Transesterification of β-keto esters catalysed by transition metal complexes in a novel heterogeneous way [*]

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β-keto esters have been successfully transesterified with primary, secondary, tertiary, allyl and alkynic alcohols by recyclable Mn(III) salen or vanadyl(IV) acetate catalysts realised while conducting the reaction deliberately for the first time in a novel heterogeneous media to afford good to excellent yields.

Keywords: transesterification, β-keto esters, Mn(III) salen complex, vanadyl(IV) acetate, heterogeneous system, reusability

1. Introduction

Transesterification is an important organic transformation to synthesise a variety of organic esters [1,2]. Transesterification is a preferred process to the esterification of alcohols with carboxylic acids of low solubility, because esters that are starting materials for transesterification are commonly soluble in most of the solvents. Transesterification of β-keto esters provides important synthons for a number of complex natural products [3] and intermediates for oil and paint industry.

Typically transesterification is catalyzed by strong acids [4], soluble base catalysts [5,6], carbonates [7] and enzymes [8]. The reaction employing acids and bases is incompatible to the modern synthetic industrial chemistry that desires to be highly efficient, selective, ecofriendly and preferably catalytic. Consequently, evolution of titanium(IV) alkoxides [9,10] and alkyldistannoxanes [11], homogeneous catalysts and kaolinite [12], zeolites [13] and alumina oxides [14], a tin-based superacid [15], heterogeneous catalysts for transesterification of β-keto esters reflects the current status of research in this area. These catalysts possess inherent and serious disadvantages that limited the scope of their utility in the transesterification reactions such as (1) expensive and tedious preparation of the catalysts, (2) confining the utility to some kind of esters only. Based on a simple insolubility principle, we have recently designed heterogeneous catalytic systems, Mn(III) salen complex and vanadyl(IV) acetate for Knoevenagel condensation [16] and acetylations [17], respectively. The simple preparation, low cost, and easy handling of these complexes prompted us to study their application for the transesterification, an industrially important reaction.

2. Experimental

2.1. Preparation of the catalysts

2.1.1. [N,N′-ethylene bis(salicylideneaminato)] manganese(III) chloride (Mn(III) salen complex)

[N,N′-ethylene bis(salicylideneaminato)] manganese(III) chloride was prepared following Jacobsen's procedure [18]. The Mn(III) salen complex was prepared by adding 6.127 g (25 mmol) of $Mn(OAc)_2 \cdot 4H_2O$ to 2.68 g (10 mmol) of salen ligand dissolved in ethanol (50 ml) and refluxing this mixture under air for 3 h at 80 °C. 1.27 g (30 mmol) of LiCl was added to the above mixture, refluxed for a further period of 2 h and cooled in ice. The brown Mn salen complex was filtered, washed with ethanol, ice-cold water and dried under vacuum for 6 h. Chemical analysis for $C_{16}H_{14}N_2O_2MnCl$: calcd. Mn, 15.40; C, 53.9; H, 3.9; N, 7.8, Cl, 9.9; found Mn, 15.24; C, 51.8; H, 3.6; N, 7.2; Cl, 9.86. The complex was analysed by UV and IR spectrometry and its spectrum is similar to that of Kochi's $[Mn(III)\ salen]^+PF_6^-$ complex [19].

2.1.2. Preparation of vanadyl(IV) acetate

Vanadyl(IV) acetate was prepared according to the literature procedure [17].

2.2. A typical experimental procedure for transesterification reaction

Mn(III) salen complex (25 mg, 0.07 mmol)/vanadyl(IV) acetate (25 mg, 0.135 mmol) was suspended in dry toluene (10 ml) followed by the addition of a mixture of methyl acetoacetate (1 mmol, 0.116 g), cinnamyl alcohol (1 mmol, 0.134 g) and heated to 100 °C in two-necked round bottomed flask provided with Dean–Stark apparatus to remove the methanol. The reaction was monitored by TLC. After completion of the reaction, the catalyst was filtered and used

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Table 1
Transesterification of β-keto esters catalysed by transition metal complexes.

Entry	Substrate (1)		Alcohol (2)	Time (h)		Yields of product (3)[a]	
	R	R$'$	R$''$	(A)	(B)	Mn(III) salen (A)	VO(OAc)$_2$ (B)
1	CH$_3$	CH$_3$	Propargyl	6	8	90	70
2	CH$_3$	CH$_3$	Menthyl	8	12	98	95
3	CH$_3$	CH$_3$	Dodecyl	4	6	98	98
4	CH$_3$	CH$_3$	Crotyl	6	8	95	65
5	CH$_3$	CH$_3$	Geranyl	6	8	94	43
6	CH$_3$	CH$_3$	Cyclohexyl	3	6	94	87
7	CH$_3$	CH$_3$	Cinnamyl	8	7	90[b]	50
8	CH$_3$	CH$_3$	Benzyl	8	8	93	75
9	CH$_3$	CH$_3$	2-phenylethyl	8	8	98	45
10	CH$_3$	CH$_3$	*Tert*-butyl	6	12	56	0
11	CH$_3$	CH$_3$	1-octyl	2	6	97	80
12	CH$_3$	CH$_3$	1-hexyl	2	5	98 (95)[c]	91 (90)[c]
13	CH$_3$	CH$_3$	2-pentyl	4	6	88	81
14	CH$_3$	CH$_3$	2-methoxy ethyl	3	4	95	87
15	CH$_3$	CH$_3$	2-amino, 1-butyl	8	8	90	77
16	CH$_3$	CH$_3$	Benzyl amine	4	4	98	98
17	CH$_3$	CH$_2$CH$_3$	1-hexyl	6	8	98	98
18	Ph	CH$_2$CH$_3$	1-hexyl	12	12	95	80

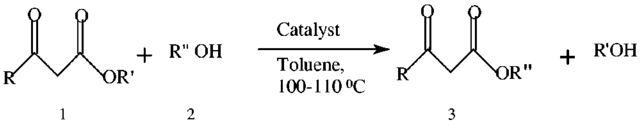
[a] Yields determined by ^{1}H NMR, based on β-keto ester.
[b] Yield of isolated pure product.
[c] Yield after fifth cycle.

for a recycling experiment since it is practically insoluble in toluene solvent media. The filtrate was concentrated and purified by column chromatography (hexane/ethylacetate, 95/5 v/v) to afford the *3-phenyl-2-propenyl-3-oxobutanoate* (table 1, entry 7) as a viscous colourless liquid, yield: 0.196 g (90%). ^{1}H NMR (200 MHz, Gemini Varian, using TMS as an internal standard in CDCl$_3$): δ 2.25 (s, 3H), 3.4 (s, 2H), 4.8 (d, 2H), 6.14–6.35 (m, 1H), 6.6–6.75 (m, 1H), 7.2–7.4 (m, 5H); IR (KBr pellets, recorded on a Nicolet DX-5 spectrometer): 3060, 3020, 2940, 1740, 1720, and 1620 cm^{-1}; MS (EI, 70 eV, scanned on VG 70–70H (micromass)): m/z 218 (M$^+$ peak), 160, 133, 105, 91, 85, 77, 69, 65, 55, and 43.

Recycling of the catalyst. After completion of the reaction, the catalyst is filtered, washed thoroughly with toluene, dried under vacuum and used for the transesterification reaction following the procedure as described above.

3. Results and discussion

We report in this letter the designing of the process of transesterification of the β-keto esters with a wide scope of utility, possible with varied primary, secondary, tertiary, allyl and alkynic alcohols catalysed by Mn(III) salen or vanadyl(IV) acetate deliberately in a heterogeneous media by a simple insolubility principle to realise reusability of the catalyst by filtration to afford good to excellent yields (scheme 1, table 1). The reactions are in general very clean and no by-product has been isolated.



Scheme 1. Transesterification of β-keto esters catalysed by transition metal complexes.

This method is found to be applicable for a wide range of compounds (table 1) and offers distinct advantages over the existing methods. The salient features of this methodology are summed up: (1) Aliphatic and aromatic esters are successfully transformed into synthetically useful esters. (2) The transesterification of allylic alcohols is difficult since the product readily undergoes a decarboxylative rearrangement, the Caroll rearrangement [20]. With our catalytic system unsaturated alcohols such as crotyl, cinnamyl and propargyl underwent transesterification affording esters in high yields (entries 1, 4 and 7). (3) It is interesting to note here that even tertiary butyl esters (entry 10) were prepared using the Mn(III) salen complex. The bulky tertiary alcohol failed to react under the same conditions with vanadyl(IV) acetate probably due to difficulty of the tertiary alkoxide species formation because of its acidic nature, whereas in case of the Mn(III) salen complex the formation of tertiary alkoxide is possible because of its basic nature. In general, the formation of alkoxide is sluggish in case of tertiary alcohols compared to the primary and secondary alcohols [21]. (4) Aryl alcohols (entries 7, 8 and 9), cyclic and hindered alcohols (entries 2 and 6) and long chain primary alcohols underwent transesterification affording the corresponding esters of commercial use (entries 3 and 11) in high yield in short time. (5) The scope of the present catalytic system is widened for the transamidation (entry 16) of an ester affording excellent yield. (6) Selective amidation of an ester with aliphatic amino alcohols is another striking example (entry 15). (7) The catalysts are recycled for five times without any significant loss in activity.

In conclusion, we have demonstrated that Mn(III) salen and vanadyl(IV) acetate act as efficient, convenient and reusable catalysts to effect transesterification. The superiority and flexibility of our method over the existing methods coupled with the ease of operation and the simplicity in the work-up involving mere filtration of the catalyst and recyclability should find widespread application in transesterification of many β-keto esters. The resolution of racemic esters and amines (aminolysis of esters) with Jacobsen catalyst (R,R)-(−)-N,N′-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclo-hexane diamino-manganese(III) chloride, is under progress in our laboratory.

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