



Transesterification over various zeolites under liquid-phase conditions

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Abstract

Transesterification of β -keto esters with a variety of alcohols to the corresponding β -keto esters has been carried out efficiently over aluminosilicates simply by refluxing in toluene under liquid-phase conditions. Aliphatic β -keto esters exhibit the higher reactivity than the aromatic and/or cyclic β -keto esters, whereas other esters such as α -keto esters, α,β -unsaturated esters, normal esters, and α -halo esters fail to undergo the transesterification. The reaction proceeds smoothly with primary alcohols than the tertiary-, cyclic-, and allylic alcohols. The large-pore zeolites such as Y, mordenite, and β show higher activity than the medium-pore ZSM-5 and the partial removal of framework aluminum from the large-pore zeolites by dealumination increases their activity. The aluminum containing mesoporous MCM-41 shows poor activity. Among the different solvents used toluene leads to the highest activity and the optimum catalyst concentration found was ca. 20 wt.% of the substrate. The activity increases with increasing reaction temperature. The reaction pathway consists of formation of acyl ketene intermediate by the interaction of β -keto esters with Brønsted acid sites of the catalyst, followed by nucleophilic attack of the alcohol at the electrophilic center and successive elimination of the proton to give the product.

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1. Introduction

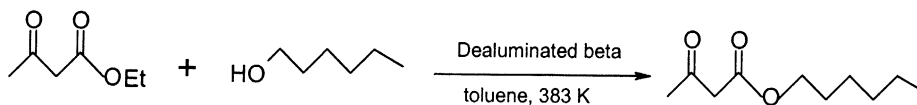
β -Keto esters are widely used as synthons in several natural product synthesis and industrial applications. For example, terpene esters, commonly used as flavor and fragrance compounds for a variety of foods and beverages, are synthesized using various homogeneous chemical reagents via transesterification [1]. However, since the transesterification is an equilibrium process, it is accelerated by the simultaneous removal of low-boiling coproduct alcohol during the process [2] by azeotropic distillation. The transesterification reaction has been effected with various homogeneous catalysts such as distannoxanes [3], InCl_3 [4], LiClO_4 [5], titanium(IV) alkoxide [6], and sulphated SnO_2 [7]. A few heterogeneous catalysts like envirocat EPZG [8,9], amberlyst-15 [10], and polymer supported lipase [11] have also been employed recently. Although many methods are

available for this reaction, the transesterification of allylic alcohols is rather difficult as it leads to successive decarboxylation and rearrangement [12,13]. Moreover, the reaction failed with aromatic substrates over sulphated SnO_2 catalyst [7]. Distannoxanes are reported to give good yields of β -keto esters but the catalysts are difficult to prepare. Furthermore, due to environmental demands, there has been considerable interest in developing new inorganic solid-acid catalysts such as zeolites to replace the homogeneous catalysts.

The availability of a range of zeolites with different pore-size and tunable acidity coupled with high thermal stabilities in the protonic form had considerable impact over their utility in the field of various fine chemicals synthesis. Zeolite β was found to be a suitable catalyst for the transesterification reaction to prepare a variety of building blocks for the synthesis of natural products like podophyllotoxin [14,15]. Herein we report the detailed study over the transesterification of different β -keto esters and alcohols by changing the experimental parameters such as influence of solvent, temperature, amount of catalyst used as well as strength of acid sites, and pore-size vis-à-vis void space.

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Scheme 1.

2. Experimental

2.1. Catalysts

The commercial catalysts Na-Y, mordenite, and ZSM-5 were obtained from United Catalyst India Ltd (Bombay). All the catalysts were treated with 1 M ammonium acetate solution and heated at 673 K for 6 h to give the active protonic form. H-Y was converted to rare-earth (RE)-Y by treatment with a rare-earth solution containing a mixture of La, Ce, Sm, Pr, and Nd at 373 K, this exchange process was repeated three times to achieve the exchange of 2.8 wt.% and the resultant material was finally calcined at 673 K for 6 h.

2.2. Synthesis of zeolite β

In a typical synthesis of Al- β , 1.32 g of NaOH was dissolved in 70 g of TEAOH (Aldrich, 40%) and added slowly under constant stirring to a slurry of 20 g fumed silica (Cab-o-sil M5) in 100 g H₂O. To the above mixture, a solution containing 4 g of Al₂(SO₄)₃·16H₂O was added and stirred for additional 2 h to give a homogeneous gel. The resultant gel (composition: 0.33 SiO₂; 0.033 NaOH; 0.19 TEAOH; 0.006 Al₂O₃; 8.3 H₂O) was crystallized at 413 K under static condition. The solid product after crystallization was centrifuged, washed thoroughly with distilled water, dried at 373 K and finally calcined in air at 793 K for 12 h. Similarly other metallosilicate analogues of Ga- β and Fe- β were synthesized by using Ga₂(SO₄)₃ and Fe(NO₃)₃·9H₂O, respectively. In the synthesis of Fe- β , Fe(NO₃)₃·9H₂O was treated with oxalic acid to form the metal complex and added to the synthesis gel. Al-MCM-41 was synthesized according to the reported procedure [16] using cetyltrimethylammonium bromide and tetramethylammonium hydroxide.

2.3. Dealumination of zeolite β

Zeolite β was dealuminated using the (NH₄)₂SiF₆ method reported by Beyer et al. [17]. In a typical dealumination experiment, 5 g of NH₄-form of zeolite β (parent sample) was added to an aqueous solution of ammonium acetate (50 ml, 10 M) at 348 K. To this mixture 4.5 ml of 0.75 N solution of ammonium hexafluorosilicate in water was added slowly through a syringe fitted with a metering pump (Sage Syringe Pump). Then, the slurry was heated to 363 K and stirred for 16 h. Finally, the contents were washed thoroughly with distilled water in order to remove extracted aluminum and dried at 373 K. This procedure was repeated until the required Si/Al ratio is obtained and the product was finally calcined

at 673 K for 6 h. A similar procedure has been adopted for the dealumination of zeolite Y and mordenite.

2.4. Typical transesterification procedure

In a typical experiment, 10 mmol of β -keto ester and 10 mmol of alcohol were mixed in dry toluene (25 ml) in a round bottom flask to which 20 wt.% (with respect to β -keto ester) of catalyst was added. Then the flask was fitted with a distillation condenser and heated to 383 K using an oil bath with azeotropic removal of the lower alcohol formed (Scheme 1). After 10 h, the reaction mixture was cooled, the catalyst was filtered off, washed with 3 × 10 ml of toluene, and the combined toluene washing were distilled off under vacuum. Products identification was made using authentic samples and GC–MS splitting patterns. Purification by column chromatography and distillation was also employed to separate and identify the reaction products.

3. Results and discussion

3.1. Influence of solvents, temperature, and substrate/catalyst ratio

Table 1 exhibits the physico-chemical properties of various zeolites investigated for the transesterification under liquid-phase conditions. All the catalysts were activated under a flow of air at 573 K for 5 h before transferring into the reaction vessel. The zeolite catalyzed liquid-phase reactions

Table 1
Physico-chemical properties of various metallosilicates

Entry	Catalyst	Si/M ratio (product) ^a	Particle size (μm) ^b	Surf. Area ($\text{m}^2 \text{g}^{-1}$) ^c
1	H-ZSM-5	40.0	0.1–0.2	465
2	H-ZSM-12	78.0	1–2	346
3	H-Y	2.5–3.0	0.5–0.7	737
4	H-Y ^d	11.5	0.5–0.7	737
5	H-mordenite	12.5	0.3–0.5	492
6	H-mordenite ^d	26.8	0.3–0.5	492
7	H- β	27.5	0.2–0.3	630
8	H- β ^d	75.0	0.2–0.3	630
9	H-Ga β	61.0	0.2–0.5	611
10	H-Fe β	55.0	0.2–0.3	595
11	H-MCM-41	76.0	1–2	985

^a Si/M ratio was estimated from ICP analysis.

^b Particle size measurements were made from SEM observation.

^c Surface area was measured by N₂ adsorption at 77 K on a BELSORB 28SA analyzer.

^d The parent aluminosilicate was dealuminated with ammonium hexafluorosilicate.

Table 2

Effect of different solvents, temperature, and substrate/catalyst ratio in transesterification reaction over dealuminated zeolite β^a

Entry	Solvent	Temperature (K)	Substrate/catalyst ratio (w/w)	Conversion ^b (%)
1	Toluene	383	5	92.0
2	Nitromethane	383	5	60.5
3	Acetonitrile	383	5	45.0
4	Benzene	383	5	31.0
5	Toluene	353	5	55.4
6	Toluene	363	5	72.9
7	Toluene	373	5	86.0
8	Toluene	383	10	78.0
9	Toluene	383	3.3	92.0
10	Toluene	383	2.5	93.0
11	Toluene	383	1.5	93.0

^a Reaction conditions: 10 mmol of ethylacetoacetate, 10 mmol of 1-hexanol, 20 ml of dry solvent, reaction time 10 h.

^b Estimated from GC analysis and the rest is unreacted starting materials.

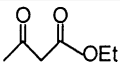

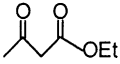

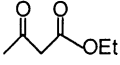

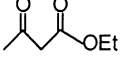

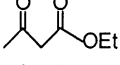

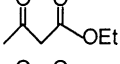

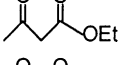

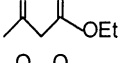

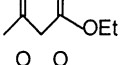

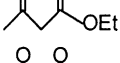

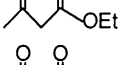

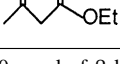

often depend on the solvent used, which produces a crucial effect on the activity and selectivity; the solvent can also govern the intraporous concentration of reactants or may participate/assist in the catalytic cycle. Therefore, the transesterification reaction has been optimized by considering the solvent and temperature effect as well as the critical amount of catalyst required to attain the maximum conversion. Entries 1–4 in Table 2 show the effect of different solvents over the transesterification. Toluene provided the best activity and the use of solvents such as acetonitrile, nitromethane, and benzene led to less conversion. Probably due to their low boiling point, they adversely affect the removal of co-product ethanol by azeotropic distillation, driving down the equilibrium. The conversion is reduced (entries 5–7) when the temperature is decreased. Increase in conversion with increasing temperature is attributed to increased activation at higher temperature coupled with facile desorption of chemically adsorbed intermediate. Entries 8–11 exhibit the influence of substrate/catalyst ratio (w/w) in the transesterification of ethylacetoacetate. When the substrate/catalyst ratio was changed from 10 to 5, the conversion of the catalyst increased from 78 to 92% (entries 1 and 8). However, further increase in the catalyst amount did not increase the conversion significantly as the reaction almost attained the equilibrium. Hence, the substrate/catalyst (w/w) ratio of 5 was chosen for further investigation along with toluene as the reaction medium.

3.2. Activity of various aluminosilicates

The activity of various aluminosilicates as well as other metallosilicates for the reaction between ethylacetoacetate and *n*-hexanol is shown in Table 3. Entries 1–3 show the activity of unmodified large-pore Y, mordenite, and β , respectively. Although both Y (Si/Al = 2.5–3.0), and mordenite (Si/Al = 12.5) contain a large amount of aluminum than β (Si/Al = 27.5), the former exhibits lower activity,

Table 3

Activity of various aluminosilicates towards transesterification^a

Entry	Catalyst	β -keto ester	Alcohol	Yield ^b (%)
1	H-Y			72
2	H-mordenite			65
3	H- β			80
4	H Y ^c			85
5	H-mordenite ^c			86
6	H- β^c			92
7	H-Ga β			55
8	H-Fe β			36
9	H-ZSM-12			30
10	H-ZSM-5			28
11	RE-Y ^d			40
12	H-MCM-41			25

^a Reaction conditions: 10 mmol of β -keto ester, dry toluene, temperature 383 K, time 10 h.

^b Quantified by using GC and the remaining is unreacted starting materials

^c Dealuminated zeolites.

^d Rare earths exchanged Y-zeolite.

possibly there are not many strong acid-sites to promote the reaction. Furthermore, the activity of these aluminosilicates increased considerably by dealumination (entries 4–6) of the parent aluminum-rich zeolites. Both dealuminated Y (Si/Al = 11.5) and mordenite (Si/Al = 26.8) show similar activity (85 and 86%, respectively) even though Y still contains a large amount of aluminum than mordenite. Similarly the enhanced conversion over dealuminated zeolite β (Si/Al = 75) cannot be explained on the basis of Si/Al ratio alone. Generally, the acid strength of a zeolite, particularly the Al-rich ones, is increased with an increase in the Si/Al ratio [18–21]. However, an increase in the Si/Al framework molar ratio of zeolites also leads to their increased hydrophobicity. Hence it is expected that the ingress of the organic reactants and egress of the products will be more facile in more hydrophobic zeolites, where hydrophilic or relatively less hydrophobic compounds like ethanol compared to esters will be repelled, shifting the equilibrium towards the

formation of desired products. In addition to hydrophobic nature, large void space of the catalysts, as in the case of dealuminated β and Y zeolites, will be a primary factor for their higher activity.

When the acid-strength of zeolite β is modified with substitution of either gallium (entry 7) or iron (entry 8) in the framework position, the conversion decreased significantly, as expected. It is well known that the acid-strength of metallosilicates follows the order: Al- β > Ga- β > Fe- β [22,23]. Quite interestingly, ZSM-12 (entry 9) and ZSM-5 (entry 10) exhibit low activity in this transesterification reaction in spite of being high-silica Brønsted acid zeolites. Hence, the relatively low activity of these two high silica zeolites is attributable to the diffusion limitations.

Entries 1 and 11 compare the influence of charge compensating cations in zeolite Y. When H-Y is converted to RE-Y, the conversion decreased significantly. Although this observation is rather difficult to explain on the basis of acid strength, the hydrophobic nature of the catalyst may be a significant contributing factor. It is expected that RE-Y with large number of non-framework RE-OH groups may increase the hydrophilicity compared to that of H-Y. Al-MCM-41 exhibits the least activity despite its mesoporous structure probably be due to their lower acid-strength compared to microporous aluminosilicates. It is, therefore, quite likely that increased conversion over dealuminated zeolites vis-à-vis parent zeolites may largely be due to the increased hydrophobicity of the former, particularly when the diammonium hexafluorosilicate method was used for dealumination where the defect sites created by dislodged Al are healed by Si incorporation. Dealuminated zeolite β was used for all further study in the transesterification of different alcohols with various β -keto esters.

3.3. Transesterification of various β -keto esters with different alcohols

The reactivity of various β -keto esters with different alcohols using dealuminated β /toluene as the catalytic system is given in Table 4. Entries 1–4 exhibit the transesterification of ethylacetoacetate with different aliphatic alcohols. All the aliphatic alcohols undergo smooth reaction but the reactivity for *tert*-butyl alcohol (entry 4) is considerably lower than the primary 1-butanol (entry 2). The observed reactivity can be explained on the basis of a steric factor and nucleophilicity/basicity of the alcohols. Although the *tert*-butoxide ion (Me_3CO^-) is a stronger base than either OEt^- or OH^- , its relative bulkiness may hinder it from closely approaching a substrate leading to the less reactivity of *tert*-butyl alcohol. However, cyclic and aromatic alcohols (entries 5 and 6) realized comparable reactivity. Interestingly, unsaturated aromatic alcohol (entry 7) also exhibits quite high reactivity. It is worth mentioning that transesterification of β -keto esters with unsaturated alcohols is rather difficult as it leads to facile decarboxylation and rearrangement as the side reactions [15]. However, in the present case using ze-

olite catalyst, β -keto esters underwent smooth transesterification even with unsaturated alcohols. Entries 8–13 exhibit the reactivity of different β -keto esters with 1-hexanol under similar conditions. The open-chain β -keto ester (methyl acetoacetate, entry 8) shows higher reactivity than the cyclic β -keto ester (entry 9). However, other esters like α -keto esters, α -halogenated ester, normal ester, and α,β -unsaturated esters (entries 10–13) completely fail to undergo the reaction. Thus, the observed reactivity reveals that nucleophilicity of alcohols as well as bulkiness of both alcohols and β -keto esters influence the transesterification activity. The used dealuminated β was reactivated at 773 K for 5 h under O_2 flow and reused for the transesterification of ethylacetoacetate with 1-hexanol. The activity of the catalyst was reduced by merely 5% after three successive uses with reactivation.

3.4. Effect of reaction time

Fig. 1 exhibits the progress of transesterification of ethylacetoacetate with 1-hexanol over dealuminated β zeolite as a function of reaction time. The reaction progressed steadily from the beginning until the conversion reached about 90% in 8 h. The rapid increase in the activity may possibly be due to the formation and removal of azeotropes (mixture of toluene and ethanol) which drives the equilibrium to favor the product formation by shifting the equilibrium. Very little improvement in the conversion was noticed after prolonged reaction time.

3.5. Reaction pathways

The proposed reaction mechanism [14,15,24] and different equilibrium steps involved in the transesterification are shown in Scheme 2. The interaction of Brønsted acid sites with the carbonyl groups of β -keto esters gives the protonated intermediate complex which undergoes nucleophilic

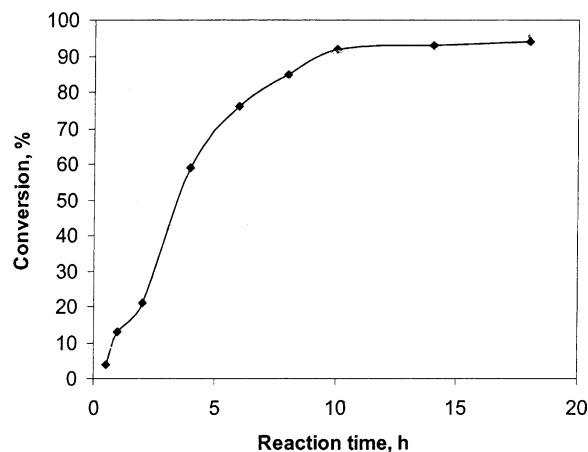
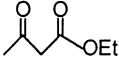

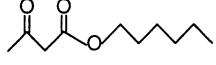
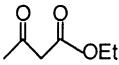
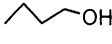
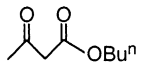
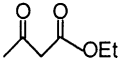
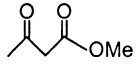
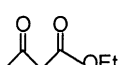

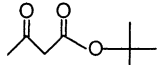
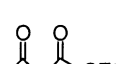

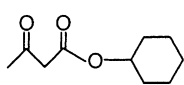
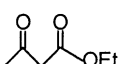
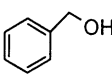
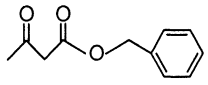
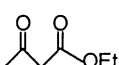
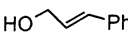
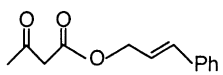
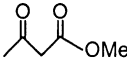

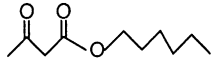
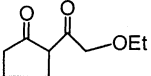

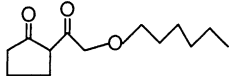
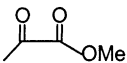

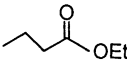

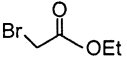

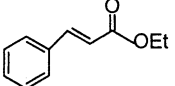



Fig. 1. Effect of reaction time over the activity of dealuminated β /toluene catalytic system for the transesterification of ethylacetoacetate with 1-hexanol.

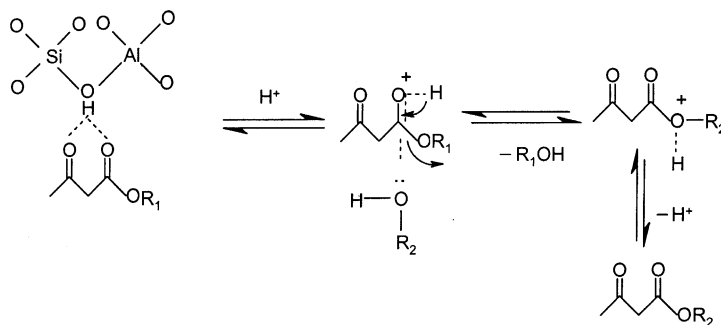
Table 4

Activity of various β -keto esters and alcohols towards transesterification over dealuminated H- β ^a

Entry	β -keto ester	Alcohol	Product	Yield ^b (%)
1				92
2				87
3		MeOH		85
4				66
5				87
6				80
7				88
8				85
9				79
10			Nil	Nil
11			Nil	Nil
12			Nil	Nil
13			Nil	Nil

^a Reaction conditions: 10 mmol of β -keto ester; 10 mmol of alcohol; 20 ml of dry toluene; 20 wt.% of dealuminated; β temperature 383 K; reaction time 10 h.

^b The products were isolated by column chromatography technique.



Scheme 2.

reaction with the alcohols followed by elimination of H^+ to give the final product. Furthermore, the observed lower reactivity of *tert*-butyl alcohol, vis-à-vis 1-butanol, indicates the involvement of nucleophilic species, as the former with lower nucleophilicity due to its bulkiness, exhibits lower reactivity. Moreover, other esters such as α -keto esters, α -halogenated ester, normal ester, and α,β -unsaturated esters completely failed to undergo the reactions. The difference in reactivity of β -keto esters from that of the other esters in transesterification may presumably be due to the formation of an acyl ketene intermediate in the former as proposed by Campbell and Lawrie [24]. None of the other esters has the possibility of forming a 6-membered intermediate which can stabilize the charge polarization. Therefore, the typical enol form of the β -keto esters enables them to undergo facile and efficient transesterification with various alcohols.

4. Conclusions

The large-pore high silica aluminosilicates with large void space such as zeolite β and Y can be used for the effective transesterification of various β -keto esters with different alcohols like primary, tertiary, benzylic, and allylic alcohols. The dealuminated zeolites β and Y exhibited quite high activity compared to the respective parent materials, probably due to the increased acid strength and hydrophobicity. The isomorphously substituted Ga- β and Fe- β gave significantly lower conversion compared to Al- β . ZSM-5 and ZSM-12 zeolites exhibited poor activity due to diffusion limitations. The β -keto esters exhibited higher transesterification activity than the α -keto esters, α -halogenated ester, normal ester, and α,β -unsaturated esters. Aliphatic primary alcohols realized quite high yield than the tertiary alcohols in accordance with the high nucleophilicity. Bulky β -keto esters as well as alcohols showed the decreased reactivity due to steric hindrance at the active sites. Time on stream study re-

vealed that azeotropic removal of coproduct ethanol assists the product formation by shifting the equilibrium. The probable mechanism involves the complexation of β -keto esters with the Brønsted acid sites of the catalyst followed by the nucleophilic attack of the alcohol.

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