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# Liquid phase reaction of 2′-hydroxyacetophenone and benzaldehyde over ZSM-5 catalysts

S. Saravanamurugan[1], M. Palanichamy, Banumathi Arabindoo, V. Murugesan*

*Department of Chemistry, Anna University, Sardar Patel Road, Chennai 600025, India*

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**Abstract**

The reaction of 2′-hydroxyacetophenone with benzaldehyde was studied over H-ZSM-5, Mg-ZSM-5 and Ba-ZSM-5 catalysts at 140 °C. The products were 2′-hydroxychalcone and flavanone. The conversion of 2′-hydroxyacetophenone increased with time and attained a maximum of 40–50% conversion over all the catalysts. Though the yield of chalcone and flavanone increased with increase in time, the yield of flavanone was less than 2′-hydroxychalcone over all the catalysts. The order of activity of the catalysts was Mg-ZSM-5 > Ba-ZSM-5 > H-ZSM-5. The influence of temperature in the range of 100–160 °C on conversion and products yield was studied over Mg-ZSM-5. The increase in conversion was small between 100 and 120 °C, but above 120 °C there was a marked increase in conversion. The optimal catalyst loading was found to be 0.75 g for 10 mmol reactants. Study of influence of time on Mg-ZSM-5 at 160 °C revealed a rapid increase in conversion and products yield up to 3 h and a steady state afterwards. The role of solvent in this reaction was studied with DMSO, nitrobenzene and a mixture of DMSO and nitrobenzene. High conversion was observed with DMSO.


*Keywords:* 2′-Hydroxychalcone; Flavanone; Mg-ZSM-5; DMSO; Nitrobenzene

## 1. Introduction

The members of flavanoid family are attracting increasing attention due to their applications as anticancer, anti-inflammatory, antibacterial and anti-AIDS pharmacological activities [1–4]. Flavanone, a member of this family, is an important intermediate in the synthesis of many pharmaceuticals. Flavanoids are commonly synthesised via the Claisen–Schmidt condensation between 2′-hydroxyacetophenone and benzaldehyde and subsequent isomerisation of 2′-hydroxychalcone intermediate [5,6]. Both the reactions are catalysed by acids and bases under homogeneous conditions. There are many drawbacks for reactions under homogeneous conditions such as catalyst recovery and waste disposal problems [7–11]. In this respect heterogeneous catalysis is considered as an eco-friendly alternative. The feasibility of utilising heterogeneous catalysts for the production of flavanone was demonstrated by Corma et al. [6] and Blanco et al. [12]. But there is no report in the literature for the use of H-ZSM-5 zeolite as a catalyst for this reaction.

Solvents play an important role in fine chemical and pharmaceutical synthesis [13]. While the ultimate goal of many heterogeneous catalytic processes is to eliminate the use of solvent, it is equally important to understand the role of solvents in these syntheses. Solvents are used to facilitate liquid phase reactions by improving the heat and mass transfer characteristics of the system. They also extend the catalyst life by preventing coke build-up on the catalyst surface [14]. Variations in the solvent polarity, solubility, reactivity and chemisorption property can influence the chemo-, regio-, and in some cases, stereo-selectivity of the products. Recently, Drexler and Amiridis [13] have reported the detailed kinetic results both in the presence and absence of DMSO solvent for the synthesis of flavanone over MgO. They suggested modification of MgO surface and its adsorption behaviour

* Corresponding author. Tel.: +91-44-22200660; fax: +91-44-22200660.
*E-mail addresses:* s_rsaravanan2002@yahoo.co.in (S. Saravanamurugan), v_murugu@hotmail.com (V. Murugesan).
[1] Tel.:+91-44-22203150; fax: +91-44-22203150.

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for the reactants in the presence of DMSO. Borax [15], $Al_2O_3$ [16], and zeolites [17] were also used as catalysts for the synthesis of chalcones, but the solvent influence was not investigated. Since the reaction is both acid and base catalysed, in the present study acid catalyst H-ZSM-5 and base catalysts Mg-ZSM-5 and Ba-ZSM-5 were examined for the activity. In addition, the influence of solvents such as DMSO and nitrobenzene on the yield of flavanone was also investigated.

## 2. Experimental

$NH_4$-ZSM-5 zeolite with Si/Al = 40 purchased from United Catalysis India Ltd., Baroda, was subjected to ion exchange with barium nitrate and magnesium nitrate, respectively, by the following procedure: 15 ml of 0.1 M aqueous solution of metal nitrate was added to 1 g of $NH_4$-ZSM-5 zeolite. The mixture was stirred at 80 °C for 6 h, cooled to room temperature, filtered and dried at 80 °C for 6 h. The same procedure was repeated thrice in order to get maximum ion-exchange. The ion-exchanged materials were calcined at 550 °C in air for 6 h. The ion-exchanged catalysts were activated prior to use.

The in situ DRIFT spectra were recorded in a Nicolet Avatar 360 FTIR spectrophotometer equipped with a high temperature vacuum chamber. About 15 mg of the powdered catalyst sample was dehydrated at 500 °C under vacuum ($10^{-5}$ mbar) and then cooled to room temperature. Pyridine was adsorbed at the same temperature and allowed to equilibrate. The catalyst was then evacuated at 150 °C under vacuum ($10^{-5}$ mbar) for 30 min. The sample was then cooled to room temperature and the spectrum was recorded.

## 3. Catalytic reaction

The title reaction was carried out in the liquid phase in a batch reactor consisting of a three-necked round bottomed flask fitted with a condenser, a connector for nitrogen purge, and sampling apparatus. The reaction mixture, 2′-hydroxyacetophenone (10 mmol), benzaldehyde (10 mmol) and solvent (5 ml) was heated in an oil bath to the requisite temperature and stirred simultaneously with a magnetic stirrer. Prior to each experiment the empty reactor was purged with nitrogen to remove oxygen to avoid oxidation of benzaldehyde to benzoic acid [3]. Aliquots of the reaction mixture were withdrawn at regular intervals and subjected to GC analysis (Shimazdu 17A; cross-linked 5% phenylmethyl siloxane capillary column, FID detector). The products were also identified by GC–MS using a Perkin-Elmer Auto System XL Gas Chromatograph with Turbo Mass Spectrometer (EI, 70 eV) using helium as carrier gas.

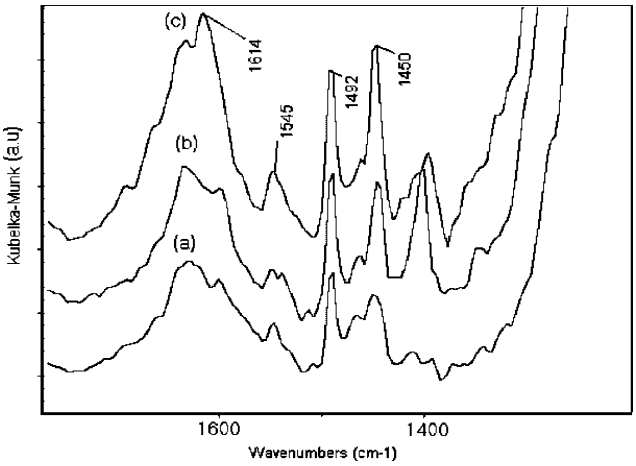



Fig. 1. In situ DRIFT spectra of pyridine adsorbed catalysts: (a) H-ZSM-5; (b) Ba-ZSM-5; (c) Mg-ZSM-5.

## 4. Results and discussion

The in situ DRIFT spectra of pyridine-adsorbed catalysts are shown in Fig. 1. The characteristic band due to pyridine adsorbed on Brønsted acid sites (pyridinium ions) appears at 1545 $cm^{-1}$ while the band due to pyridine coordinated to Lewis acid sites appears at 1450 $cm^{-1}$ [18]. The peak at 1450 $cm^{-1}$ is more intense for Mg-ZSM-5 and Ba-ZSM-5 than for H-ZSM-5 thus confirming coordination of pyridine with $Mg^{2+}$ and $Ba^{2+}$ ions. Desorption study was performed for pyridine adsorbed Mg-ZSM-5 at 150, 200, 300 and 400 °C and the spectrum was recorded at each temperature (Fig. 2). The intensity of the peak at 1450 $cm^{-1}$ decreases gradually with increasing temperature. The intensity of the peak at 1545 $cm^{-1}$ does not vary upto 300 °C but a major decrease in intensity for the same peak is observed at 400 °C. These observations demonstrate strong bonding of pyridine with Brønsted acid sites and weak bonding with

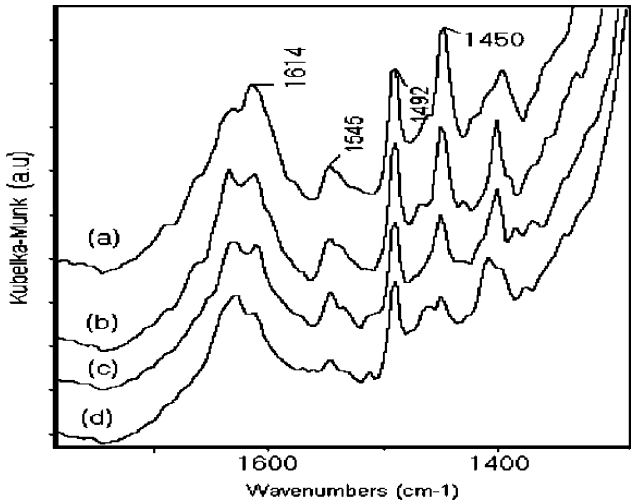
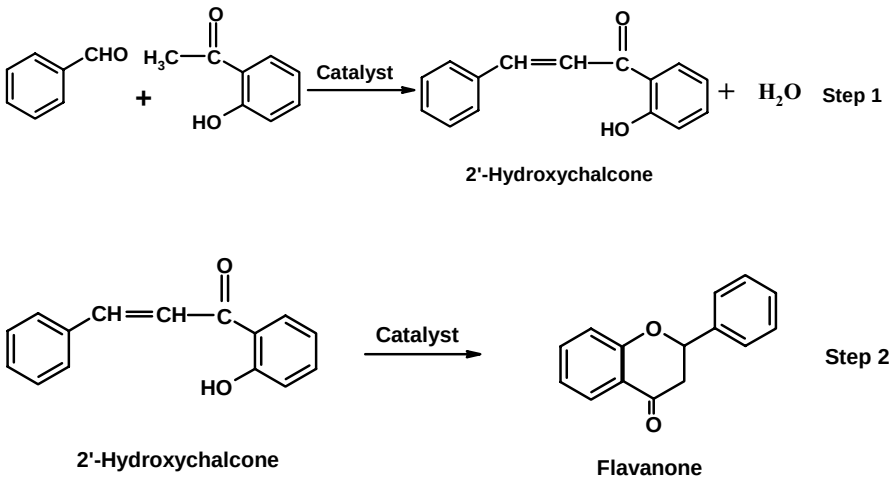



Fig. 2. DRIFT spectra of pyridine desorbed over Mg-ZSM-5 at: (a) 150 °C; (b) 200 °C; (c) 300 °C; (d) 400 °C.




Scheme 1.

Lewis acid sites. Further the gradual decrease in intensity of the peak at 1450 $cm^{-1}$ indicates presence of Lewis acid sites of varying strength.

The synthesis of flavanone from benzaldehyde and 2′-hydroxyacetophenone at 140 °C over H-ZSM-5, Mg-ZSM-5 and Ba-ZSM-5 involves two steps as illustrated in the reaction (Scheme 1). The Claisen–Schmidt condensation of benzaldehyde with 2′-hydroxyacetophenone takes place in the first step to yield 2′-hydroxychalcone. In the second step, 2′-hydroxychalcone undergoes intramolecular cyclisation to yield flavanone. Steps one and two are both acid and base catalysed reactions. Protonation of the carbonyl oxygen of the aldehyde by acids in step one making it more susceptible to nucleophilic attack. Similarly, protonation of 2′-hydroxyacetophenone makes the $–CH_3$ hydrogens more acidic to provide nucleophilicity for the resulting $–CH_2$ ion. The step 2 is catalysed by protonation of the carbonyl oxygen of the chalcone permitting the distant methine carbon more susceptible to nucleophilic attack by the phenolic oxygen.

The results of 2′-hydroxyacetophenone conversion and the yields of chalcone and flavanone over H-ZSM-5 are illustrated in Fig. 3. Conversion increases with time and reaches a maximum of 40% at the end of 3 h. The yield of 2′-hydroxychalcone and flavanone increases with increase in time and the yield of 2′-hydroxychalcone is larger than that of flavanone. Since the catalyst contains more strong Brønsted acidic sites, 2′-hydroxyacetophenone might be protonated at the carbonyl carbon thus providing greater mobility to $CH_3$ hydrogens. When the $CH_3$ hydrogens are close to protonated benzaldehyde, the dipole–dipole interaction between the protonated carbonyl group of benzaldehyde and methyl hydrogens of 2′-hydroxyacetophenone would facilitate condensation. The expected decrease in entropy of the process, and increase in resonance in 2′-hydroxychalcone may be the driving forces for this intermolecular condensation. The intramolecular cyclisation of 2′-hydroxychalcone to flavanone is further favoured by decrease in enthalpy. As the catalyst is of medium pore type, it will also provide additional driving force for intramolecular cyclisation. As the yield of 2′-hydroxychalcone and flavanone increases with increase in time, there must be attainment of steady state in the formation 2′-hydroxychalcone and its cyclisation to flavanone.

In order to study the influence of Lewis acid sites ion on conversion and products yield, the reaction was also carried over Mg-ZSM-5. There is a linear increase in conversion with time (Fig. 4). The overall conversion over Mg-ZSM-5 is about 8–10% higher than over H-ZSM-5 with slight increase in the yield of 2′-hydroxychalcone and flavanone. This suggests nearly same influence of the Brønsted and Lewis acid sites. The yield of 2′-hydroxychalcone is higher and the yield of flavanone is lower over Ba-ZSM-5 at 140° C (Fig. 5). This observation illustrates steric hindrance to the diffusion of 2′-hydroxychalcone into the pores of the catalyst due to the size of the cation. In addition, flavanone may not easily

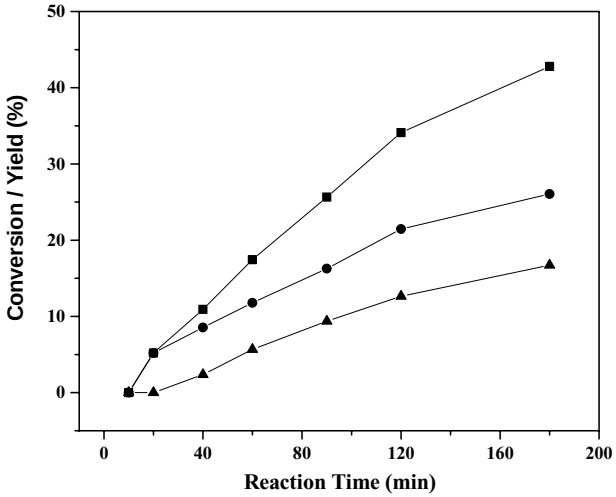



Fig. 3. Conversion and products yield as a function of reaction time in DMSO over H-ZSM-5 ((■) conversion of 2′-hydroxyacetophenone; (●) yield of 2′-hydroxychalcone; (▲) yield of flavanone); (catalyst weight, 0.5 g; temperature, 140 °C; reaction time, 3 h).

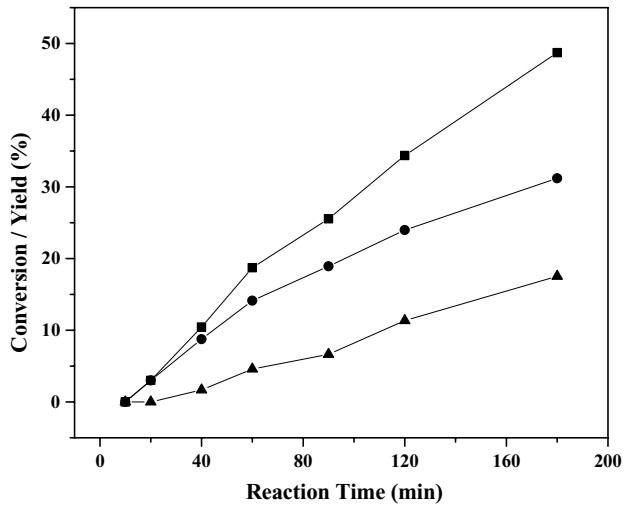



Fig. 4. Conversion and products yield as a function of reaction time in DMSO over Mg-ZSM-5 ((■) conversion of 2′-hydroxyacetophenone; (●) yield of 2′-hydroxychalcone; (▲) yield of flavanone); (catalyst weight, 0.5 g; temperature, 140 °C; reaction time, 3 h).

diffuse out of the catalyst due to the large $Ba^{2+}$ ion [19]. While the yield of chalcone increases with increase in time, the yield of flavanone increases up to 2 h and attains a steady state afterwards. This indicates steric congestion due to large size of $Ba^{2+}$ for cyclisation of 2′-hydroxychalcone to flavanone within the pores. In order to confirm that of the reaction occurs mostly inside the pore, the reaction was carried out over surface passivated Ba-ZSM-5 catalyst. The surface passivation was carried out using tetraethyl orthosilicate by the reported procedure [20]. The conversion is 36.8% for surface passivated Ba-ZSM-5, which is by only 8% lower than the unpassivated Ba-ZSM-5. This observation clearly confirms the occurrence of the reaction mostly in side the pore.

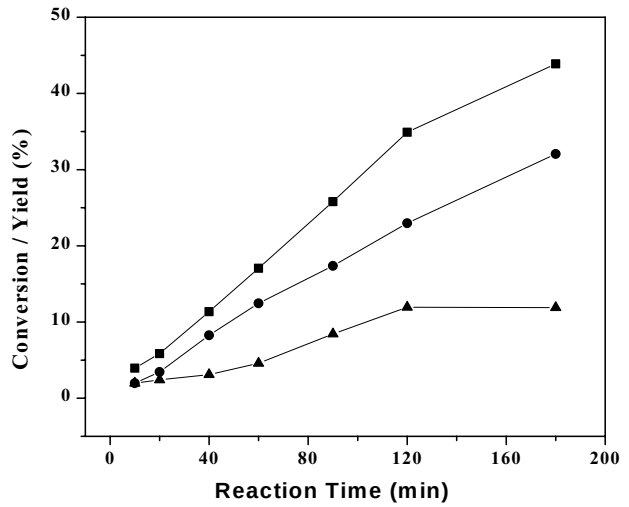



Fig. 5. Conversion and products yield as a function of reaction time in DMSO over Ba-ZSM-5 ((■) conversion of 2′-hydroxyacetophenone; (●) yield of 2′-hydroxychalcone; (▲) yield of flavanone); (catalyst weight, 0.5 g; temperature, 140 °C; reaction time, 3 h).

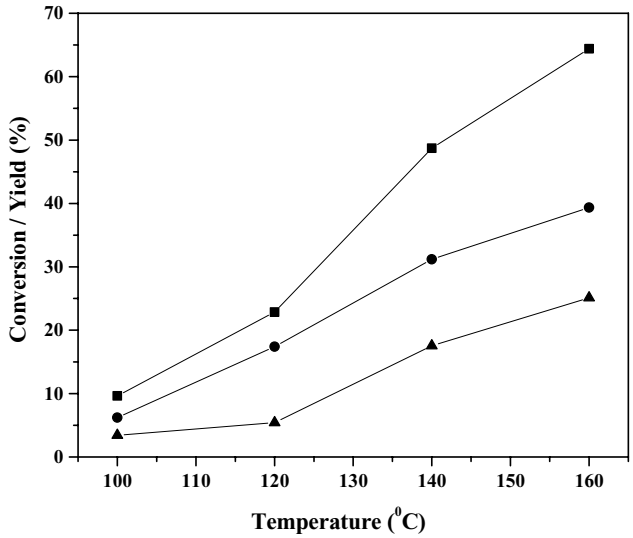



Fig. 6. Effect of temperature on conversion and products yield in DMSO over Mg-ZSM-5 ((■) conversion of 2′-hydroxyacetophenone; (●) yield of 2′-hydroxychalcone; (▲) yield of flavanone); (catalyst weight, 0.5 g; reaction time, 3 h).

The influence of temperature on conversion and products yield was studied between 100 and 160 °C over Mg-ZSM-5 catalyst. The results are illustrated in Fig. 6. Conversion as well as yield of 2′-hydroxychalcone increase with increasing temperature, whereas the yield of flavanone does not increase significantly between 100 and 120 °C. The increase in the yields of both products is almost parallel with further increase of temperature. The effect of catalyst loading on conversion and products yield was studied over Mg-ZSM-5 at 160 °C (Fig. 7). Conversion and products yield increase with increase in the catalyst loading upto 0.75 g and thereafter

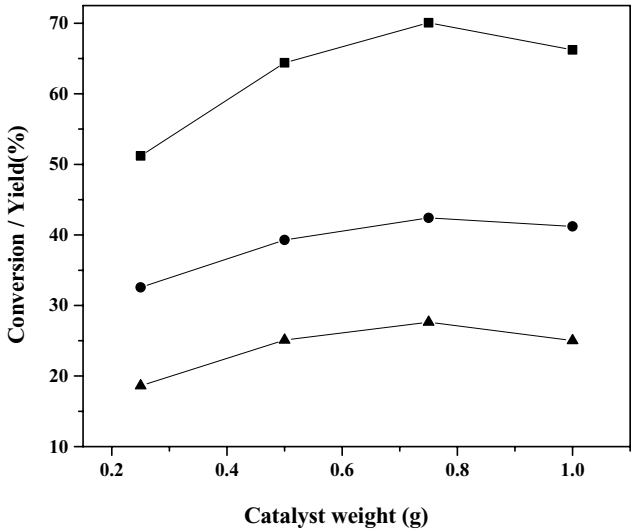



Fig. 7. Effect of catalyst loading on conversion and products yield in DMSO over Mg-ZSM-5 ((■) conversion of 2′-hydroxyacetophenone; (●) yield of 2′-hydroxychalcone; (▲) yield of flavanone); (temperature, 160 °C; reaction time, 3 h).

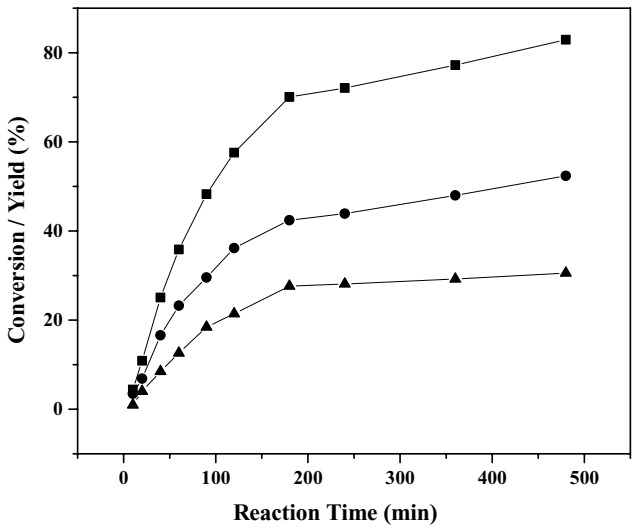



Fig. 8. Effect of reaction time on conversion and products yield in DMSO over Mg-ZSM-5 ((■) conversion of 2′-hydroxyacetophenone; (●) yield of 2′-hydroxychalcone; (▲) yield of flavanone); (catalyst weight, 0.75 g; temperature, 160 °C; reaction time, 8 h).

decrease in both conversion and products yield. Macquarrie et al. [21] reported similar observation in the synthesis of flavanones and 2′-hydroxychalcones using KF/natural phosphate catalysts. In order to attain equilibrium, the reaction time was extended upto 480 min. There was a gradual increase in conversion and products yield even upto 180 min thus illustrating unattainment of equilibrium (Fig. 8).

The role of solvent in this reaction was studied with DMSO, nitrobenzene and a mixture of DMSO and nitrobenzene and the results are presented in Table 1. High conversion with DMSO is attributed to the chemisorption of DMSO on the Brønsted acid sites of the catalyst which may provide enhanced polarisation of the carbonyl group of 2′-hydroxycacetophenone. The ultimate aim is to increase the acidity of $–CH_3$ hydrogens which can easily condense with benzaldehyde to yield chalcone. In addition, it can also bring benzaldehyde on its surface as its positive charge is well dispersed and simultaneously permits both benzaldehyde and 2′-hydroxyacetophenone to condense on its surface to yield 2′-hydroxychalcone. Thus, protonated DMSO could act as a matchmaker with which intermolecular condensation of aldehyde and ketone is more facile. The kind of modified adsorption in the presence of DMSO as suggested by previous workers prompted us to propose this pathway [13]. The conversion decreases with nitrobenzene suggesting that it is incapable of activating 2′-hydroxyacetophenone. The addition of a few drops of DMSO to nitrobenzene has increased the conversion in line with our expectations.

The selectivity to 2′-hydroxychalcone is high in DMSO while the selectivity for flavanone is high in nitrobenzene. As intramolecular cyclisation of 2′-hydroxychalcone depends on the acid sites, such free sites is less in DMSO due to protonation and hence the selectivity for the flavanone is lowered. Nitrobenzene does not lead to such protonation and hence formation of flavanone is more favourable. As expected, nitrobenzene–DMSO mixture increases the selectivity of flavanone.

Table 1
Effect of solvent on conversion and selectivity of products

| Solvent | Conversion of 2′-hydroxy acetophenone (%) | Selectivity of products (%) | |
|---|---|---|---|
| | | 2′-Hydroxy chalcone | Flavanone |
| DMSO | 70.06 | 60.5 | 39.5 |
| Nitrobenzene | 6.21 | 30.9 | 69.1 |
| Nitrobenzene[a] | 18.70 | 46.3 | 53.7 |

Reaction temperature: 160 °C; catalyst weight: 0.75 g; time: 3 h.
[a] Few drops DMSO was added to nitrobenzene system.

## 5. Conclusion

H-ZSM-5, Mg-ZSM-5 and Ba-ZSM-5 are found to be active catalysts for the formation of flavanone from 2′-hydroxyacetophenone and benzaldehyde through the Claisen–Schmidt condensation. Increase in temperature increases both conversion and products yield. The catalytic study with passivated Ba-ZSM-5 confirms the occurrence of the reaction inside the pores. The study shows higher conversion with DMSO than with either nitrobenzene or a DMSO–nitrobenzene mixture.

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