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Esterification of salicylic acid over zeolites using dimethyl carbonate

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Abstract

The esterification of salicylic acid (SA) using dimethyl carbonate (DMC) is reported for the first time. The reaction is studied in detail over zeolites Hβ, HZSM5 and HY in the temperature region 370–425 K in an autoclave under autogenous pressure. The molar ratio of SA to DMC, the reaction period and the weight of zeolite catalysts are varied. The SA conversion is over 90% for both Hβ and HZSM5 at 423 K. HY is not as effective a catalyst as the other two. Irrespective of the conversion levels the selectivity towards methyl salicylate is greater than 95%. A comparative study on the esterifying ability of DMC and methanol is reported. From the kinetic data, the energy of activation (E_a) for the esterification reaction using DMC over Hβ and HZSM5 is calculated to be 25 and 36 kcal/mol, respectively. A reaction mechanism for the esterification of SA with DMC over zeolites is proposed.

Keywords: Esterification; Salicylic acid; Dimethyl carbonate; HZSM5; Hβ

1. Introduction

Organic esters represent an important class of intermediates widely used in fine chemicals, drugs, plasticizers, food preservatives, pharmaceuticals, solvents, perfumes, cosmetics and chiral auxiliaries [1]. Esterification of carboxylic acids is an important reaction in synthetic organic chemistry, e.g. it provides protection of a carboxylic acid group in a molecule [2]. Although many useful and reliable methods for the esterification of carboxylic acids exist, there is still a need towards finding a versatile process. Methyl esters of carboxylic acids are generally prepared by refluxing the acid and methanol with a small amount of sulfuric acid, hydrogen chloride or sulfonic acid as catalysts [3]. The use of these catalysts is nowadays undesirable from the environmental point of view. Keeping in mind the stringent environment requirement, there has been a global effort to replace hazardous and environmentally harmful chemicals with more benign and less hazardous alternatives [4]. Zeolites are a class of solid acids, which have been widely studied as viable alternatives to conventional acids. The use of zeolites as catalysts for organic reactions began in the early 1960s. In addition to the increased use in petrochemicals manufacture [5], zeolite catalysis is expanding into areas of specialty and fine chemical synthesis [6,7]. We have focused our research on the use of zeolites and zeolitic materials in various organic transformations like alkylation and esterification reactions

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[8–12]. The main draw back of esterification reactions using alcohol is that water is formed as a by-product, requiring azeotropic distillation to remove water during the reaction which otherwise would deactivate the catalyst [7]. When dimethyl carbonate (DMC) is used to prepare the methyl esters, the by-product formed is methanol and not water and it does not require azeotropic distillation. The methylating activity of DMC has been widely studied in recent years [13–18]. Aromatic amines and phenols have been selectively methylated using DMC over different catalysts. DMC is an environment friendly methylating agent and can replace undesirable methyl halides and dimethyl sulphate. In addition to this, it can also be used as a methoxy carbonylating agent [14]. A very important feature of DMC is its selectivity which is crucial in any organic synthesis, e.g. in the methylation of phenol anisole is produced selectively [14] and in the methylation of aniline very selective mono-*N*-methylation has been reported [16,18]. Use of DMC in esterification results in methanol as a by-product, which can be recycled for the production of DMC [19]. There are not many reports on the use of DMC in the esterification of acids. Lee and Shimizu [15] have reported the use of DMC to esterify mycophenolic acid to its methyl ester over cesium carbonate catalyst. In this case, both the carboxylic acid group and the hydroxyl groups were methylated. Methyl salicylate, the methyl ester of salicylic acid (SA) is an important chemical as it finds use in pharmaceutical industries and as a flavoring agent [20,21]. Conventionally, it is prepared with SA and methanol using H_2SO_4 as a catalyst.

In the present work, the selective esterification of SA (2-hydroxybenzoic acid) using DMC in liquid phase over zeolites Hβ, HZSM5 and HY has been reported for the first time. The esterifying ability of DMC and methanol under similar conditions has been compared. An attempt has also been made to study the kinetics and mechanism of the reaction involving DMC.

2. Experimental

Zeolites β, Y and ZSM5 having different Si/Al ratios and characteristic properties were used in the esterification of SA by DMC and methanol. Protonated forms of the zeolites Y and ZSM5 were obtained from Conteka, The Netherlands. The sodium form of zeolite β was obtained from United Catalysts India Limited and was converted to its protonated form by exchange using aqueous NH_4NO_3 followed by calcination. All the zeolite samples were characterized for surface area. Acidity of the zeolites was measured by stepwise temperature programmed desorption of ammonia on a Micromeritics pulse chemisorb 2700 by bracketing the temperature of desorption. The details of acidity measurements are described elsewhere [22]. The relevant physico-chemical properties of the zeolites used are given in Table 1. The esterification reactions were carried out in a stainless steel autoclave reactor (internal volume: 300 cm^3) under autogenous pressure in the temperature region 373–423 K. The reactants were taken directly in the autoclave along with the catalyst, kept in a hot air oven and the reaction was carried out for a definite period of time. The total volume of the reactants was kept constant at 20 cm^3. The reaction was studied by varying the reaction parameters such as molar ratio of the reactants, reaction temperature, reaction period, weight of the catalyst and the zeolite type. After the stipulated reaction time, the reactor was cooled to room temperature and acetone was added to dissolve the unreacted SA in the reaction mixture and then filtered to separate the catalyst. The filtrate was analyzed by a Chemito 8510 gas chromatograph using 20% SE-30 column, coupled with FID. The products were

Table 1
Physico-chemical characteristics of zeolites[a]

Zeolite	Si/Al	BET area (m^2/g)	Acidity (mmol/g) NH_3			
			Physisorbed (A)	Weak (B)	Medium (C)	Strong (D)
Hβ	8	434	0.35	1.03	2.30	4.50
HZSM5	25	400	0.42	1.89	1.16	3.05
HY	30	730	1.30	1.51	1.70	0.99

[a] Desorption temperature region: A, 353–423 K; B, 423–523 K; C, 523–623 K; D, 623–723 K.

identified by comparing with the standards. The products were further confirmed by HPLC and by GC–MS. The major product of the reaction was identified as methyl salicylate and the minor side product as phenol.

Blank reactions were also carried out in the absence of a catalyst. The efficiency of DMC and that of methanol was compared by carrying out the reactions under similar conditions. The conversion and selectivity were calculated based on the GC results using the following expressions:

$$\text{conversion of salicylic acid (SA) (\%)} = 100 - 100 \times \frac{[\text{salicylic acid}]}{[\text{salicylic acid}] + [\text{methyl salicylate}] + [\text{phenol}]}$$

$$\text{selectivity for methyl salicylate (\%)} = 100 \times \frac{[\text{methyl salicylate}]}{[\text{methyl salicylate}] + [\text{phenol}]}$$

3. Results and discussion

Initial analysis of the reaction mixture showed that the major product obtained was methyl salicylate and the other product was phenol. Preliminary results of the experiments carried out are given in Table 2. From this, it is clear that while zeolites Hβ and HZSM5 were effective catalysts for this esterification reaction, zeolite HY was not found to be so. When the acidity values of these zeolites were scrutinized, it was found that a linear relationship exists between the conversion of SA and acidity, especially in the strong acid region D (Table 1, Fig. 1). Detailed investigations of this reaction were carried out on zeolite Hβ and HZSM5 only.

Table 2
Effect of the catalyst type[a]

Catalyst	Conversion (%)		Selectivity (%)	
	1:2	1:4	1:2	1:4
Hβ	65	70	99	100
HZSM5	44	48	98	98
HY	4	6	100	100

[a] SA:DMC, 1:2 and 1:4 (mol/mol); reaction temperature, 408 K; reaction time, 4 h; zeolite weight, 1.5 g.

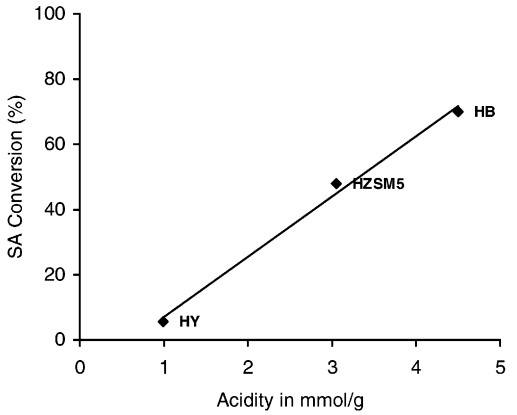


Fig. 1. Conversion of salicylic acid as a function of strong acid sites (region D, Table 1) over zeolites Hβ, HZSM5 and HY: SA:DMC, 1:4 (mol/mol); reaction temperature, 408 K; reaction time, 4 h; zeolite weight, 1.5 g.

3.1. Influence of molar ratio of the reactants

The reaction was carried out using different acid to DMC molar ratios, the results of which are summarized in Fig. 2. The conversion of SA increases from 60 to 71% on varying the acid to DMC molar ratio from 1:1 to 1:6 for Hβ. In the case of HZSM5, for the same molar ratio region 1:1 to 1:6, the conversion levels are lower than those of Hβ and remain between 40 and 50%. Selectivity for methyl salicylate in all cases remains above 95% irrespective of the type of catalyst used and conversion levels.

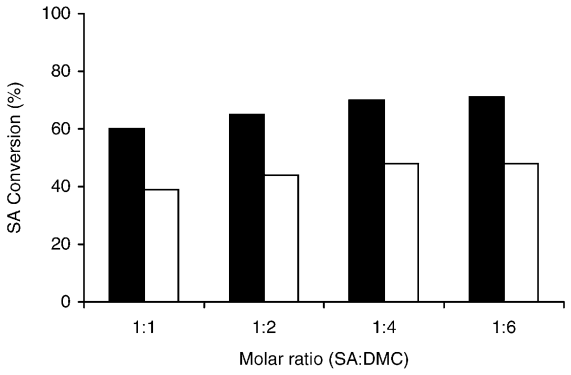


Fig. 2. Esterification of salicylic acid with dimethyl carbonate, effect of salicylic acid to dimethyl carbonate molar ratio: Hβ (■) and HZSM5 (□); zeolite weight, 1.5 g; reaction time, 4 h; reaction temperature, 408 K.

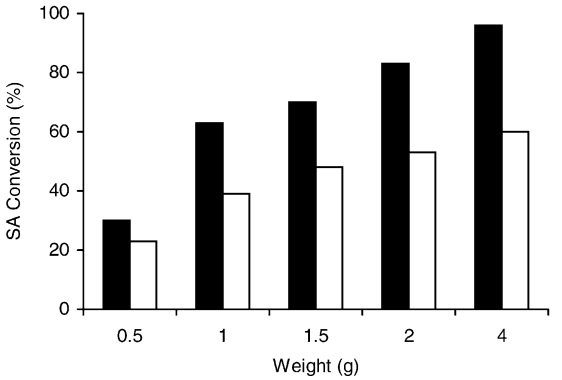


Fig. 3. Esterification of salicylic acid with dimethyl carbonate, effect of zeolite weight: Hβ (■) and HZSM5 (□); SA:DMC, 1:4 (mol/mol); reaction time, 4 h; reaction temperature, 408 K.

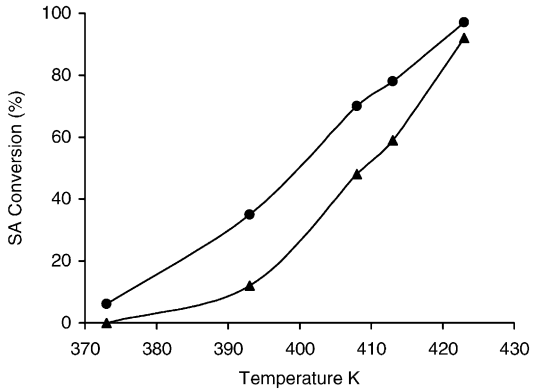


Fig. 4. Esterification of salicylic acid with dimethyl carbonate, effect of reaction temperature: Hβ (●) and HZSM5 (▲); zeolite weight, 1.5 g; reaction time, 4 h; SA:DMC, 1:4 (mol/mol).

3.2. Influence of the catalyst concentration

The amount of the catalyst was varied between 0 and 4 g keeping SA to DMC molar ratio at 1:4 and reaction temperature at 408 K. The reaction was carried out for 4 h and the products were analyzed. The results are represented in Fig. 3. This reaction did not take place in the absence of a catalyst. There is an increase in the conversion of SA from 30 to 96% as the amount of Hβ is increased. For HZSM5, this increase is from 25 to 60%. In all reactions, the selectivity for methyl salicylate is greater than 95%.

3.3. Influence of temperature

The reaction was carried out in the temperature region 370–430 K. The effect of temperature on the conversion of SA is illustrated in Fig. 4. At 373 K, HZSM5 showed no detectable conversion of SA, whereas Hβ gave 6%. The conversion over HZSM5 is always around 20% less than that over Hβ at lower temperatures. The conversion over both catalysts reached around 95% at 423 K.

3.4. Influence of the reaction time

The effect of reaction time on the conversion of SA is given in Fig. 5. The conversion increases with reaction time on both Hβ and HZSM5 zeolites. Even though both zeolites gave the same conversions of about 30% for 2 h of reaction time, the difference in the conversion widens at higher reaction times. For a 10 h reaction, Hβ gave a conversion of 95% while HZSM5 gave 64%. The selectivity towards methyl salicylate remains above 95% in all cases.

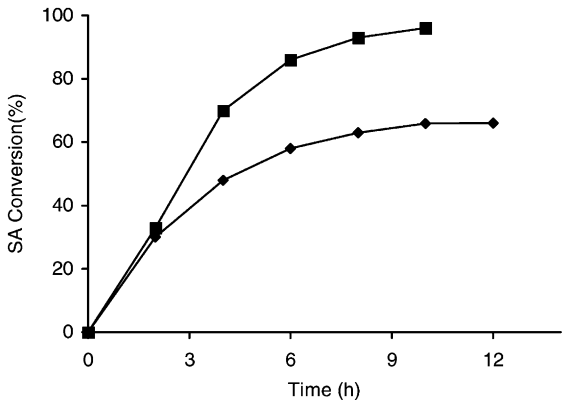


Fig. 5. Esterification of salicylic acid with dimethyl carbonate, effect of reaction time: Hβ (■) and HZSM5 (◆); zeolite weight, 1.5 g; reaction temperature, 408 K; SA:DMC, 1:4 (mol/mol).

3.5. Esterification using methanol

In order to understand the esterifying behaviour of DMC in relation to methanol, esterification reaction was carried out over Hβ and HZSM5 zeolites under similar experimental conditions using methanol as the esterifying agent. The results of this study are presented in Table 3. It is interesting to note that the

Table 3
Esterification of salicylic acid using methanol[a]

Reaction time (h)	Hβ		HZSM5		Blank	
	Conversion (%)	Selectivity (%)	Conversion (%)	Selectivity (%)	Conversion (%)	Selectivity (%)
2	34	96	31	93	24	94
4	49	92	44	92	35	94
6	58	92	54	92	44	92
8	66	93	58	91	47	92

[a] Zeolite weight, 1.5 g; reaction temperature, 408 K; SA:methanol, 1:4 (mol/mol).

esterification of SA with methanol proceeds to an appreciable extent even in the absence of a catalyst. For example, at 408 K and SA to methanol molar ratio of 1:4, the conversion is between 24 and 47% depending on the time of reaction. The presence of Hβ or HZSM5 does increase the conversion, the increase being 10–20% in the case of Hβ and about 10% over HZSM5. This is in contrast to the esterification reaction using DMC, where there is no reaction in the absence of a catalyst. Comparing the esterifying activity of the two esterifying agents, it can be said that the use of DMC always results in higher SA conversion. Generally, DMC is used in excess quantity for the esterification reaction. During the reaction other than the major product methyl salicylate, methanol and carbon dioxide are formed as by-products along with the minor product phenol. Even though methanol is an esterifying agent, its contribution is limited or nearly nil in presence of excess of DMC. Moreover, DMC is more reactive than methanol, and hence, the methanol formed is not expected to be consumed during the reaction. The fact that methanol esterifies SA in the absence of a catalyst while DMC does not, indicates that the mechanisms by which esterification takes place in both the cases are different. This is discussed in the following section.

3.6. Kinetics and mechanism of salicylic acid esterification using dimethyl carbonate

As the amount of the catalyst increases in the esterification of SA using DMC, the conversion also increases (Fig. 3). This suggests that the transfer of reactants from the liquid phase to the catalyst phase is not a rate limiting step, implying the rate is independent of the catalyst mass [23]. A plot of $-\ln(1-\text{conversion})$ versus reaction time for reactions carried out at 408 K is drawn in Fig. 6. This plot shows

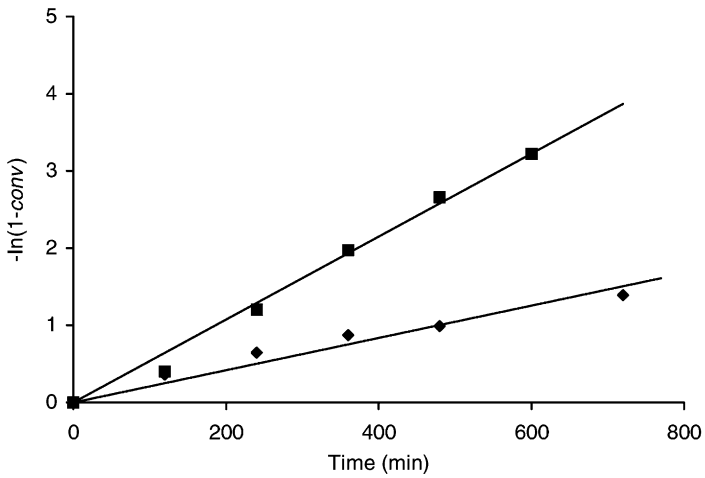


Fig. 6. Plot of the first-order rate equation for the esterification of salicylic acid with dimethyl carbonate at 408 K: Hβ (■) and HZSM5 (◆).

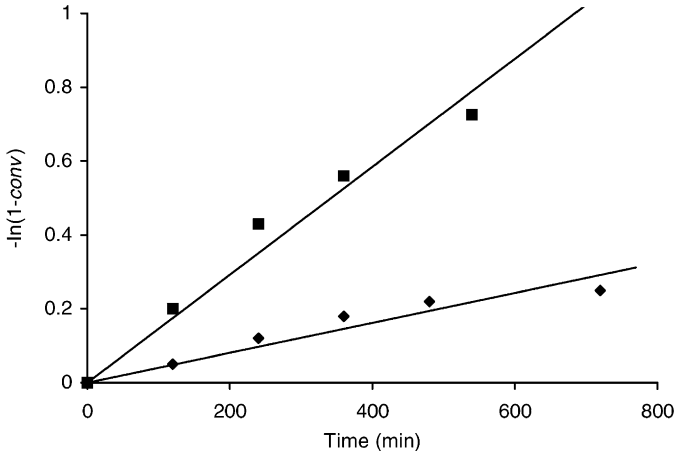


Fig. 7. Plot of the first-order rate equation for the esterification of salicylic acid with dimethyl carbonate at 393 K: Hβ (■) and HZSM5 (◆).

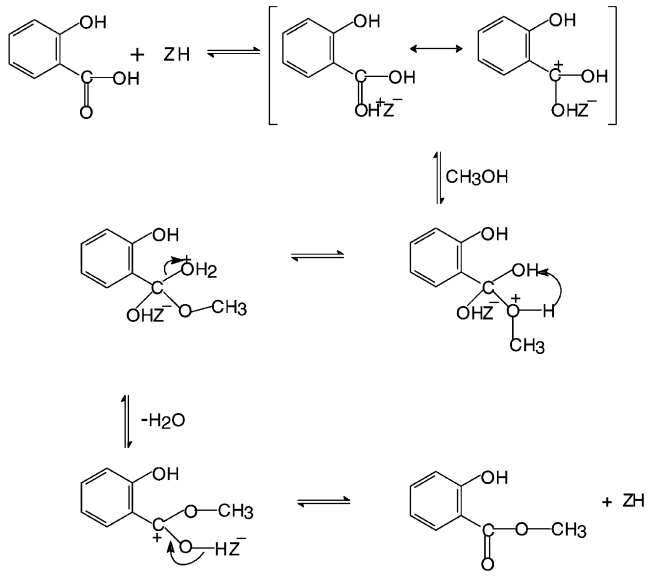
a near linear character over both the zeolites. This suggests a first-order dependence of the rate of the reaction on SA concentration. A similar first-order rate dependence is observed for the reactions carried out at 393 K (Fig. 7). The rate constants calculated from the slopes of plots in Figs. 6 and 7 are given in Table 4. The energy of activation (E_a) for this reaction was calculated for the two zeolites using Arrhenius equation and they were found to be 25 and 36 kcal/mol for Hβ and HZSM5, respectively. The fact that E_a is less in the case of Hβ indicates that the reaction is more facile over Hβ than over HZSM5. Even though the mechanism of the reaction on the two zeolites may be the same, the differences in their activity can be attributed to their acid site strengths and distribution, and there is no evidence of the involvement of pore sizes. Studies on the variation of molar concentration of the reactants, temperature and reaction period on both Hβ and HZSM5 zeolites indicate that in general Hβ is more active catalytically than HZSM5 as indicated by SA conversion. However, the variations in conversion with respect to these parameters are similar and irrespective of the conversion levels the selectivity for methyl salicylate is always higher than 95% over both Hβ and HZSM5 zeolites under the reaction conditions studied. This also suggests that there is no difference in the reaction mechanism on both these catalysts for this reaction and the difference in their conversion levels can only be attributed to their acidic properties.

Table 4
Reaction rate constant for esterification of salicylic acid with dimethyl carbonate over zeolites[a]

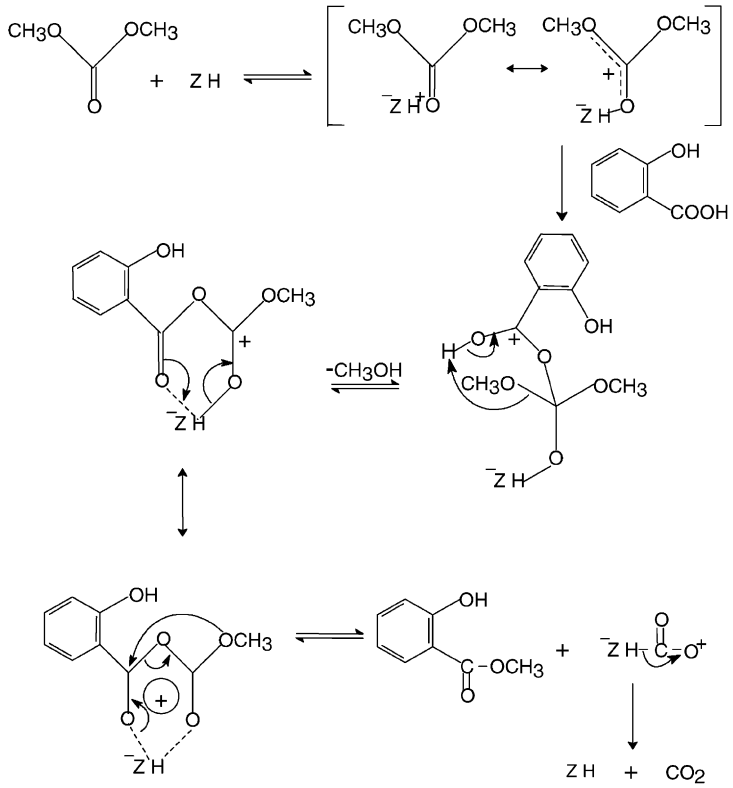
Catalyst	Reaction temperature (K)	Rate constant, K (min^{-1})
Hβ	393	1.44×10^{-3}
	408	4.69×10^{-3}
HZSM5	393	0.42×10^{-3}
	408	2.27×10^{-3}

[a] Molar ratio of SA:DMC, 1:4; catalyst weight, 1.5 g.

The mechanism of the esterification of salicylic acid using methanol over zeolites (Scheme 1) is similar to the conventional mechanism, which involves the nucleophilic attack by methanol on the carboxyl atom [24]. The resulting loss of water would give the methyl ester. The role of an acid catalyst here is to facilitate the formation of the carbocation, and to help remove OH^- from the carboxylic group. We observed that this is possible even in the absence of a catalyst, although to a lesser extent (Table 3). As mentioned earlier, the water that is formed during the course of reaction would deactivate the catalyst necessitating its removal by azeotropic distillation during the reaction. On the other hand, the mechanism involving DMC would be different as no reaction takes in the absence of a catalyst. Beutel [25] has envisaged a mechanism for the alkylation of phenol with DMC, where the DMC is activated on a Lewis acid site by its carbonyl oxygen and phenol on an adjacent Lewis base site by H-bonding. Jyothi et al. [26] have also proposed



Scheme 1. Mechanism for the esterifiaction of salicylic acid with methanol over protonic zeolites (ZH).



Scheme 2. Plausible mechanism for the esterification of salicylic acid with dimethyl carbonate over zeolites (ZH).

a similar mechanism for the alkylation of catechol by DMC over hydrotalcites. These have been proposed for the alkylation reactions of DMC making use of both the acid and the basic sites on the catalyst. Based on all these information, we propose the mechanism as shown in Scheme 2 for the esterification reaction using DMC. Dimethyl carbonate is adsorbed on the acid site of the zeolite (represented as ZH) through its carbonyl carbon to form an activated complex. Dimethyl carbonate may also be activated in the electrostatic field in the zeolite super cages [14]. Through a series of steps involving the nucleophilic attack from SA and subsequent loss of methanol, the formation of the methyl salicylate takes place. CO_2 is evolved by the decomposition of the carbonic acid type complex in the final step. The absence of any water formation during the reaction favors the use of DMC over methanol as an esterifying agent for this reaction.

4. Conclusion

From the detailed studies on the esterification of SA using DMC, the following conclusions may be derived. Dimethyl carbonate can be employed effectively to esterify SA to methyl salicylate and this is reported for the first time. The important observation of this study is the high selectivity for methyl salicylate by exclusive esterification of the –COOH group of SA while the –OH group remains unaffected. Zeolites Hβ and HZSM5 are suitable catalysts for this reaction, whereas HY is not. The differences in the catalytic activity are attributed very much to the acid site strengths and their distribution. Hβ seems to have an edge over HZSM5 and the selectivity for methyl salicylate is always greater than 95% irrespective of the concentration levels and the type of zeolites used. The deactivation is more pronounced when methanol is used as an esterifying agent compared to DMC. A mechanism involving zeolitic acid sites and DMC is proposed. The activation energy for the reaction is 25 and 36 kcal/mol over Hβ and HZSM5, respectively.

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