried out in the absence of any solid acid catalyst, low yield of acetyl salicylic acid was observed. This indicates that *o*-acetylation of salicylic acid is a catalyzed reaction and a suitable catalyst required.

In order to obtain highest possible yield of acetyl salicylic acid, *o*-acetylation reaction was optimized by varying parameters such as, molar-ratio of reactants (salicylic acid: acetic anhydride), amount of the zeolite catalyst, reaction temperature and reaction time.

Effect of type of zeolite catalyst on the yield of acetyl salicylic acid:

The following Table 2 shows the yield (%) of acetyl salicylic acid over different zeolite under a set of reaction conditions. The yield (%) of acetyl salicylic acid over zeolite catalyst was in the range 69-92%.

The order of reactivity was found to be: Zeolite-β >Zeolite-ZSM5 > Zeolite-Y.

Table 2. Effect of type of zeolite catalyst on the yield of acetyl salicylic acid.

Zeolite Catalysts	Yield of acetyl salicylic acid (%)
Naβ	16
NaY	10
NaZSM5	13
Hβ	76
HY	65
HZSM5	71
Pt-Hβ	98
Pt-HY	86
Pt-HZSM5	92

[Reaction conditions: Weight of catalyst = 0.05g; molar ratio of SA:AA = 1:3; reaction temperature = 85 ^{0}C; reaction time = 45 min].

Yield of acetyl salicylic acid was found to be affected by the surface acidity of zeolites. As platinated zeolites possessed more acidity than their sodium or protonated forms, platinated zeolites were more active in *o*-acetylation than their other forms. The order of reactivity of different forms of zeolites in *o*-acetylation was:

Pt–Hzeolites > Hzeolites > Na-zeolites

Since highest yield of acetyl salicylic acid was obtained over β-zeolites, optimization studies were carried out over Hβ and Pt-Hβ catalysts.

Effect of molar ratio on the yield (%) of acetyl salicylic acid:
In order to study the effect of concentration of reactants (salicylic acid or acetic anhydride) on the yield (%) of acetyl salicylic acid, the molar ratio of SA: AA was varied from 1:2 to 1:5 and the results of which are presented in Table 3. Since highest yield of acetyl salicylic acid was obtained over β-zeolites, optimization studies were carried out over this catalyst.

Table 3: Effect of molar ratio on the yield (%) of acetyl salicylic acid.

Sl. No.	Molar ratio of SA: AA	Yield of acetyl salicylic acid (%)	
		Hβ	Pt-Hβ
1	1:2	71	90
2	1:3	76	98
3	1:4	72	84
4	1:5	68	76

[Reaction conditions: Reaction temp = 85 ^{0}C; reaction time = 45 min; catalyst = 0.05 g of Hβ or Pt-Hβ].

As acetic anhydride acts both as a solvent and as a reactant in *o-acetylation*, the excess of acetic anhydride is used to facilitate the reaction. At a molar ratio of 1:3, salicylic acid can be well dispersed in acetic anhydride medium driving the reaction to completion. However, further increase in concentration of acetic anhydride (molar ratio = 1:4 and 1:5) lead to decrease in the yield of acetyl salicylic acid due to dilution effect. Hence optimum molar ratio was used for further studies 1:3.

Effect of reaction temperature on the yield (%) of acetyl salicylic acid:
To study the effect of reaction temperature on the yield (%) of acetyl salicylic acid, *o*-acetylation reactions was carried out over Hβ and Pt-Hβ in the temperature range from 55 – 115 ^{0}C (Figure 3). In fact, the yield of acetyl salicylic acid increased with an increase in the reaction temperature up to 85 ^{0}C. However, when the reaction temperature exceeds 85 ^{0}C the yield decreased which may be due to product decomposition at high temperatures. Hence 85 ^{0}C was found to be optimum reaction temperature for the synthesis of acetyl salicylic acid over zeolite catalyst.

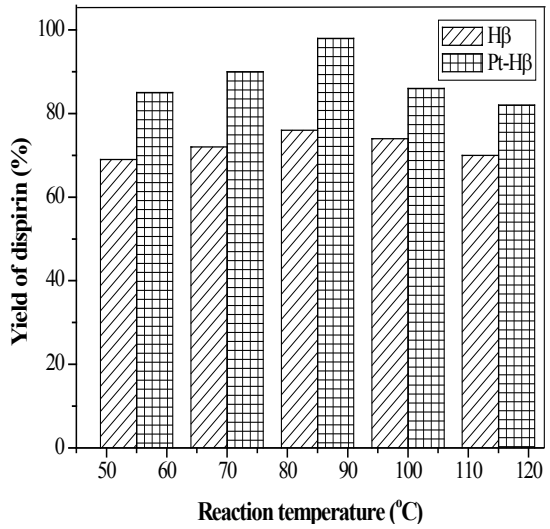


Figure 3. Effect of reaction temperature on the yield of (%) of acetyl salicylic acid.

[Reaction conditions: Molar ratio of SA: AA = 1:3; catalyst = 0.05 g of Hβ or Pt-Hβ; reaction time = 45 min].

Effect of reaction time on the yield (%) of acetyl salicylic acid:
In order to study the effect of reaction time on the synthesis of acetyl salicylic acid, salicylic acid and acetic anhydride were allowed to react in presence of Hβ or Pt-Hβ as a catalyst in the time range from 15 min to 75 min. The yield (%) of acetyl salicylic acid got increased when the reaction time was increased. At 45 minutes a maximum yield of acetyl salicylic acid was obtained over Hβ or Pt-Hβ and as reaction time increased beyond 45 min the yield of acetyl salicylic acid got decreased (Figure 4). This can be attributed to the formation of side products along with the condensation of SA molecules in the reaction system. Hence, 45 min was chosen as an appropriate reaction time for the better yield of acetyl salicylic acid.

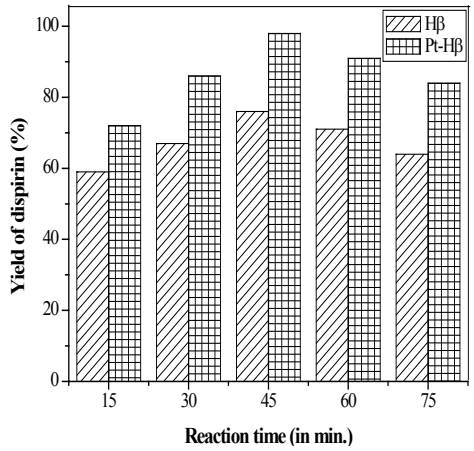


Figure 4. Effect of reaction time on the yield (%) of acetyl salicylic acid.

[Reaction conditions: Molar ratio of SA: AA = 1:3; catalyst = 0.05 g of Hβ or Pt-Hβ; reaction temperature = 85 ^{0}C].

Effect of weight of zeolite catalyst (Hβ or Pt-Hβ) on the yield (%) of acetyl salicylic acid:
The effect of weight of zeolite catalyst (Hβ or Pt-Hβ) was studied by varying the catalyst weight from 0.025 g to 0.15 g and the results are presented in Figure 5. The yield of acetyl salicylic acid increases with an increase in the weight of the catalyst. And a good yield of acetyl salicylic acid (98%) was achieved at 0.05 g of Pt-Hβ and 76% over Hβ zeolite catalyst. The yield of acetyl salicylic acid was found to decrease when the weight of the catalyst was increased beyond 0.05 g, which may be because of the fact that, when the weight of the catalyst is increased beyond a limit may lead to a delay in attaining reaction equilibrium which further results to the formation of more side products.

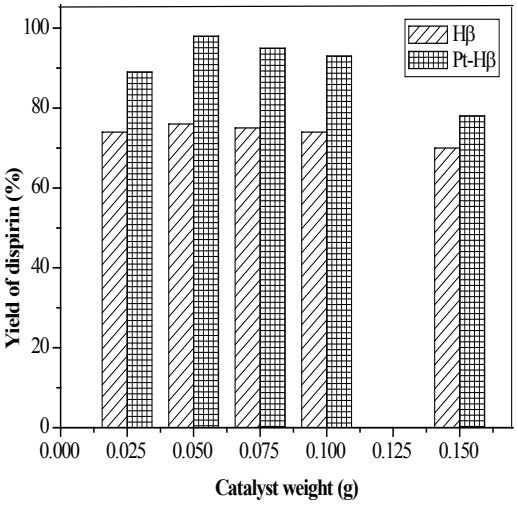


Figure 5. Effect of weight of zeolite catalyst on the yield of (%) of acetyl salicylic acid.

[Reaction conditions: Molar ratio of SA: AA = 1:3; catalyst = 0.05 g Hβ or Pt-Hβ; reaction temperature = 85 ^{0}C].

Effect of re-usability of zeolite catalyst (Hβ and Pt-Hβ) on the yield (%) of acetyl salicylic acid:

To study the regeneration and reusability of the catalyst, Hβ or Pt-Hβ were recovered from the reaction mixture by filtration, washed with acetone followed by drying in an oven at 120 °C for 5 h and thermal activation at 550 °C in a muffle furnace for 1 h. Thus regenerated zeolites were re-used as catalysts in *o*-acetylation reaction. This process of regeneration and reusability was carried out for 5 reaction cycles and the results are shown in the form of a graph (Figure 6). It is observed that, the yield of acetyl salicylic acid was slightly decreased over Hβ catalyst. However, Pt-Hβ was found to be much active even after it's used for 5 reaction cycles. This indicates that incorporation of platinum on zeolites can decrease their deactivation. Thus platinum incorporated zeolites can be successfully used in *o*-acetylation reaction for more number of cycles and it can be a better green catalyst for the synthesis of acetyl salicylic acid.

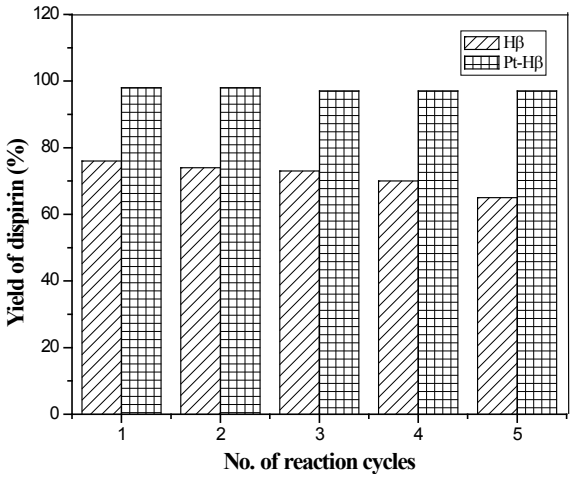
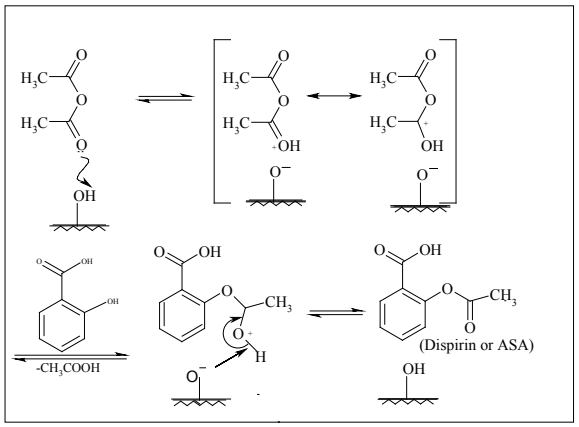


Figure 6. Effect of re-usability of zeolite catalyst on the yield (%) of acetyl salicylic acid.

[Reaction conditions: Molar ratio of SA: AA = 1:3; catalyst = 0.05 g Hβ or Pt-Hβ; reaction temperature = 85 ^{0}C; reaction time = 45 min].

Mechanism of *o*-acetylation over Brönsted (protonic) acid sites of zeolites:

A probable mechanism for the synthesis of acetyl salicylic acid over an zeolite catalyst is illustrated in Scheme 2, where the Brönsted acid sites (-OH) of the zeolites catalyst helps in the formation of carbocation intermediate (CH_3CO^+) which attacks the phenolic oxygen of salicylic acid to form acetyl salicylic acid .



Scheme 2. Probable mechanism for *o*-acetylation of salicylic acid with acetic anhydride over Brönsted acid sites of an acid catalyst.

Conclusion:

Investigation of *o*-acetylation of salicylic acid with acetic anhydride using zeolite (protonated & platinated) was carried out. Platinum modified zeolites were found to be more acidic and active in *o*-acetylation resulting in the highest yield of acetyl salicylic acid upto 98% when compared to protonated or Na-zeolites. Incorporation of platinum in zeolites not only increased their acidity but also prevent their deactivation. These solid acid catalysts were found to be green, eco-friendly, reusable and reasonably economical when compared to conventional catalysts such as H_2SO_4 and H_3PO_4.

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