Aldol and Knoevenagel condensations catalysed by modified Mg–Al hydrotalcite: a solid base as catalyst useful in synthetic organic chemistry

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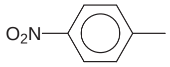
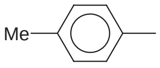
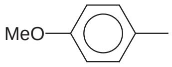
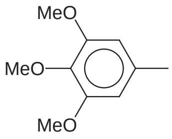
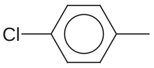
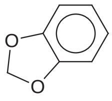
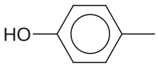
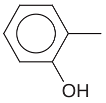
Aldol and Knoevenagel condensations were performed with suitably activated Mg–Al hydrotalcite as catalyst in quantitative yields in the liquid phase under mild reaction conditions at a faster rate for the first time.

In recent years, there has been increasing emphasis on the use and design of environment-friendly solid acid–base catalysts to reduce the amount of toxic waste and by-products arising from the chemical processes prompted by stringent environment protection laws. The challenge is to perform heterogeneous catalysis reactions leading to C–C bond formation which are widely employed in organic synthesis.[1] The versatile Knoevenagel and aldol condensations have numerous applications in the elegant synthesis of fine chemicals[2] and are classically catalysed by bases[3,4] in the liquid phase system. On the laboratory scale, many catalysts have been known to effect the Knoevenagel and aldol condensations and include alumina,[5] sepeolite,[6] zeolites,[7] clays,[8] hydrotalcites[9–11] and anionic resins.[12]

Table 1 Aldol condensation between acetone and substituted benzaldehydes catalysed by MHT catalyst at 60 °C[a]

Entry	R¹	*t*/h	Yields (%)[b]
1		1	97[c]
2		1	96
3		1.5	95
4		0.5	98
5		1.5	94
6		1	96[d]
7		14	8[c]
8		15	No reaction

[a] All reactions were performed on 2 mmol substrate in 10.3 ml (140 mmol) acetone using 0.2 g of MHT. [b] ¹H NMR yields based on aldehyde. [c] Aldol to dehydrated product (1 : 1). [d] Isolated yield.

Layered double hydroxides (LDHs) or hydrotalcite-like compounds (HTLCs) have recently received much attention[13] in view of their potential usefulness as adsorbents, anion exchangers and most importantly as basic catalysts.[14] LDHs upon thermal decomposition at about 450 °C give a highly active homogeneous mixed oxide which is a potential basic catalyst used for a variety of organic transformations such as aldol condensation,[15] nucleophilic halide exchange,[16] alkylation of diketones,[17] epoxidation of activated olefins with hydrogen peroxide[18] or Claisen–Schmidt condensation.[19]

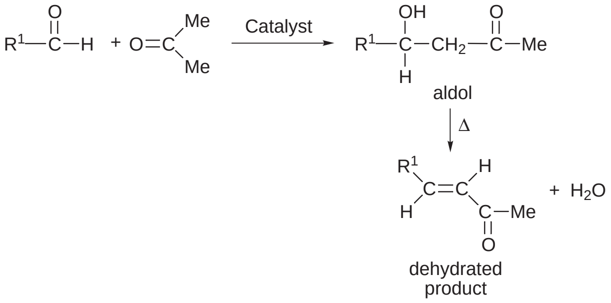
The previous work[10,15,17,19] on aldolisations using HTLCs was performed generally at higher temperatures. Recently, we reported[20] a modified method for the activation of the hydrotalcite catalyst whose basicity was tuned for base catalysed condensation reactions in the liquid phase under very mild reaction conditions. Herein, we report Knoevenagel and aldol condensations catalysed by this modified hydrotalcite (MHT) with quantitative yields at a faster rate of reaction under very mild liquid phase conditions (Tables 1 and 2) for the first time as part of our investigation into the scope and applicability of MHT for a variety of organic reactions.

In the case of aldol reactions, the aldol was the major product when the reaction was conducted at room temperature but the yields were poor except in the case of benzaldehyde.[20] When the reaction was conducted at 60 °C, yields were improved drastically but the reaction proceeded to give the dehydrated product (entries 2–6) predominantly except in the case of *p*-nitrobenzaldehyde (entry 1) where the ratio of aldol to α,β-unsaturated product was 1 : 1. In the case of *o*-hydroxybenzaldehyde (entry 8) there was no reaction, while the *p*-hydroxybenzaldehyde (entry 7) showed little activity (< 10%) with the formation of both the aldol and the dehydrated product (1 : 1) (Scheme 1). The inactivity of these compounds may be attributed to the fact that the basic sites present on the

Table 2 Knoevenagel condensation catalysed by MHT[a]

Entry	R¹	R²	Y	Solvent	*t*/h	Yields (%)[b]
1	Ph	H	CN	Toluene	1	100
2	Ph	H	CO_2Et	Toluene	2	50
3	PhCH=CH	H	CN	Toluene	2	87
4	PhCH=CH	H	CO_2Et	DMF	1	61
5	3-MeOC_6H_4	Me	CN	Toluene	1	100
6	3-MeOC_6H_4	Me	CO_2Et	Toluene	4	61
7	2-Furyl	H	CN	Toluene	0.5	100
8	2-Furyl	H	CO_2Et	Toluene	2	100
9	$4\text{-NO}_2C_6H_4$	H	CN	Toluene	1	100
10	$4\text{-NO}_2C_6H_4$	H	CO_2Et	Toluene	2	100
11	2-MeOC_6H_4	H	CN	Toluene	1	96.0[c]
12	2-MeOC_6H_4	H	CO_2Et	Toluene	4	83.0
13	$-cC_5H_{10}-$		CN	Toluene	0.5	100
14	$-cC_5H_{10}-$		CO_2Et	DMF	1	33.3

[a] All reactions were performed on 2 mmol substrate and 2 mmol active methylene compound using 0.05 g of MHT in 10 ml dry toluene at room temperature. [b] ¹H NMR yields based on aldehyde. [c] Isolated yield.



Scheme 1 Aldol condensation between acetone and substituted benzaldehydes

catalyst surface were neutralised by the adsorption of the phenolic moiety which is acidic in nature. All other substrates irrespective of the nature of the substituent present on the phenyl ring shown in Table 1 resulted in good yields in shorter reaction times.

Knoevenagel condensations (Scheme 2) involving various aromatic carbonyl compounds and aliphatic ketone, cyclohexanone with (a) malononitrile and (b) ethyl cyanoacetate as the active methylene compounds were carried out with MHT at room temperature (Table 2). The results are quite impressive, when compared with results reported for solid catalysts requiring vapour phase conditions and longer reaction times, and this present modified hydrotalcite is the first heterogeneous catalyst reported in the literature which perform the reactions at room temperatures in excellent yields. All the reactions proceeded smoothly in toluene with the exception of cinnamaldehyde and cyclohexanone with ethyl cyanoacetate. However, when DMF was used as the solvent, cinnamaldehyde and cyclohexanone condensed affording the corresponding product. The solvent effect established here is in consonance with the results reported by others.[21]

Scheme 2 Knoevenagel condensation of different carbonyl compounds with malononitrile or ethyl cyano acetate

Thus, good yields of aldol and Knoevenagel products can be obtained in heterogeneous catalysis using hydrotalcites provided that the solid is suitably activated. This new solid base catalyst is a practical alternative to soluble bases both in Knoevenagel and aldol reactions in view of the following advantages: (a) high catalytic activity under very mild liquid phase conditions in general for both the reactions described above and specifically at room temperature for the accomplishment of Knoevenagel reactions, (b) easy separation of the catalyst by simple filtration, (c) waste minimisation and (d) possibility of reuse.

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Notes and References

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20 K. Koteswara Rao, M. Gravelle, J. Sanchez and F. Figueras, *J. Catal.*, 1998, **173**, 115; Mg–Al hydrotalcite synthesised with Mg : Al in a ratio of 2.5 was first calcined at 450 °C in a flow of air at the rate of 10 °C min^{-1} to reach 450 °C and maintained for 8 h. The solid was then rehydrated at room temperature under flow of nitrogen gas (6 l h^{-1}), saturated with water vapour for about 6 h and used for the reactions. Reusability of the catalyst: after completion of the reaction, the catalyst was filtered off and then activated in a similar way as fresh catalyst and found to be active for both aldol and Knoevenagel reactions.
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