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# Layered Double Hydroxides-Supported Diisopropylamide: Synthesis, Characterization and Application in Organic Reactions

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**Abstract:** The layered double hydroxides-supported diisopropylamide (LDH-DA) catalyst is found to be an efficient and selective solid base for aldol, Knoevenagel, Henry, Michael, transesterification and epoxidation reactions under liquid phase conditions. LDH-DA is synthesized by the interaction of lithium diisopropylamide with LDH-$NO_3$ (as-synthesized) and calcined LDH-$NO_3$. The LDH-DA (Mg/Al, 3/1) and their precursors are well characterized by using various instrumental techniques such as FT-IR, TGA and DTA, powder XRD, solid state $^{27}$Al MAS NMR spectroscopy, SEM and XPS (ESCA).

**Keywords:** aldol reaction; epoxidation; Henry reaction; Knoevenagel reaction; layered double hydroxides; Michael addition; transesterification

## Introduction

There has been increasing attention on the design and use of environmentally compatible solid acid-base catalysts targeted to minimize the emission of effluents in chemical industries. The challenge is to perform heterogeneous catalytic reactions for C–C or C–O bond formation in the laboratory, bulk and fine chemical industries. The versatile aldol, Knoevenagel, Henry, Michael, epoxidation and transesterification reactions have numerous applications in the elegant syntheses of fine chemicals[1–6] and are classically catalyzed by bases[7–9] such as alkali metal hydroxides, carbonates, bicarbonates, alkoxides, barium and calcium hydroxide, magnesium aluminium ethoxides, potassium-exchanged zirconium phosphate and also organic bases like primary, secondary, tertiary amines[10] in liquid phase systems. At the laboratory scale, many catalysts are known to effect the aldol, Knoevenagel, Henry and Michael reactions, e.g., alumina,[11] sepeolite,[12] zeolites,[13] clays,[14] LDHs,[15] anionic resins,[16] xonotlite/potassium *tert*-butoxide,[17] alkali-containing MCM-41,[18] $AlPO_4$–$Al_2O_3$,[19] alumina-KF[20] and amberlyst.[21] The incorporation of alkali metal cations,[12,18] such as $Cs^+$ or $Na^+$, in zeolites and mesoporous molecular sieves by 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[22] afford strongly basic sites, which catalyze side chain alkylations also. The development of an efficient, selective and recyclable solid base catalyst for the construction of a C–C and C–O bond continues to be a challenging field in organic synthesis.

We believe that the layered double hydroxides (LDHs) or layered double hydroxides-like compounds could be a material of choice for C–C and C–O bond forming reactions in view of their specific properties as underlined.[23] The structure of LDHs consists of brucite [$Mg(OH)_2$] type octahedral layers in which a part of the $M^{II}$ cations are isomorphously substituted by $M^{III}$ cations. The excess positive charge of the octahedral layers resulting from this substitution is compensated by interstitial layers built of anions. These materials are represented by the general formula, $[M^{II}_{(1-x)}\ M^{III}_x(OH)_2]^{x+}$ $[(A^{y-})_{x/y} \cdot n\ H_2O]^{x-}$, where $M^{II}$ and $M^{III}$ are the divalent and trivalent cations, respectively, $A^{n-}$ is the interlayer anion and the value of $x$ is in the range of 0.1 to 0.33. The basicity and activity can be easily tuned up by choosing a set of hetero elements $M^{II}/M^{III}$ and changing their ratio for brucite sheet and/or by incorporating different anions in the interlayer of brucite from a wide range of multiple options.[24] The interesting characteristic of these materials is their anionic exchange ability, which makes them unique inorganic materials for the adsorp-

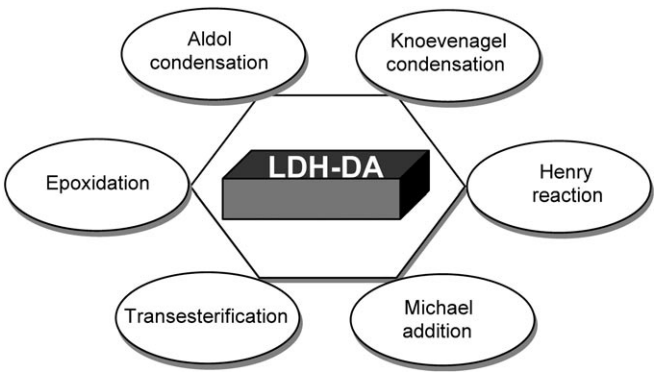
tion of organic and inorganic anions. LDHs are found to be very useful as adsorbents, anion exchangers and most importantly as catalysts.[23] Upon thermal decomposition at about 450 °C, layered double hydroxides are transformed into a highly active homogeneous mixed oxide phase useful for a variety of organic transformations.[25] The rehydrated LDHs[26] composed of Brönsted hydroxide anions displayed superior activity over the LDHs composed of $Cl^-$, $NO_3^-$ or $CO_3^{2-}$ anions or calcined LDHs. Later, we designed and developed LDH-O-*t*-Bu for the first time in our laboratory, as a solid base that displayed manifold activity in various organic reactions.[27] In this article, we have devised a strategy to design, develop and evolve the recyclable LDH-diisopropylamide (LDH-DA) by the interaction of lithium diisopropylamide (LDA) with the uncalcined LDHs (cat. **A)** and calcined LDHs (cat. **B**) that catalyzes C–C and C–O bond forming reactions such as aldol, Knoevenagel, Henry, Michael, epoxidation and transesterification reactions efficiently at ambient temperature (Scheme 1). The LDH-DA and their precursors (Mg/Al, 3/1) were prepared and well characterized by using various instrumental techniques such as FT-IR, TGA and DTA, XRD, solid state $^{27}$Al MAS NMR spectroscopy, SEM and XPS (ESCA).

## Results and Discussion

The catalysts LDH-DA (Mg/Al, 3/1) (hereafter, cat. **A**) using uncalcined LDH-$NO_3$ as a precursor, LDH-DA (hereafter, cat. **B**) (Mg/Al, 3/1) using calcined LDH-$NO_3$ as a precursor were prepared as detailed in the Experimental Section. The LDH-O-*t*-Bu,[27] LDH-OH[26a] and LDH-F[24b] were prepared as reported.

### Applications of LDH-DA in Organic Reactions

Layered double hydroxides composed of Mg/Al (3/1) with different anions (i.e., $OH^-$, $F^-$, $NO_3^-$, *t*-$BuO^-$, diisopropylamide) were evaluated in the aldol reaction of




**Scheme 1.**

**Table 1.** The aldol condensation between *p*-nitrobenzaldehyde and acetone using various LDHs as catalysts.[a]

| Entry | Catalyst | Time [min] | Yield[b] |
|---|---|---|---|
| 1 | LDH-DA (3:1) (cat. **A**) | 30 | 93 |
| 2 | LDH-DA (3:1) (cat. **B**) | 30 | 95 |
| 3 | LDHs (calcined)[c] | 30 | NR[d] |
| 4 | LDH-OH (rehydrated) (cat. **C**) | 60 | 97[e] |
| 5 | LDH-F (cat. **D**) | 30 | NR[d] |
| 6 | LDH-O-*t*-Bu (cat. **E**) | 30 | 91[f] |
| 7 | LDH-$NO_3$ | 60 | NR[d] |

[a] Reaction conditions as exemplified in the Experimental Section.
[b] Isolated yields.
[c] LDH-$NO_3$ was calcined at 450 °C in a flow of air at the rate of 10 °C $min^{-1}$ to reach 450 °C in 6 h.
[d] No reaction
[e] Reaction was carried out in refluxing acetone, only dehydrated product was isolated.
[f] Reaction was carried out at 0 °C.

*p*-nitrobenzaldehyde with acetone at room temperature and the results are summarized in Table 1. LDHs composed of diisopropylamide anion, LDH-DA (3:1) (cat. **A**) (Table 1, entry 1) and LDH-DA (3:1) (cat. **B**) (Table 1, entry 2) showed slightly better activity compared to LDH-O-*t*-Bu (cat. **E**) (Table 1, entry 6). On the other hand, the reactions conducted with other LDHs comprising of anions such as $NO_3^-$, $OH^-$, $F^-$ showed less activity.

The LDH-$NO_3$ precursor for cat. **A** and cat. **B** is essentially inactive for this reaction (Table 1, entries 3 and 7). Surprisingly, there is no reaction with LDH-F (cat. **D**) (Table 1, entry 5) although it is an active catalyst for Michael reactions.[24b]

The catalytic activities of catalysts **A** and **B** were followed with time and the results are presented in graphical form (Figure 1). The initial rate of reaction displayed by the calcined cat. **B** is far superior to that of the uncalcined cat. **A**. Furthermore, cat. **A** required an induction period as can be seen in Figure 1. The slow reaction and delayed response of the cat. **A** may be attributed to the presence of unexchanged nitrate anions which prevent the free access of reactants to the basic sites.

Buoyed with these results that established the superiority of cat. **B**, we further carried out aldol condensations with a variety of substrates in order to extend the scope of the reaction (Scheme 2 and Table 2). The aldol products **3a** were obtained selectively in quantitative yields under mild reaction conditions. These results were quite impressive compared with the earlier reports, wherein the corresponding unsaturated carbonyl compounds **3b** are the major products.

It is worthy of mention here that the reaction between *p*-nitrobenzaldehyde and acetone resulted in 45% of dehydrated product **3b** at room temperature using LDH-O-*t*-Bu[27] as catalyst. Whereas the use of LDH-DA cat-

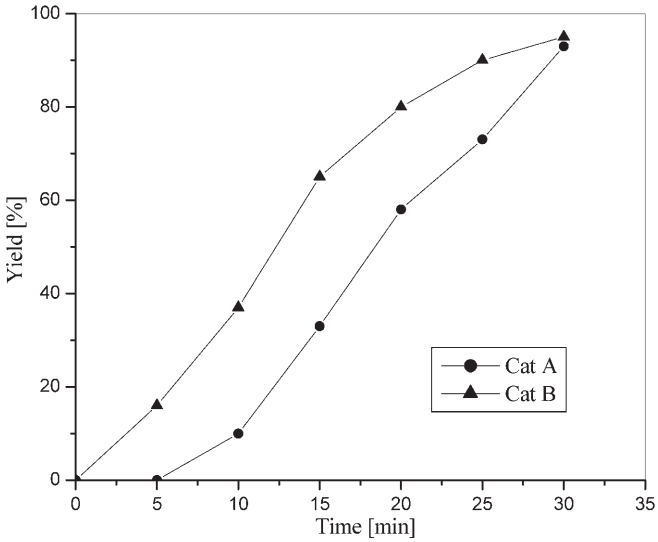
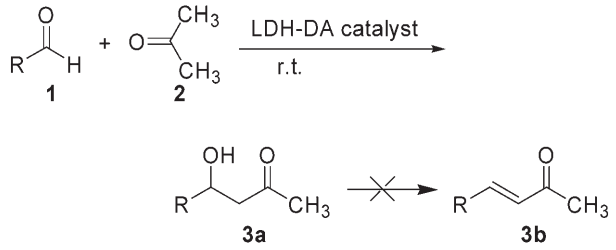



**Figure 1.** Comparison of the catalytic activities of cat. **A** and cat. **B** for the aldol reaction of *p*-nitrobenzaldehyde with acetone.



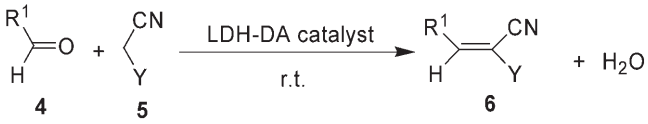

**Scheme 2.** The aldol reaction of between various aldehydes and acetone catalyzed by LDH-DA (cat. **B**).

alyst gave 95% isolated yield of the aldol product (Table 2, entry 2) with 100% selectivity, these data clearly indicate that the LDH-DA has its own merit in terms of selectivity and yield over LDH-O-*t*-Bu in the case of aldol reactions.

The interaction of layered double hydroxide with diisopropylamide anions increases the activity many times since the Claisen–Schmidt condensation of benzaldehyde and acetone, which affords about 90% yield of aldol product in 3 h on a layered double hydroxide first calcined, then rehydrated, is now achieved with a similar efficiency in about 30 min. This increase in activity is indicative of a deep modification of the basic properties of the solid accentuated by incorporation of the diisopropylamide anion. The presence of diisopropylamide anion in the used catalyst was confirmed by elemental analysis and FT IR, which indicates the strong binding of the diisopropylamide anion onto the solid LDHs support.

Knoevenagel condensations involving various aromatic carbonyl compounds with (a) malononitrile and (b) ethyl cyanoacetate (Scheme 3) as the active methylene compounds were carried out with cat. **B** at room temperature (Table 3). The aromatic aldehydes readily condensed with malononitrile, while with ethyl cyanoacetate, the reaction is slightly slower. This may be attributed to the fact that abstraction of a proton from the active methylene group of ethyl cyanoacetate is more difficult due to the lower acidity. All the reactions proceeded smoothly in DMF.

As can be seen from Table 3, all the reactions proceeded selectively to the dehydrated products without any side reaction. No self-condensation, Cannizaro products or hydrated products of Knoevenagel adducts were obtained. The reaction between benzaldehyde and ethyl cyanoacetate in the presence of cat. **B** (Table 3, entry 2) gave selectively the Knoevenagel adduct while the same reaction promoted by an alkali metal-containing MCM-41 yielded a mixture of hydrated and dehydrated products. The xonotlite-*tert*-butoxide catalyst fails to in-




**Scheme 3.** The Knoevenagel reaction between various aldehydes and active methylene compounds catalyzed by LDH-DA (cat. **B**).

**Table 2.** Aldol condensations catalyzed by LDH-DA (cat. **B**).

| Entry | R in **1** | Time [min] | Conversion [%][a] | Yield [%][b] of **3a** |
|---|---|---|---|---|
| 1 | $C_6H_5$ | 30 | 100 | 95 |
| 2 | 4-$NO_2$-$C_6H_4$ | 30 | 100 | 95, 80[c] |
| 3 | 3-$NO_2$-$C_6H_4$ | 30 | 100 | 97 |
| 4 | 4-MeO-$C_6H_4$ | 40 | 90 | 88 |
| 5 | 2-MeO-$C_6H_4$ | 30 | 100 | 93 |
| 6 | 3-MeO-$C_6H_4$ | 30 | 100 | 97 |
| 7 | 3,4,5-MeO-$C_6H_4$ | 30 | 100 | 92 |
| 8 | 4-Cl-$C_6H_4$ | 45 | 100 | 93 |

[a] Reaction conditions as exemplified in the Experimental Section, conversions based on $^1$H NMR spectroscopic integration.
[b] Isolated yields.
[c] Yield after 5$^{th}$ cycle.

**Table 3.** Knoevenagel condensation catalyzed by LDH-DA (cat. **B**).[a]

| Entry | $R^1$ in **4** | Y in **5** | Time [h] | Yield [%] of **6** |
|---|---|---|---|---|
| 1 | $C_6H_5$ | CN | 0.5 | 98 |
| 2 | $C_6H_5$ | $CO_2Et$ | 2.0 | 95 |
| 3 | 4-MeO-$C_6H_4$ | CN | 0.5 | 70 |
| 4 | 4-MeO-$C_6H_4$ | $CO_2Et$ | 1.5 | 60 |
| 5 | 4-Cl-$C_6H_4$ | CN | 0.5 | 98 |
| 6 | 4-Cl-$C_6H_4$ | $CO_2Et$ | 0.5 | 90 |
| 7 | 2-furyl | CN | 0.25 | 98 |
| 8 | 2-furyl | $CO_2Et$ | 0.5 | 98 |
| 9 | 4-$NO_2$-$C_6H_4$ | CN | 0.5 | 98, 90[b] |
| 10 | 4-$NO_2$-$C_6H_4$ | $CO_2Et$ | 0.5 | 98 |
| 11 | 2-MeO-$C_6H_4$ | CN | 0.25 | 98 |
| 12 | 2-MeO-$C_6H_4$ | $CO_2Et$ | 0.25 | 98 |

[a] Reaction conditions as exemplified in the Experimental Section.
[b] Yield after 4th cycle.

**Table 4.** Henry reactions between nitromethane and various aldehydes catalyzed by LDH-DA (cat. **B**).[a]

| Entry | R in **7** | Time [h] | Yield [%][b] of **9a** |
|---|---|---|---|
| 1 | $C_6H_5$ | 1.0 | 98 |
| 2 | 2-furyl | 1.0 | 98 |
| 3 | 4-$NO_2$-$C_6H_4$ | 0.5 | 98, 85[c] |
| 4 | $(CH_3)_2CH_2$ | 1.0 | 95 |
| 5 | 2-MeO-$C_6H_4$ | 0.5 | 98 |
| 6 | 3-$NO_2$-$C_6H_4$ | 0.5 | 98 |
| 7 | 4-Br-$C_6H_4$ | 0.5 | 98 |

[a] Reaction conditions as exemplified in Experimental Section.
[b] Determined by $^1$H NMR spectroscopic integration, based on aldehyde.
[c] Yield after 4th cycle.

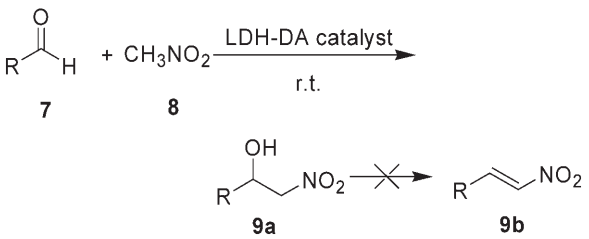
itiate the condensation of furfuraldehyde with malononitrile (Table 3, entry 7). However, the use of untreated xonotlite led to moderate yields of the adduct after a longer reaction time. The Knoevenagel condensation of furfuraldehyde in the presence of $AlPO_4$-$Al_2O_3$ catalyst required a large amount of catalyst and afforded poor yields of adducts. In contrast to all of the above mentioned methodologies, the cat. **B** is very effective for the said reaction, involving a small amount of the catalyst and a much faster rate, *viz.* 15 min.

The superior activity of the catalyst, cat. **B**, in comparison with the catalysts previously described for Knoevenagel reaction is well established as is evident from Table 3.

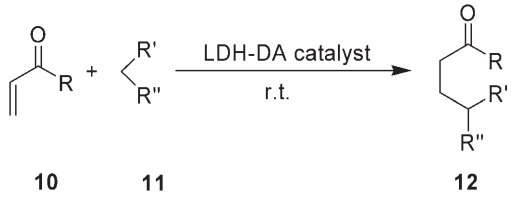
The Henry reaction (Scheme 4) represents one of the classical C–C bond forming processes and the products of the Henry reaction, 2-nitroalkanols, **9a**, have been used extensively in syntheses of insecticides, fungicides and pharmacologically active substances.[4,28] Careful control of the basicity of the reaction medium is crucial for achieving better yields of β-nitro alcohols and such efforts demand longer reaction times with moderate yields. The significance of 2-nitroalkanols in organic synthesis and our continued interest involving LDHs prompted us to explore the Henry reaction using cat. **B**. Herein, we present a convenient and selective synthesis of 2-nitroalkanols *via* the Henry reaction affording 100% selectivity to β-nitro alcohols **9a** in quantitative yields using cat. **B**. The results of Henry reaction with cat. **B** are given in Table 4. No dehydrated product **9b** was observed even after continuing the reaction for prolonged period when we deliberately used aryl aldehydes **7** as one of the reactants.

The Michael reactions (Scheme 5) have numerous applications in the elegant synthesis of fine chemicals. Results of Michael addition reactions are compiled in Table 5. Cat. **B** was found to be an efficient and selective catalyst for 1,4 addition. Several structurally varying donors **10** such as diethyl malonate, nitromethane, dimethyl malonate and ethyl acetoacetate underwent clean and remarkably fast Michael addition with a variety of acceptors **11** including cyclopentenone, chalcones and substituted chalcones to afford he corresponding Michael adducts **12**.

The Michael addition of nitroalkanes is a convenient method for the preparation of a number of useful synthetic intermediates, since the nitro group can be transformed into various functionalities (Table 5, entry 1). The Michael addition of cyclic enones (Table 5, entry 5) with malonic ester was performed to demonstrate the versatility of the method with acceptors other than the usual Michael acceptors such as methyl vinyl ketone or acrylic esters. Excellent yields of adducts were obtained.



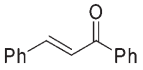
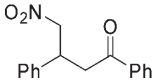
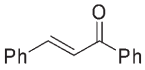
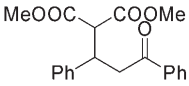
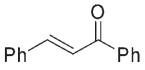
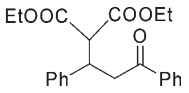
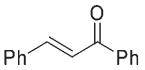
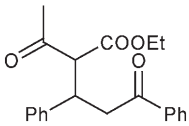
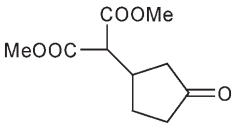
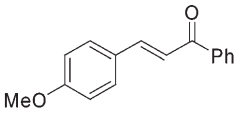
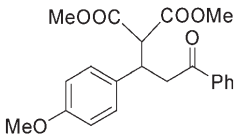
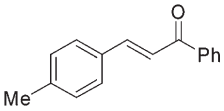
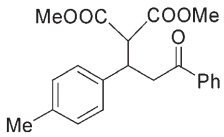

**Scheme 4.** The Henry reaction between various aldehydes and active nitroalkanes catalyzed by LDH-DA (cat. **B**).




**Scheme 5.** The Michael addition reaction catalyzed by LDH-DA (cat. **B**).

**Table 5.** Michael additions catalyzed by LDH-DA (cat. **B**).[a]

| Entry | Acceptor **10** | Donor **11** | Product **12** | Time [h] | Yield[b][%] |
|---|---|---|---|---|---|
| 1 |  | $CH_3NO_2$ |  | 3 | 93, 75[c] |
| 2 |  | DMM[d] |  | 4 | 98 |
| 3 |  | DEM[e] |  | 7, 48[f] | 98, 75[f] |
| 4 |  | EAA[g] |  | 7 | 88 |
| 5 |  | DMM |  | 24 | 98 |
| 6 |  | DMM |  | 24 | 98 |
| 7 |  | DMM |  | 24 | 98 |

[a] Reaction conditions as exemplified in Experimental Section.
[b] Isolated yield.
[c] Yield after 4th cycle.
[d] Dimethyl malonate.
[e] Diethyl malonate.
[f] Using potassium *tert*-butoxide on xonotlite as catalyst.
[g] Ethyl acetoacetate.

The recently reported rehydrated LDHs[29] show several disadvantages in the Michael additions such as high catalyst loading, longer reaction times and limited scope of utility (activating only the methylene group flanked by at least one electron-withdrawing nitrile group), when compared with the present method using cat. **B**. The base strength derived from Brönsted hydroxy anions intercalated in the rehydrated LDHs catalyst is not adequate to abstract a proton from the active methylene group of compounds such as dimethyl malonate, diethyl malonate and ethyl acetoacetate and, consequently, there is no reaction with these substrates. In contrast, in the case of cat. **B**, the diisopropylamide anions are sufficiently strongly basic to deprotonate even weakly activated methylene groups to facilitate Michael reactions.

Transesterification is an important organic transformation and provides essential synthons for a number of complex natural products, pheromones and additives for paints.[30] Although solid acids, such as clays, zeolites, alumina oxides, are widely explored, only LDHs in the class of solid bases are reported to give higher yields in transesterification reactions[31] at elevated temperatures or pressures or both.

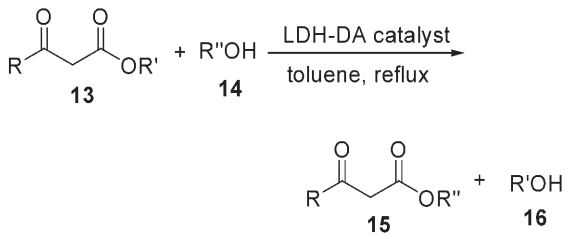
The transesterification of β-keto esters was carried out with a variety of primary, unsaturated, allylic, aromatic and hindered alcohols for the first time in excellent yields with cat. **B** at faster reaction rates (Scheme 6). β-Keto esters were successfully transformed into synthetically useful esters. Transesterification of allylic alcohols is difficult since the product readily undergoes decarboxylative rearrangement, i.e., Caroll rearrangement.[32] With our catalytic system, unsaturated alcohols, such as cinnamyl and propargyl alcohols, underwent transesterification affording esters in high yields (Table 6, entries 1 and 7). Long-chain primary alcohols un-

**Table 6.** Transesterification reactions catalyzed by LDH-DA (cat. **B**).[a]

| Entry | Ester **13** | Alcohol **14** | Time [h] | Yield[%][b] **15** |
|---|---|---|---|---|
| 1 | Methyl acetoacetate | Cinnamyl alcohol | 5 | 93, 85[c] |
| 2 | Ethyl acetoacetate | 1-Pentanol | 5 | 95 |
| 3 | Ethyl acetoacetate | 1-Decanol | 5 | 81 |
| 4 | Methyl acetoacetate | 1-Decanol | 5 | 81 |
| 5 | Ethyl acetoacetate | 1-Octanol | 5 | 85 |
| 6 | Methyl acetoacetate | 1-Octanol | 5 | 85 |
| 7 | Methyl acetoacetate | Propargyl alcohol | 5 | 92 |
| 8 | Ethyl acetoacetate | Benzyl alcohol | 5 | 88 |
| 9 | Ethyl acetoacetate | Phenol | 2.5 | 60 |

[a] Reaction conditions as exemplified in Experimental Section.
[b] Isolated yields.
[c] Yield after 5th cycle.

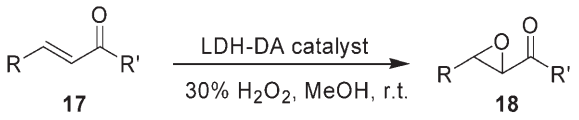



**Scheme 6.** The transesterification reactions catalyzed by LDH-DA (cat. **B**).

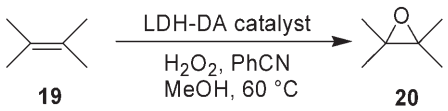
derwent transesterification affording the corresponding esters of commercial use (entries 5 and 6) in high yield in shorter durations.

Epoxides are versatile building blocks for organic synthesis.[33] LDHs as synthesized, calcined, and LDH-O-*t*-Bu samples have been probed for the epoxidation of unfunctionalized and electron-deficient olefins, respectively, and found to be active.[27b]

In the present endeavors, we describe the epoxidation of unfunctionalized as well as electron-deficient olefins by employing cat. **B** as a solid-base catalyst and using hydrogen peroxide as an oxidant under a set of different conditions as described in Schemes 7 and 8. The results of epoxidation of α,β-unsaturated ketones catalyzed by




**Scheme 7.** Epoxidation of electron-deficient olefins catalyzed by LDH-DA using aqueous hydrogen peroxide (cat. **B**).




**Scheme 8.** Epoxidation of unfunctionalized olefins catalyzed by LDH-DA (cat. **B**) using aqueous hydrogen peroxide.

LDH-DA (cat. **B**) and calcined LDHs are compiled in Table 7. Cat. **B** displayed excellent activity over simple calcined LDHs in the epoxidation of chalcone (Table 7, entry 1).[27b] Chalcones with electron-withdrawing or electron-donating groups are epoxidized in quantitative yields. Under the conditions mentioned in Scheme 7, the epoxidation of unfunctionalized olefins remained unsuccessful. The use of benzonitrile, which gives peroxycarboximidic acid[34] by the interaction of hydrogen peroxide, however, promoted the epoxidation reaction of unfunctionalized olefins with cat. **B** (Table 8). The results with cat. **B** are compared with those from the LDH carbonates of Kaneda et al.[35] in Table 8. Cat. **B** showed excellent activity over the best LDHs (Table 8, entry 7). The epoxidation of terminal olefins to racemic epoxides in excellent yields is noteworthy and assumes further significance since value added optically pure epoxides and 1,2-diols could be easily obtained from the racemic epoxides through kinetic resolution.[33]

### Recyclabilty

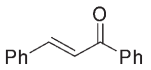
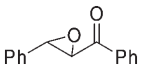
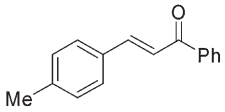
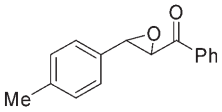
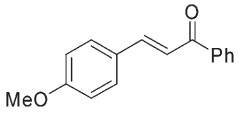
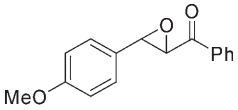
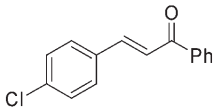
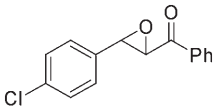
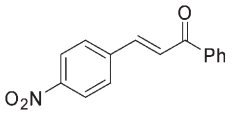
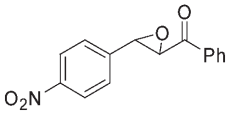
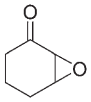
The catalyst was reused for 4 to 5 cycles in each of the aldol, Knoevenagel, Henry, Michael, transesterification and epoxidation reactions and the results are presented in parenthesis in Tables 2–8 and in Figure 2 for a selected substrate. As can be seen in Figure 2, the catalyst displays good recyclability, which is better than LDH-O-*t*-Bu. The loss of the activity at the end of 4/5 cycles is in the range 8 to 12% in the above reactions. A small decrease in activity is attributed to the loss of the catalyst in each cycle and blocking of some of the basic sites by residual organics.[27d]

## Conclusions

Thus, we have developed a recyclable LDH-DA catalyst with compatible basic sites for C–C and C–O bond forming reactions such as the aldol, Henry, Knoevenagel,

**Table 7.** The epoxidation of electron-deficient alkenes by LDH-DA Cat **B**[a]

| Entry | Substrate **17** | Time [min] | Product **18** | Yield [%][b] |
|---|---|---|---|---|
| 1 |  | 50, 10[c] |  | 98, 93,[c] 97,[d] 85[e] |
| 2 |  | 50 |  | 98 |
| 3 |  | 45 |  | 95 |
| 4 |  | 55 |  | 98 |
| 5 |  | 55 |  | 98 |
| 6 |  | 55 |  | 95 |

[a] Reaction conditions as exemplified in Experimental Section.
[b] Isolated yields.
[c] Yield with LDH-O-*t*-Bu.
[d] Yield after 24 h with 0.150 g of calcined LDHs.
[e] Yield after 4$^{th}$ cycle.

Michael, epoxidation and transesterification reactions that operates efficiently at ambient temperature and finds wide applications both in laboratory and industry for the preparation of aldols, α,β-unsaturated nitriles, esters, β-nitroalkanols, substituted esters, epoxides and transesterified products.

## Experimental Section

### General Remarks

$Mg(NO_3)_2 \cdot 6\,H_2O$, $Al(NO_3)_3 \cdot 9\,H_2O$, NaOH, LDA and all other substrates were purchased from Aldrich or Fluka and were used as such. All the other solvents (HPLC grade, otherwise stated) and chemicals were obtained from commercial sources and used as such without further purification. Tetrahydrofuran (THF) was freshly distilled from sodium/benzophenone prior to use. All the reactions were conducted under a nitrogen atmosphere. The preparation of catalyst was performed under a nitrogen atmosphere in a glove box. Proton nuclear magnetic resonance ($^1$H NMR) spectra were recorded on a Varian Gemini at 200 MHz, as solutions in $CDCl_3$ at 25 °C, δ values are given in ppm downfield from tetramethylsilane (TMS). Mass spectra were obtained at an ionization potential of 70 eV, scanned on a VG 70–70H (micro mass). Infrared spectra were recorded on a Nicolet 740 FT-IR spectrometer either as neat liquids or KBr pellets. Thin layer chromatography was performed on silica gel 60$F_{254}$ plates procured from E. Merck. ACME silica gel (60–120 mesh) was used for column chromatography.

### Preparation of Catalysts

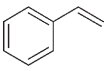
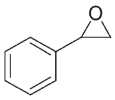
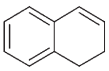
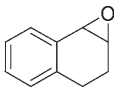
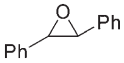
The preparation of LDH-$NO_3$ (Mg/Al, 3/1) was based on a literature procedure.[23] The LDH-$NO_3$ catalyst was prepared in a nitrogen atmosphere to avoid carbonation in air. $Mg(NO_3)_2 \cdot 6\,H_2O$ (30.8 g, 0.12 mol) and $Al(NO_3)_3 \cdot 9\,H_2O$ (15.0 g, 0.04 mol) were dissolved in deionized and decarbonated water (100 mL). The pH of the solution was adjusted to 10 by the addition of NaOH (2 M). The slurry was stirred for 2 h at room temperature, filtered and then dried under vacuum at 80 °C.

### LDH-DA (cat. A)

LDH-DA was prepared from uncalcined LDH-$NO_3$. LDH-$NO_3$ (1.214 g) was added to a solution of lithium diisopropylamide (LDA) (0.1 M) prepared by dissolving lithium diisopropylamide (1.07 g, 10 mmol) in freshly dried THF (100 mL). The solution was stirred for 24 h at room temperature in nitrogen atmosphere and then filtered under nitrogen. A white solid, LDH-DA (1.412 g) was obtained. The DA content on LDH was found to be 7.1% as indicated by elemental analysis. All the catalysts were well dried under vacuum.

**Table 8.** The epoxidation of various unfunctionalized olefins catalyzed by LDH-DA Cat. **B**.[a]

| Entry | Substrate **19** | Time [h] | Product **20** | Yield [%][b] |
|---|---|---|---|---|
| 1 |  | 2.0 |  | 98, 90[d] |
| 2 |  | 1.5 |  | 83 |
| 3 |  | 2.0 |  | 90 |
| 4 |  | 1.5 |  | 98 |
| 5 |  | 1.5 |  | 90 |
| 6 |  | 1.5 |  | 91 |
| 7 |  | 1.5, 24[c] |  | 90, 95[c] |

[a] Reaction conditions as exemplified in Experimental Section.
[b] Isolated yields.
[c] Reaction conducted with LDHs carbonate using 0.050 g of catalyst.[35]
[d] Yield after 4th cycle.

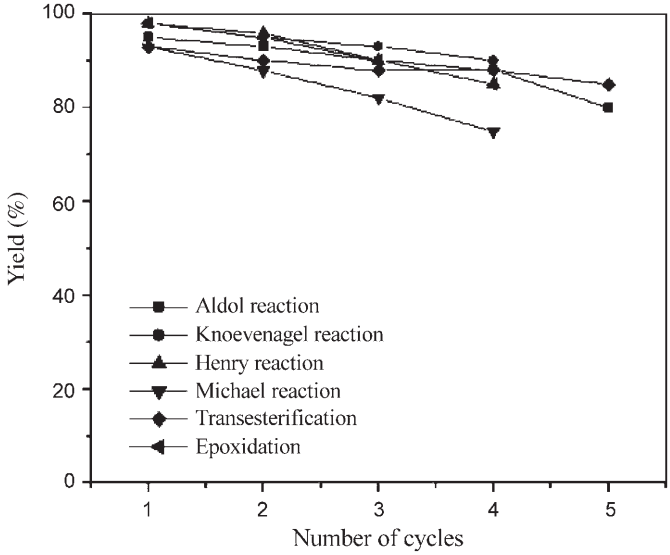



**Figure 2.**

## LDH-DA using Calcined LDH-$NO_3$ (cat. B)

LDH-$NO_3$ (Mg/Al, 3/1) was calcined at 450 °C in a flow of air for 6 h (temperature raised at 10 °C/min) and cooled to room temperature in a flow of dry nitrogen to obtain calcined LDHs. Calcined LDHs (1.214 g) was added to a solution of lithium diisopropylamide (0.1 M) prepared by dissolving lithium diisopropylamide (LDA) (1.07 g, 10 mmol) in freshly dried THF (100 mL). The solution was stirred for 24 h at room temperature in a nitrogen atmosphere and then filtered under nitrogen. A white solid, LDH-DA (1.732 g) was obtained, which was washed with excess of THF. The DA content on LDH was found to be 7.5% as indicated by elemental analysis.

The LDH-OH (cat. **C**) catalyst was obtained using a reported procedure.[26]

The LDH-F (cat. **D**) catalyst was obtained using a reported procedure.[24b]

## General Procedure for Aldol Reaction

A two-necked flask was charged with 4-nitrobenzaldehyde (2 mmol), 50 mg of cat. **B**, 5 mL of acetone and the contents were stirred at room temperature. After the completion of reaction, as monitored by thin layer chromatography (TLC), the catalyst was filtered and filtrate was concentrated under reduced pressure. The crude product was purified by column chromatography.

## Typical Procedure for Recycle Studies

The reusability of the catalyst was carried out with 4-nitrobenzaldehyde and acetone by adopting the following protocol under similar experimental conditions as described above. After the completion of reaction, the catalyst was allowed to settle and the supernatant solution was pumped out from the reaction flask. Fresh quantities of 4-nitrobenzaldehyde and acetone were introduced under nitrogen atmosphere. The cat. **B** was used for 4 cycles with consistent activity.

## General Procedure for Knoevenagel Condensation

Aldehyde (2 mmol) and 0.05 g of cat. **B** were stirred in 5 mL of dimethylformamide for 5 min. Then the active methylene compound (2 mmol) was added and stirring was continued at room temperature until the completion of the reaction, as monitored by thin layer chromatography (TLC). The catalyst was filtered and the product was extracted with ethyl acetate, dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude product was purified by column chromatography.

## General Procedure for Henry reaction

To a mixture of nitroalkane (10 mmol), and benzaldehyde (2 mmol), 0.03 g of cat. **B** was added at room temperature and stirred till completion of the reaction, as monitored by TLC. The catalyst was filtered and washed with dichloromethane (3 × 10 mL). Then, the filtrate was concentrated under reduced pressure to obtain the product. The crude product was purified by column chromatography.

### General Procedure for Transesterification Reaction

In a two-necked, round-bottomed flask, 1 mmol of ester, 1 mmol of alcohol and 0.025 g of cat. **B** in 10 mL dry toluene were stirred at 90–100 °C and reaction was monitored by thin layer chromatography (TLC). Work-up consisted of simple filtration followed by concentration of the filtrate under reduced pressure. The crude product was purified by column chromatography.

### General Procedure for the Epoxidation of Functionalized Olefins

1 mmol of enone and 0.03 g of cat. **B** were taken in 10 mL of methanol in a 50-mL, two-necked, round-bottomed flask. To this solution, 0.35 mL (3 mmol) of aqueous hydrogen peroxide (30% w/w) were added slowly at room temperature under continuous stirring. The reaction was monitored by thin layer chromatography (TLC) until the completion, the solid was separated by filtration and washed with diethyl ether. The solution was evaporated, the residue was redissolved in dichloromethane, dried over sodium sulfate, and the solvent was concentrated under reduced pressure to obtain the crude product. The crude product was subjected to chromatography using a mixture of *n*-hexane-EtOAc (40:1, v/v) as an eluent to afford the pure product.

### General Procedure for the Epoxidation of Unfunctionalized Olefins

Into a round-bottomed flask with a reflux condenser were successively placed 0.03 g of cat. **B**, 10 mL of methanol, 4 mmol of alkene, 1.0 mL of benzonitrile (10.5 mmol) and 2.4 mL of 30% hydrogen peroxide. The resulting mixture was stirred at 60 °C and monitored by thin layer chromatography. After the completion of reaction, the LDHs was separated by filtration and filtrate was treated with $MnO_2$ (0.03 g) to decompose the remaining $H_2O_2$. The filtrate was diluted with deionized water (20 mL) and extracted with $CHCl_3$ ($3 \times 20$ mL). The extract was concentrated under reduced pressure and subjected to chromatography using a mixture of *n*-hexane-EtOAc (40:1, v/v) as eluent to afford the pure product.

### General Procedure for Michael Reaction

The acceptor (2 mmol) and 0.05 g of cat. **B** were stirred in 10 mL of methanol for 5 min, then the donor (2 mmol) was added and stirring was continued until the completion of the reaction which was 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.

All the products gave satisfactory $^1$H NMR, mass and IR data as compared to previously reported spectra.

### Supporting Information

Detailed characterization (powder XRD, SEM, TGA-DTA, FT-IR, $^{27}$Al MAS NMR, and XPS) data of the LDH-DA (cat. **A**, cat. **B** and their precursors) catalysts and general instrumental conditions.

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## References

[1] a) B. M. Trost, *Comprehensive Organic Synthesis*, Pergamon, Oxford, **1991**, *2*, 133; b) J. H. Clark, *Chem. Rev.* **1980**, *80,* 429.
[2] a) S. Ganesh, A. Sarkar, *Tetrahedron Lett.* **1991**, *32,* 1085; b) S. Machida, Y. Hashimoto, K. Saigo, J. Inoue, M. Hasegawa, *Tetrahedron* **1991**, *47,* 3737.
[3] A. W. A. Brown, D. B. W. Robinson, H. Hurtig, B. J. Wenner, *Can. J. Res.* **1948**, *26D,* 177.
[4] P. W. Brian, J. F. Grove, J. C. McGowan, *Nature* **1946**, *158,* 876.
[5] A. G. M. Barrett, G. G. Graboski, *Chem. Rev.* **1986**, *86,* 751.
[6] A. G. M. Barrett, *Chem. Soc. Rev.* **1991**, *20,* 95.
[7] a) E. Knoevenagel, *Ber. dtsch. chem. Ges.* **1894**, *27,* 2345; b) G. Jones, *Org. React.* **1967**, *15,* 204.
[8] a) E. D. Bergmann, D. Ginsburg, R. Pappo. *Org. React.* **1959**, *10,* 179; b) D. A. Oare, C. H. Heathcock, *Topics in Stereochemistry*, (Eds.: E. L. Eliel, S. H. Willen), Wiley, New York, **1989**, Vol. *19*, p 277.
[9] a) M. B. Smith, J. March, *Advanced Organic Chem*istry, 5th edn., J. Wiley & Sons, New Yorkl, **2001**, p 486, p 1024, p 1053, p 1218, p 1225; b) C. H. Heathcock, *Comprehensive Organic Synthesis*, (Ed.: B. M. Trost), Pergmon Press, Oxford, **1991**, Vol. *2*, p 341.
[10] G. Rosini, in: *Comprehensive Organic Synthesis*, Vol. 2, (Eds.: C. H. Heathocock, B. M. Trost, I. Fleming), Chapter 1.10, Pergamon Press, Oxford, **1991**, p 321, and references cited therein.
[11] a) J. Muzart, *Synth. Commun*. **1985**, *15,* 285; b) J. Muzart, *Synthesis* **1982**, 60.
[12] A. Corma, R. M. Martin-Aranda, *J. Catal*. **1991**, *130,* 130.
[13] A. Corma, V. Fornes, R. M. Martin-Aranda, A. Garcia, J. Primo, *Appl. Catal.* **1990**, *59*, 237.
[14] Y. V. Subba Rao, B. M. Choudary, *Synth. Commun.* **1991**, *21,* 1163.
[15] a) J. M. Climent, A. Corma, S. Iborra, J. Primo, *J. Catal.* **1995**, *60,* 151; b) D. Tichit, M. H. Lhouty, A. Guida, B. H. Chiche, F. Figueras, A. Auroux, D. Bartalini, E. Garronne, *J. Catal.* **1995**, *50,* 151.
[16] W. Richardhein, J. Melvin, *J. Org. Chem.* **1961**, *26,* 4874.
[17] S. Chalais, P. Laszlo, A. Mathy, *Tetrahedron Lett.* **1985**, *26,* 4453.

  

[18] K. R. Kloetstra, H. Van Bekkum, *J. Chem. Soc. Chem. Commun*. **1995**, 1005.
[19] J. A. Cabello, J. M. Campelo, A. Garcia, D. Luna, J. M. Marinas, *J. Org. Chem.* **1984**, *49,* 5195.
[20] J. M. Melot, F. Texier- Boullet, A. Foucaud, *Tetrahedron Lett.* **1986**, *27,* 493.
[21] R. Ballini, G. Bosica, P. Forconi, *Tetrahedron* **1996**, *52,* 1677.
[22] L. Martens, P. Grobet, P. A. Jocobs, *Nature* **1985**, *315,* 568.
[23] a) F. Cavani, F. Trifiro, A. Vaccari, *Catal. Today* **1991**, *11,* 173; b) F. Trifiro, A. Vaccari, in: *Comprehensive Supramolecular Chemistry*, Vol. 7, (Eds.: G. Alberti, T. Bein), Pergmon Press, Oxford, **1996**, p 251; c) B. Sels, D. De Vos, M. Buntinx, F. Pierard, A Kirsch-De Mesmaeker, P. Jacobs, *Nature* **1999**, *400,* 855; d) B. M. Choudary, M. Lakshmi Kantam, A. Rahman, Ch. Venkat Reddy, K. K. Rao, *Angew. Chem. Int. Ed.* **2001**, *40,* 763; e) T. Matsushita, K. Ebitani, K. Kaneda, *Chem. Commun*. **1999**, 265; f) M. Ballabeni, R. Ballini, G. Bigi, R. Maggi, M. Parrini, G. Predieri, G. Satori, *J. Org. Chem.* **1999**, *64,* 1029; g) B. M. Choudary, N. S. Chowdari, M. Sateesh, M. Lakshmi Kantam, *Angew. Chem. Ed.* **2001**, *40,* 4620; h) R. K. Allada, A. Navrotsky, H. T. Berbeco, W. H. Casey, *Science* **2002**, *296,* 721; i) B. F. Sels, D. De Vos, P. A. Jacobs, *Catal. Rev.* **2001**, *43*, 443; j) F. Prinetto, M. Manzoli, G. Ghiotti, M. J. M. Ortiz, D. Tichit, B. Coq, *J. Catal*. **2004**, *222*, 238; k) K. Motokura, D. Nishimura, K. Mori, T. Mizugaki, K. Ebitani, K. Kaneda, *J. Am. Chem. Soc.* **2004**, *126,* 5662; l) F. Winter, V. Koot, A. J. van Dillen, J. W. Geus, K. P. de Jong, *J. Catal.* **2005**, *236,* 91; m) F. Ahmed Khan, Nilam Sahu, *J. Catal*. **2005**, *231,* 438; n) F. Wypych, A. Bail, M. Halma, S. Nakagaki, *J. Catal*. **2005**, *234*, 431; o) S. Abell, F. Medina, D. Tichit, J. P.-Ramírez, J. C. Groen, J. E. Sueiras, P. Salagre, Y. Cesteros, *Chem. Eur. J.* **2005**, *11*, 728; p) F. Winter, A. Jos van Dillen, K. P. de Jong, *Chem. Commun*. **2005**, 3977; q) S. Abell, F. Medina, D. Tichit, J. Perez-Ramirez, X. Rodriguez, J. E. Sueiras, P. Salagre, Y. Cesteros, *Appl. Catal. A. General*. **2005**, *281*, 191.
[24] a) V. Prevot, C. Forano, J. P. Besse, *J. Mater. Chem.* **1999**, *9,* 155; b) B. M. Choudary, M. Lakshmi Kantam, V. Neeraja, K. K. Rao, F. Figueras, L. Delmotte, *Green Chem.* **2001**, *3,* 257.
[25] a) W. T. Reichle, *J. Catal.* **1985**, *94,* 547; b) J. G. Numan, P. B. Himelfarb, R. G. Herman, K. Klier, C. E. Bogdan, G. W. Simmons, *Inorg. Chem.* **1989**, *28,* 3868; c) C. Busetto, G. Delpiero, G. Manara, F. Trifiro, A. Vacarri, *J. Catal.* **1984**, *85,* 260; d) K. Yamaguchi, K. Ebitani, T. Yoshida, H. Yoshida, K. Kaneda, *J. Am. Chem. Soc.* **1999**, *121,* 4526; e) V. J. Bulbule, V. H. Deshpande, S. Velu, A. Sudalai, S. Sivasankar, V. T. Sathe, *Tetrahedron* **1999**, *55,* 9325; f) E. Suzuki, Y. Ono, *Bull. Chem. Soc. Jpn*. **1988**, *61,* 1008; g) E. Suzuki, M. Okamoto, Y. Ono, *J. Mol. Catal.* **1990**, *61,* 283; h) C. Cativiela, F. Figueras, J. I. Garcia, J. A. Mayoral, M. Zurbano, *Synth. Commun.* **1995**, *25,* 1745; i) C. Cativiela, F. Figueras, J. M. Fraile, J. I. Garcia, J. A. Mayoral, *Tetrahedron Lett.* **1995**, *36,* 4125; j) W. T. Reichle, *US Patent* 4,458,026, **1984**; k) A. Corma, V. Fornes, R. M. Martin-Aranda, H. Garcia, J. Primo, *Appl. Catal.* **1990**, *59,* 237.
[26] a) K. K. Rao, M. Gravelle, J. Sanchez, F. Figueras, *J. Catal.* **1998**, *173,* 115; b) M. Lakshmi Kantam, B. M. Choudary, Ch. Venkat Reddy, K. K. Rao, F. Figueras, *J. Chem. Soc. Chem. Commun.* **1998**, 1033; c) B. M. Choudary, M. Lakshmi Kantam, Ch. Venkat Reddy, K. K. Rao, F. Figueras, *Green. Chem*. **1999**, 279; d) P. S. Kumbhar, J. S. Valente, J. Lopez, F. Figueras, *Chem. Commun.* **1998**, 535; e) P. S. Kumbhar, J. S. Valente, F. Figueras, *Chem. Commun*. **1998**, 1091.
[27] a) B. M. Choudary, M. Lakshmi Kantam, B. Kavita, Ch. Venkat Reddy, K. K. Rao, F. Figueras, *Tetrahedron Lett.* **1998**, *39,* 3555; b) B. M. Choudary, M. Lakshmi Kantam, B. Bharathi, Ch. Venkat Reddy, *Synlett* **1998**, 1203 and references cited therein; c) B. M. Choudary, M. Lakshmi Kantam, B. Kavita, Ch. Venkat Reddy, F. Figueras, *Tetrahedron* **2000**, *56,* 9357; d) B. M. Choudary, M. Lakshmi Kantam, Ch. Venkat Reddy, B. Bharathi, F. Figueras, *J. Catal.* **2003**, *218,* 191; e) B. M. Choudary, Ch. Venkat Reddy, B. V. Prakash, B. Bharathi, M. Lakshmi Kantam, *J. Mol. Catal.* **2004**, *217,* 81.
[28] a) A. W. A. Brow, D. B. W. Roninson, H. Hurtig, B. J. Wenner, *Can. J. Res.* **1948**, *26D,* 177; b) F. C. Bocobo, A. C. Curtis, W. B. Block, E. R. Harrell, E. E. Evans, R. F Haines, *Antibiol. Chemother.* **1956**, *6,* 385; c) O. Schales, H. A. Graefe, *J. Am. Chem. Soc.* **1952**, *74,* 4486; d) K. Zeecheng, C. Cheng, *J. Med. Chem.* **1969**, *12*, 157.
[29] B. M. Choudary, M. Lakshmi Kantam, Ch. Venkat Reddy, K. K. Rao, F. Figueras, *J. Mol. Catal.* **1999**, *146,* 279.
[30] J. Otera, *Chem. Rev.* **1993**, *93*, 1449.
[31] D. J. Engel, T. P Malloy, P. K. Nickl, (to UOP), *US Patent* 5,350,879, **1994**.
[32] W. Kamel, A. C. Cope, *J. Am. Chem. Soc.* **1943**, *65,* 355.
[33] M. Tokunaga, J. F. Larrow, F. Kakiuchi, E. N. Jacobsen, *Science* **1997**, *277,* 936.
[34] G. B. Payne, P. H. Deming, P. H. Williams, *J. Org. Chem.* **1961**, *26,* 659.
[35] S. Ueno, K. Yamaguchi, K. Yoshida, K. Ebitani, K. Kaneda. *Chem. Commun*. **1998**, 295.

  