# A facile and selective synthesis of β-keto esters *via* zeolite catalysed transesterification

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Crystalline microporous aluminosilicates (zeolites) efficiently catalyse the transesterification of β-keto esters with high selectivity under environmentally safe reaction conditions.
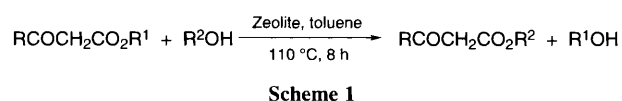
In connection with our ongoing programme on the synthesis of lignans including Podophyllotoxin[1] **29**, we were in need of various intermediate β-keto esters **23, 24, 27** and **28**. β-Keto esters represent an important class of organic building blocks[2] and are used for efficient synthesis of a number of complex natural products. Several methods exist for their synthesis;[3] however, none of them are amenable to the present requirement. In this regard, transesterification,[4] an important reaction for synthesis of esters, was chosen. Although many methods are available for the preparation of alkyl benzoylacetates,[3b,3c,3e] there are no reports on the synthesis of β-keto esters **23, 24, 27** and **28**. Transesterification of β-keto esters especially with allylic alcohols is rather difficult as it is offset by facile decarboxylated rearrangement.[5] Even modified Taber's method[6a] gives only moderate yields of allylic acetoacetates.

OH

MeO OMe

OMe

29
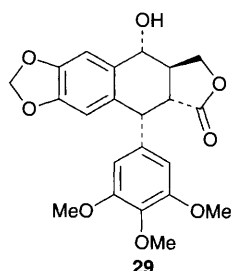
Distannoxanes[7] give good yields of β-keto esters; however the catalysts are difficult to prepare. A tin based superacid[8] was effective for the synthesis of alkyl β-keto esters but it failed with aromatic substrates. As can be clearly viewed, there is an obvious need to develop a satisfactory method for the preparation of allylic acetoacetates.

A two step strategy involving (i) preparation of alkyl benzoylacetates of the type **3, 4** and (ii) their transesterification with allyl alcohols to produce β-keto esters (Scheme 1) was adopted. Here we report a facile and selective method for the synthesis of β-keto esters employing crystalline microporous aluminosilicates (zeolites), well known environmentally safe solid materials,[9] as catalysts.

In a typical experiment 10 mmol of the β-keto ester and 10 mmol of the alcohol were mixed in dry toluene (25 ml) to which 10% (*m/m* of β-keto ester) of the catalyst was added. The
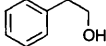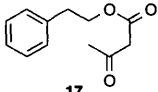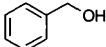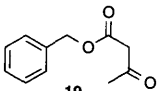
$$RCOCH_2CO_2R^1 + R^2OH \xrightarrow[110\,°C,\ 8\,h]{\text{Zeolite, toluene}} RCOCH_2CO_2R^2 + R^1OH$$

Scheme 1
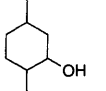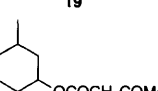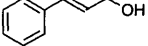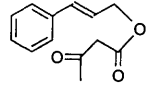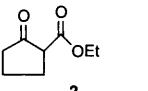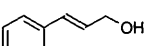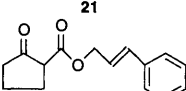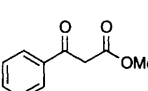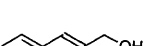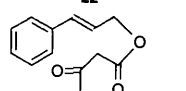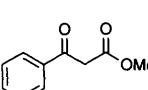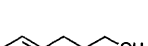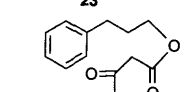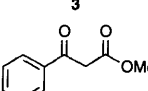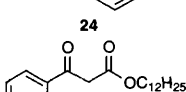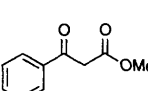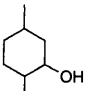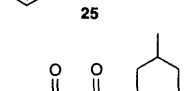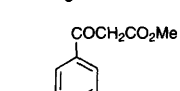
resultant mixture was heated to 110 °C (bath temp.) with azeotropic removal of the alcohol formed. After 8 h, the reaction mixture was cooled, the catalyst was filtered off, washed with 3 × 5 ml of toluene and the combined toluene distilled off under vacuum. Purification by chromatography and distillation yielded the required product.

After scanning through different zeolites, we found that H-Beta zeolite worked remarkably well. For example, transesterification of **1** with **14**, H-ZSM-5,[10a] H-ZSM-12,[10b] H-Y,† Re-Y† and H-Beta[10c] gave **21** in 85, 88, 90, 85 and 95% isolated yields. Hence, Beta, a high silica large pore zeolite with 3-dimensional open pore system, was used as a catalyst for the transesterification of several β-keto esters (Table 1). Higher acid strength of Beta (*vis-a-vis* Y-type zeolites)[11] coupled with large pore openings and void space (*vis-a-vis* ZSM-5 and ZSM-12) may be responsible for its better activity.

It is clear from Table 1 that the open chain aliphatic β-keto ester **1** with alcohols **10–14** results in higher yields of the corresponding transesterified β-keto esters **17–21**; even with the cyclic aliphatic moiety **2**, transesterification with alcohol **14** gave **22** in 85% yield. However, when β-keto esters with an aromatic moiety as in **3** and **4** were transesterified with alcohols **11, 13–16** the corresponding transesterified products **23–28** were obtained in moderate (60–70%) yields. (The starting material was recovered in all the cases to the extent of 15–20%.) This may be due to the bulkier (*vis-a-vis* aliphatic open chain substrates) nature of the substrates (entries 7–12) causing diffusional lim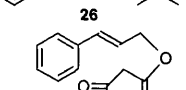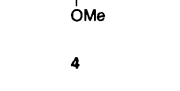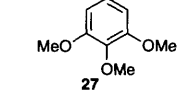itations in the pore of the zeolite catalyst. High acidity along with larger void space, as in zeolite Beta, seems to be required for high catalytic activity and selectivity in these reactions. It is noteworthy to mention that the reaction appears to be specific only for transesterification of β-keto esters. Other esters like α-keto esters, γ-keto esters, α-halogenated esters, unsaturated esters as well as normal esters fail to undergo the reaction (compounds **5–7** and **9** with **15**, and **8** with **13**). The difference in reactivity of β-keto esters from other esters in transesterification may probably be due to the formation of an acyl ketene intermediate in the former as proposed by Campbell and Lawrie.[13]

Table 1 Transesterification of various β-ketoesters with different alcohols catalysed by H-Beta[a]

Substrate	Alcohol	Product[b]	Yield (%)[c]
MeCOCH₂CO₂Et **1**	**10**	**17**	96
MeCOCH₂CO₂Et **1**	C₁₂H₂₅OH **11**	MeCOCH₂CO₂C₁₂H₂₅ **18**	86
MeCOCH₂CO₂Et **1**	**12**	**19**	81[12]
MeCOCH₂CO₂Et **1**	**13**	**20**	95[6b]
MeCOCH₂CO₂Et **1**	**14**	**21**	95
2	**14**	**22**	84
3	**14**	**23**	66
3	**15**	**24**	64
3	C₁₂H₂₅OH **11**	**25**	71
3	**13**	**26**	69
4	**14**	**27**	62
4	**16**	**28**	59

[a] No reaction in the absence of catalyst and the catalyst was reused three times without loss of activity. [b] All new compounds gave satisfactory spectral data (IR, PMR, CMR). [c] Isolated yield.

MeCOCO₂Et **5**

MeCOCH₂CH₂CO₂Et **6**

BrCH₂CO₂Me **7**

8

MeCH₂CH₂CO₂Et **9**
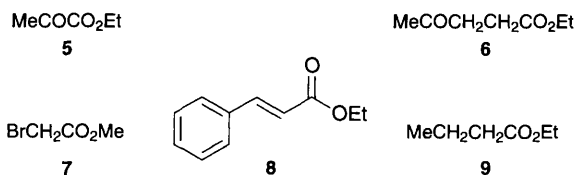
The authors thank Dr T. Ravindranathan for constant encouragement and Dr H. R. Sonawane for fruitful discussions. B. S. B. and M. S. both thank CSIR, New Delhi for the grant of research fellowships.

Footnote

† H.-Y. commerically available zeolite, was obtained from United Catalyst India Ltd. and was then partially converted into RE-Y by treatment with rare earth's solutions.

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