Mn(III) salen catalyst for Knoevenagel condensation – a novel heterogeneous system *

M. Lakshmi Kantam ** and B. Bharathi

Inorganic Chemistry Division, Indian Institute of Chemical Technology, Hyderabad 500 007, India
E-mail: iict@ap.nic.in

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Knoevenagel condensations were catalysed by Mn(III) salen complex in quantitative yields under mild reaction conditions for the first time. The catalyst was reused for several cycles with consistent activity.

Keywords: Mn(III) salen complex, Knoevenagel condensation, carbonyl compounds, heterogeneous system, reusability

1. Introduction

The versatile carbon–carbon bond forming Knoevenagel condensation [1] has numerous applications in the elegant synthesis of acids, esters, α,β-unsaturated nitriles, heterocycles and intermediates of antihypertensives and calcium antagonists [2] and is classically catalysed by bases [3,4] in a liquid-phase system. At the laboratory scale, many catalysts, viz. alumina [5], sepeolite [6], zeolites [7], clays [8], hydrotalcites [9–11], anionic resins [12], bismuth chloride [13], etc., reportedly effect the Knoevenagel condensations. Except transition metal polyhydrides [14], no other metal complexes were used till date for the Knoevenagel condensations.

Herein, we wish to report a mild catalytic method for Knoevenagel condensations of several substituted aromatic aldehydes with malononitrile and ethyl cyanoacetate as donors in moderate to excellent yields using Mn(III) salen, a reusable catalyst, for the first time. We deliberately designed and chose a heterogeneous system, in which the Mn(III) salen practically insoluble in toluene offered consistent activity for several cycles, which was possible by simple filtration. Incidentally, this forms one of the few reports on heterogenisation of a homogeneous system manoeuvred by a simple insolubility principle to evolve and act as a truly "heterogeneous system".

Knoevenagel condensations (scheme 1) involving various aromatic aldehydes with (a) malononitrile and (b) ethyl cyanoacetate as the active methylene compounds were carried out with Mn salen complex at room temperature. All the reactions proceeded smoothly in toluene with the exclusive formation of dehydrated products in quantitative yields (table 1).

An attempt was made to check the stability and heterogeneity of the Mn(III) salen catalyst, using the following procedure: 50 mg of Mn salen complex was added to 10 ml dry toluene and stirred for 1 h. The slurry was filtered and then the regular reaction was carried out with the filtrate and the residue separately. While complete conversion was observed in the reaction carried out with the residue, there was absolutely no conversion in the reaction carried out

$R_2 = H$

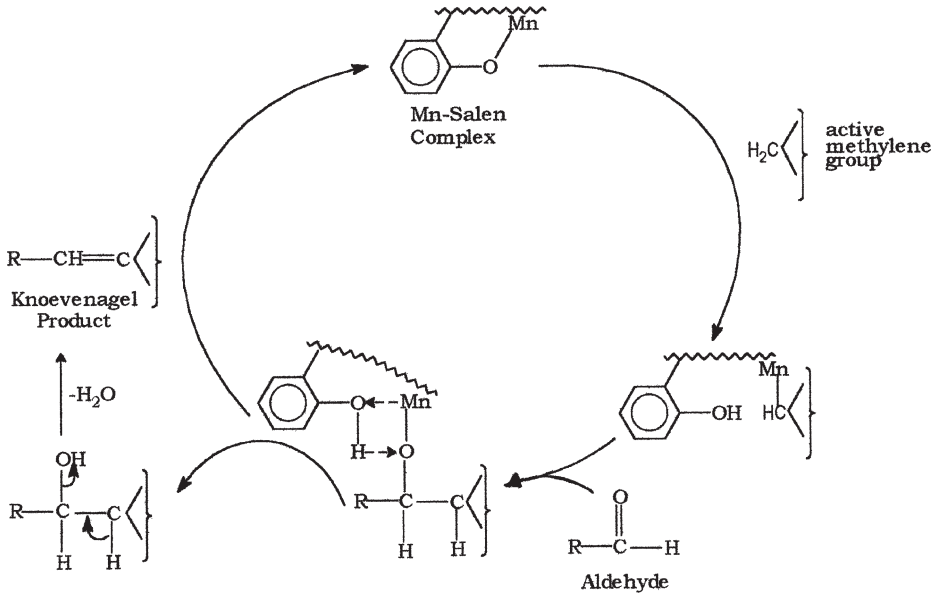
Scheme 1. Knoevenagel condensation of different carbonyl compounds with malononitrile or ethyl cyanoacetate.

Table 1
Knoevenagel condensation catalysed by Mn(III) salen complex.

Entry	R_1	Y	Time (h)	Yields[a] (%)
1	Ph	CN	1	100
2	Ph	CO_2Et	2	50
3	2-$OMeC_6H_4$	CN	1	100, 97[b]
			1/1	100[c]/93[d]
4	2-$OMeC_6H_4$	CO_2Et	3	89
5	4-ClC_6H_4	CN	1	100
6	4-ClC_6H_4	CO_2Et	2	100
7		CN	1	100
8		CO_2Et	1	100
9	4-$NO_2C_6H_4$	CN	1	100
10	4-$NO_2C_6H_4$	CO_2Et	2	100
11	3,4,5-$OMeC_6H_3$	CN	12	100
12	3,4,5-$OMeC_6H_3$	CO_2Et	14	88
13	3-$OMeC_6H_4$	CN	2	80
14	3-$OMeC_6H_4$	CO_2Et	4	50

[a] ^1H NMR yields based on aldehyde.
[b] Isolated yield.
[c] 1st recycle.
[d] 8th recycle.

* IICT communication No. 4006.
** To whom correspondence should be addressed.



Scheme 2. Plausible mechanism for the Knoevenagel condensation catalysed by Mn(III) salen complex.

with the filtrate, even after 6 h. It can, therefore, be concluded that the Mn salen complex performs the catalytic job in a heterogeneous way. In addition to this, the reusability of the catalyst with consistent activity for several cycles without any further reactivation was demonstrated. Slight deactivation was observed from the 8th cycle onwards (table 1, entry 3).

The reaction was successful with the potassium salt of salen also, thus indicating that the phenolate part of the complex will act as the (reversible) proton acceptor. Hence, it is ascribed that Mn phenolate accepts the proton from the active methylene group in a reversible fashion to form a Mn complex with the generated carbanion. Subsequently, this complex reacts with aldehyde to afford the enolate and on dehydration gives the Knoevenagel product (scheme 2).

This new catalyst becomes a practical alternative to soluble bases for Knoevenagel reactions in view of the following advantages: (a) high catalytic activity under very mild reaction conditions, (b) easy separation of the catalyst by simple filtration, and (c) reusability. Therefore, the success of heterogenisation of an otherwise homogeneous system widens the scope in several studies.

2. Experimental

The Mn(III) salen complex was prepared following Jacobsen's procedure [15].

2.1. Preparation of the salen ligand

0.67 ml (10 mmol) of ethylenediamine and 2.12 ml (20 mmol) of salicylaldehyde were refluxed in 50 ml of ethanol for 2 h. The resulting yellow solid was filtered, washed with ethanol and dried under vacuum.

2.2. Preparation of the Mn(III) salen complex

6.127 g (25 mmol) of $Mn(OAc)_2{\cdot}4H_2O$ was added to 2.68 g (10 mmol) of salen ligand dissolved in ethanol (50 ml) and refluxed 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. The complex was analysed by UV and IR spectrometry and the spectrum is similar to that of Kochi's $[Mn(III)\ salen]^+PF_6^-$ complex [16].

2.3. General procedure for Knoevenagel reaction

0.242 ml (2 mmol) of 2-methoxybenzaldehyde (entry 9) and 0.127 ml (2 mmol) of malononitrile were taken in dry toluene (10 ml) in a 50 ml round bottom flask and the reaction mixture was stirred for 10 min at room temperature. Then Mn salen complex (50 mg) was added and stirring was continued till the completion of the reaction (table 1). The reaction was monitored by TLC. On completion of the reaction, the catalyst was filtered and the filtrate was concentrated under reduced pressure to afford the crude product. The product was purified by column chromatography (hexane/ethyl acetate: 8/2). The product (yield: 0.357 g, 97.0%) was analysed by IR and ^{1}H NMR spectrometry. Proton nuclear magnetic resonance (^{1}H NMR) spectra were taken on a Gemini Varian (200 MHz) NMR spectrometer, using TMS as an internal standard. IR spectra were recorded on a Nicolet DX-5 spectrometer.

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