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The first example of Michael addition catalysed by modified Mg–Al hydrotalcite

Boyapati Manoranjan Choudary [a,*], Mannepalli Lakshmi Kantam [a], Chinta Reddy Venkat Reddy [a], Kottapalli Koteswara Rao [a], Francois Figueras [b]

[a] *Indian Institute of Chemical Technology, Hyderabad 500007, India*
[b] *Institut de Recherches sur la Catalyse, 2, Avenue Albert Einstein-69626 Villeurbanne Cedex, France*

Abstract

Selective 1,4-additions (Michael reactions) on methyl vinyl ketone, methyl acrylate, simple and substituted chalcones by donors such as nitroalkane, malononitrile, diethylmalonate, cyanoacetamide and thiols were catalysed by solid base, modified Mg–Al hydrotalcite as catalyst in quantitative yields in liquid phase under mild reaction conditions. Products of undesirable side reactions resulting from 1,2-addition, polymerisation and bis-addition are not observed. The work-up procedure is simplified by simple filtration with the use of solid bases. © 1999 Elsevier Science B.V. All rights reserved.

Keywords: Michael reactions; Activated Mg–Al hydrotalcite; Rehydration; 1,4 addition

1. Introduction

In recent years, there has been increasing emphasis on the design and development of environment-friendly solid base catalysts to replace soluble bases such as alkali metal alkoxides and hydroxides [1,2] widely employed for base induced C–C bond formation in the bulk and fine chemical industries. The objectives are first to eliminate the formation of undesirable side products resulting from polymerization, bis-addition and self condensation and secondarily to reduce the salts formed consequent to the neutralisation of soluble bases with acids. This objective is prompted by more stringent laws laid down all over the world for the protection of environment. A great challenge is the development of heterogeneous processes to coax the reactions that form carbon–carbon bonds, for instance Michael reactions which are of the most fundamental and versatile endeavours in organic chemistry [3,4]. The incorporation of alkali metals [5,6] such as Cs^+ in zeolites and mesoporous molecular sieves by an cationic exchange provides low basicity useful for a small range of organic reactions only. Na clusters introduced in the zeolites by impregnation with sodium azide [7] afford strong basic sites which even catalyse side chain alkylations but are easily deactivated by moisture. Design of anchored organic amines in the mesoporous materials such as MCM-41 offers a different approach [8] to the studies on Michael reactions. Hence, the development of efficient and selective solid acid–base catalysts [9] for the con-

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[*] Corresponding author. Tel.: +91-40-7170921; Fax: +91-40-713378; E-mail: iict@ap.nic.in

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struction of carbon–carbon bonds has been and continues to be a challenging and active exploration in organic synthesis.

Layered double hydroxides (LDHs) or hydrotalcite like compounds (HTLCs) have recently received much attention [10] in view of their potential usefulness as adsorbents, anion exchangers and most importantly as basic catalysts [11–13]. Upon thermal decomposition at about 450°C LDHs give a highly active homogeneous mixed oxide which is a potential basic catalyst used for a variety of organic transformations [14–18]. Recently, we reported [19] a modified method for the activation of the hydrotalcite catalyst whose basicity was tuned for base catalysed aldol and Knoevenagel [20] condensations in liquid phase under very mild reaction conditions. To our knowledge no report is available in the literature in which a hydrotalcite is employed to promote the Michael addition, and this reaction has therefore been investigated here.

2. Experimental section

2.1. Synthesis of Mg–Al hydrotalcite [19]

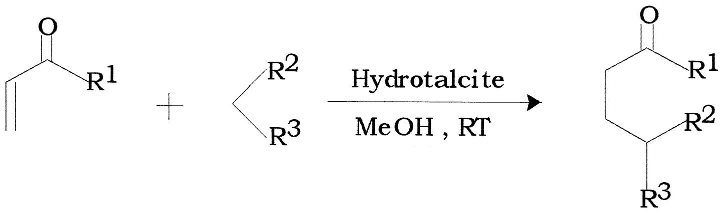
An aqueous solution (0.221 L) containing $Mg(NO_3)_2 \cdot 6H_2O$ (0.2213 mol) [Aldrich] and $Al(NO_3)_3 \cdot 9H_2O$ (0.0885 mol) [Aldrich] for a ratio Mg/Al = 2.5, was added slowly to a second solution (0.221 L) containing NaOH (0.7162 mol) and Na_2CO_3 (0.2084 mol) in a 1.0 L round-bottom flask under vigorous stirring. The addition took nearly 3 h. Then the contents were heated to 338 K for 16 h. The precipitate formed was filtered and washed with hot distilled water until the pH of the filtrate was 7. The precipitate was dried in the oven at 353 K for 15 h. The XRD pattern shows the presence of pure hydrotalcite, with lattice parameters corresponding to those reported in the literature [10].

2.2. Activation of the catalyst

The catalyst was first activated by calcining to 723 K in a flow of air. The temperature was raised at the rate of 10 K/min to reach 723 K and maintained for 8 h. The solid was then cooled in dry nitrogen and rehydrated at room temperature under a flow of dry nitrogen gas saturated with water vapour. The flow of wet nitrogen of 6 L/h was maintained for a specified period, depending on the amount of catalyst to be rehydrated. This modified hydrotalcite (MHT) was used for the Michael reactions.

2.3. Typical reaction procedure

In a typical procedure, Nitromethane (2 mmol) [Fluka, used as such] and 0.2 g of MHT were stirred in 10 ml of dry methanol for 5 min, then methyl vinyl ketone (2 mmol) (Fluka, used as such) was added and stirring was continued until the completion of the reaction, as monitored by thin layer chromatography (TLC). The catalyst was filtered and the filtrate was concentrated under reduced pressure. The crude product was purified by column chromatography (Acme Synthetic Chemicals, 60–120 mesh, silica gel) using chloroform as eluent, yield 0.251 g (96%). The product was analysed by ^1H NMR and IR spectrometry.

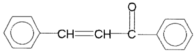
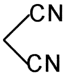
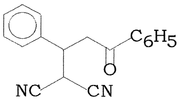
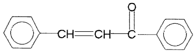
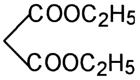
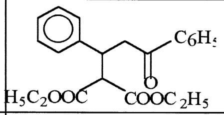
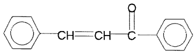
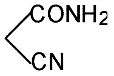
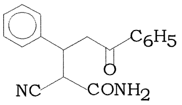
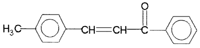
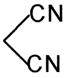
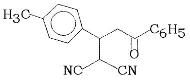
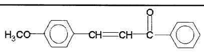
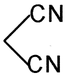
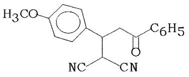
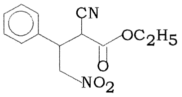
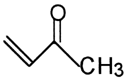
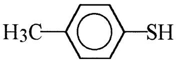
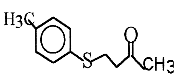
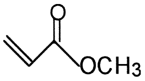
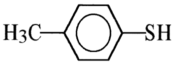
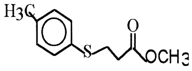
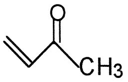
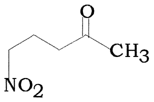


Scheme 1.

2.4. Instruments

X-ray diffraction patterns were determined on powder X-ray diffractometer Siemens, D-5000 (diffraction geometry; θ–2θ) instrument, using sealed Cu tube (2.2 kW). Proton nuclear magnetic resonance (^1H NMR) spectra were taken on a Gemini Varian (200 MHz) NMR

Table 1
Michael addition catalysed by modified Mg–Al hydrotalcite (MHT) catalyst

Entry	Acceptor	Donor	Time (h)	Product	Yield(%)[a]
1			2.0		88
2			6.0		96[b]
3			2.0		41
4			1.5		97
5			1.5		88
6	Ph—CH=CH[CN]$COOC_2H_5$	CH_3NO_2	1.5		96
7			1.5		100[c]
8			1.0		96[c]
9		CH_3NO_2	1.5		100, 96[d]

[a] Yields determined by ^1H NMR based on Michael accceptor.
[b] 1 g catalyst, hexane used as solvent.
[c] Yields determined by ^1H NMR based on Michael donor.
[d] Isolated yield.

spectrometer, using TMS as an internal standard, IR spectra were recorded on Nicolet 740 FT-IR spectrometer.

3. Results

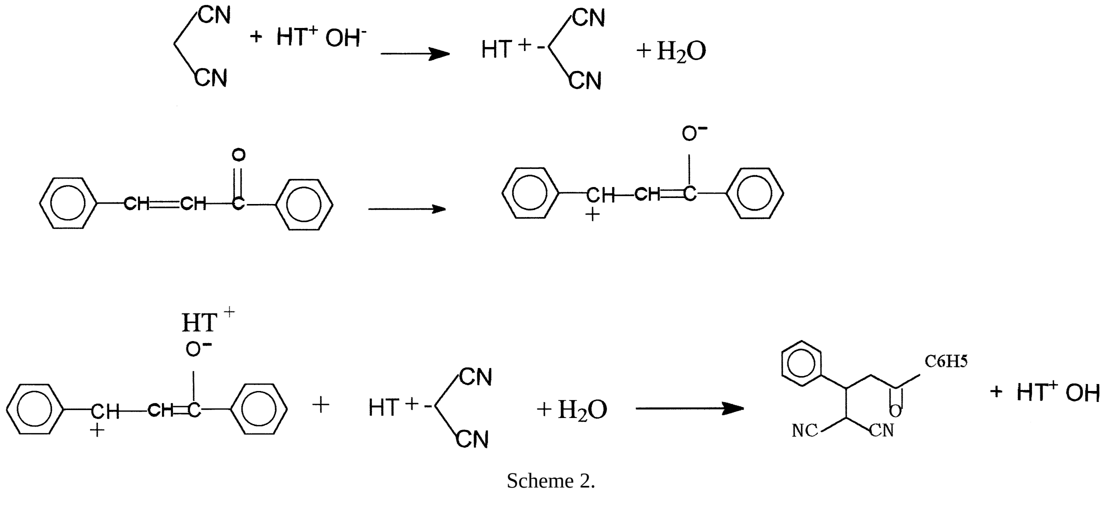
It has to be pointed out that hydrotalcite as synthesized or just calcined showed no activity for the reactions described here. The modified Mg–Al Hydrotalcite obtained by decarbonation and then rehydration of the solid is an efficient and very selective catalyst for 1,4-addition, i.e., Michael reactions (Scheme 1) as illustrated in Table 1. A reference reaction performed with chalcone and malononitrile (cf. entry 1 of Table 1), using 10% NaOH as catalyst instead of the solid base and the same experimental conditions yielded a polymerised product. Modified hydrotalcite appears to be more active than partially dehydrated barium hydroxyde since complete conversion is reached here in 2 h, compared to 8–12 h for $Ba(OH)_2$.

The procedures of Ref. [21] applied to the reaction of chalcone with different donors gave the products of Michael addition in excellent yields (entries 1, 4 and 5). All these reactions proceeded smoothly in methanol, with the exception of chalcone with diethyl malonate which offered low yields. However, using hexane as solvent the reaction of chalcone with diethylmalonate (Table 1, entry 2) afforded the Michael product in excellent yield albeit the process took 6 h. The solvent effect established here is similar to the results reported by others in the case of barium hydroxyde [22]. The slow reaction in methanol suggests a competition between methanol and the substrate favourable to methanol. In methanol as solvent the more reactive cyano acetamide as a donor gave moderate yield (Table 1, entry 3) which is likely also indicative of the importance of a solvent effect.

The Michael addition of enones with thiols and nitroalkanes was performed to demonstrate the versatility of the method with substrates other than usual active methylene compounds, such as malononitrile and malonic ester. The reaction conducted between ethyl α-cyanocinnamate with nitromethane (Table 1, entry 6) formed the Michael adduct in excellent yields. The reaction of methyl vinyl ketone and *p*-thiocresol with nitromethane (Table 1, entry 7 and 9) and the reaction of methyl acrylate with *p*-thiocresol (Table 1, entry 8) were also accomplished in high chemical yields.

4. Discussion

The reaction of Michael in organic chemistry requires hydroxyles to abstract a proton from an



Scheme 2.

active methylene of the Michael donor. It is gratifying to observe here that the same conclusion can be reached in the heterogeneous phase: the X-ray diffraction studies of the activation of hydrotalcites showed that the LDH structure which is lost upon calcination, is restored by rehydration. In that case a meixnerite-like structure is formed in which OH^- are the compensating anions. These anions are mobile and therefore basic, and catalyse several reactions proceeding by basic mechanisms like aldolisation [19,23,24] or Knoevenhagel condensations [20]. From their catalytic properties it is usually accepted that LDH have a pK_b of about 11.4 to 12, therefore, are bases of moderate strength comparable to piperidine [24]. The lack of activity of calcined hydrotalcites demonstrates then that the reaction of Michael requires here also Brônsted bases of mild strength.

The classical mechanism of the reaction of Michael [25] can therefore be applied here. The abstraction of a proton from the donor gives a carbanion which can be stabilised by the cationic charge of Al in the lattice, as suggested in Scheme 2. It could be proposed that this carbanion further adds to the chalcone to form an enolate which would take a proton from water and give the final product. The fact that the selectivity is rather high for Michael reactions, we can find two interpretations, which could be clarified only by a kinetic study not performed here: (1) either the selectivity may be high because successive reactions which would decrease the yield are unfavoured by the low basicity of the catalyst. This would be in line with the better results in homogeneous catalysis using mild bases [22,26]. (2) or chalcone is adsorbed in its enolate form (Scheme 2) and the addition can only occur then at the C atom in β position of the olefin, giving the 1,4 Michael adduct selectively. The catalytic cycle is then closed by the capture of a proton, reforming OH^- and the enolic form of the Michael adduct and finally the keto adduct. In this hypothesis competitive adsorption occurs, which should be evidenced in the kinetic study.

In any case it is interesting to observe that this reaction is very specific of Brönsted bases, such as aldolisation [19,24]. In spite of the large number of basic sites determined by the calorimetric adsorption of CO_2, hydrotalcites just decarbonated are not active.

5. Conclusion

Thus a critical requirement of selective 1,4-addition without any side reactions, condensation, dimerization, or rearrangements in Michael reaction is made possible with the hydrotalcite properly activated. It is probable that the particular properties of hydrotalcites for this class of reactions are related to their mild basicity. These catalysts bring advantages such as high catalytic activity and selectivity under very mild liquid phase conditions, easy separation of the catalyst by simple filtration, possible recycling of the catalyst, use of non-toxic and inexpensive catalysts and especially, elimination of salts and by-product pollutants. This new solid base catalyst becomes then a practical alternative to soluble bases.

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