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Synthesis of 2-nitroalkanols by Mg–Al–O-*t*-Bu hydrotalcite[☆]

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Abstract

Henry (nitroaldol) reactions were performed with Mg–Al–O-*t*-Bu hydrotalcite as catalyst in quantitative yields in liquid phase under mild reaction conditions at a faster rate. Exclusive synthesis of 2-nitroalkanols (**3**) is realised by compatible basic sites of Mg–Al–O-*t*-Bu hydrotalcite. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Henry reaction; Mg–Al–O-*t*-Bu hydrotalcite; Nitroaldols; 2-Nitroalkanols; Quantitative yields

1. Introduction

Construction of carbon–carbon bond formation is a premier reaction that finds numerous applications in synthetic organic chemistry. Henry reaction, represents one of the classical C–C bond forming processes and the products of the Henry reaction have been used extensively in syntheses of insecticides [1], fungicides [2,3] and pharmacologically active substances [4,5]. 2-Nitroalkanol is a very important intermediate especially to introduce various functionalities [6–8]. Several classical methods are available for this transformation involving the use of bases such as alkali metal hydroxides, carbonates, bicarbonates, alkoxides, barium and calcium hydroxide, magnesium and aluminium ethoxides, rhodium complex, potassium-exchanged zirconium phosphate and also organic bases like primary, secondary and tertiary amines under homogeneous conditions [9].

These methods suffer from several drawbacks such as use of stoichiometric amounts of reagents, longer

reaction times, tedious work-up procedures, requirement of large amounts of acids to neutralise bases, lack of reusability and in some cases affords condensed olefins [10]. The greatest challenge in the selective synthesis of 2-nitroalkanols in the multiple product options such as aldol olefin and its polymer and Cannizzaro products is the selection of the right type of base.

Heterogeneous catalysis induced by solid catalysts such as basic alumina [11], alumina–KF [12] and Amberlyst [13], and homogeneous phase transfer catalysis with surfactants [14] in bi-phase system, the two divergent approaches being explored are aimed at achieving higher atom selectivity. Solid base catalysts in place of soluble bases offer an eco-friendly process devoid of environmental problems associated with the salts formed on neutralisation of soluble bases [15–20]. Further, these solid base catalysts are tunable and easily separable from the liquid reaction mixture with almost zero emission of effluents.

Layered double hydroxides (LDHs) or hydrotalcite-like compounds (HTLCs) have potential application as adsorbents, anion-exchangers and most importantly as basic catalysts [1,21] for a variety of organic transformations [22–26]. We designed and developed

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Mg–Al–O-*t*-Bu hydrotalcite by the incorporation of *t*-butoxide by exchange process to tune up the hydrotalcite for higher basicity and found it to be excellent for base catalysed aldol and epoxidation reactions [27,28]. The significance of 2-nitroalkanols in organic synthesis and our continued interest on hydrotalcites prompted us to explore the Henry reaction with Mg–Al–O-*t*-Bu hydrotalcite.

2. Experimental

2.1. Preparation of catalyst

2.1.1. Preparation of Mg–Al hydrotalcite nitrates

The reaction was carried out in nitrogen atmosphere to avoid interaction with carbon dioxide in air to prevent formation of hydrotalcite carbonate as an impurity. For this 30.8 g of magnesium nitrate hexahydrate and 15.0 g of aluminium nitrate nonahydrate were dissolved in 100 ml deionised and decarbonated water. The pH of the solution was adjusted to 10 by addition of NaOH (2 M). The slurry was stirred for 2 h under nitrogen at room temperature, then filtered under nitrogen and dried under vacuum at 80°C.

2.1.2. Preparation of Mg–Al–O-*t*-Bu hydrotalcite

Mg–Al–O-*t*-Bu hydrotalcite was obtained by reacting 1.214 g of hydrotalcite nitrate with 0.1 M solution of potassium *t*-butoxide in THF under stirring for 24 h. It was then filtered and washed with THF (3 ml × 75 ml) under nitrogen atmosphere, to give Mg–Al–O-*t*-Bu hydrotalcite as a white solid (1.382 g).

2.2. General reaction procedure

To a mixture of 3 ml nitromethane and 0.280 g of *p*-chlorobenzaldehyde, 0.05 g of catalyst was added at room temperature and stirred till completion

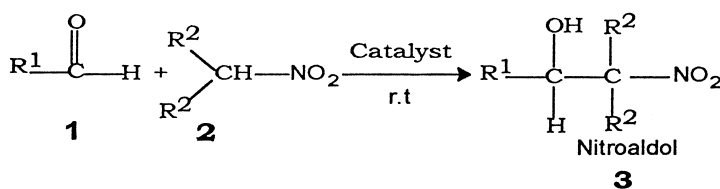
of the reaction, as monitored by TLC. The catalyst was filtered and washed with dichloromethane (3 ml × 10 ml). Then, the filtrate was concentrated under reduced pressure. The crude product was purified by column chromatography (silica gel, 60–120 mesh; hexane/ethylacetate 98/2 v/v). The products were characterised by comparing the ¹H NMR and mass spectrometry data with those reported in the literature [18–20].

A representative example: entry 5, *p*-ClPhCH(OH)-CH₂NO₂ shows ¹H NMR (200 MHz, CDCl₃) δ 2.95 (s, 1H, OH), 4.38–4.52 (m, 2H, CH₂NO₂), 5.40 (m, 1H), 7.40 (m, 5H aromatic); MS (EI, 70 eV) *m/z* (RA) 201 (4), 154 (58), 91 (70), 77 (100) identical to authentic samples. Rest of the products were characterised similarly.

3. Results and discussion

We report here a mild, simple and very convenient heterogeneous method for the selective synthesis of 2-nitroalkanols (**3**) via Henry reaction (Scheme 1), from the reaction of aldehydes and nitroalkanes at room temperature in quantitative yields.

In order to find a suitable base catalyst for the Henry reaction of benzaldehyde with nitromethane, we evaluated variety of solid bases and found Mg–Al–O-*t*-Bu hydrotalcite as the best catalyst in terms of high space-time yield and selectivity. A comparative data of the activity and selectivity of the Mg–Al–O-*t*-Bu hydrotalcite catalyst with a variety of soluble and solid bases such as sodium hydroxide, neutral aluminium oxide, magnesium oxide, diamino-functionalised MCM-41 and rehydrated Mg–Al hydrotalcite is presented in Table 1. Mg–Al–O-*t*-Bu hydrotalcite displayed increased activity by several-fold in terms of space-time yield (STY) over the other catalysts described in Table 1, i.e. an activity 256 times greater



Scheme 1.

Table 1
Henry reaction between benzaldehyde and nitromethane using various base catalysts

Entry	Catalyst	<i>T</i> (h)	Yield (%) ^a	Space time yield ^b
1	Mg–Al–O- <i>t</i> -Bu hydrotalcite	0.25	98 ^c	26.16
2	Aluminium oxide	12.0	37	0.102
3	Magnesium oxide	8.0	51	0.212
4	Sodium hydroxide with PTC	2.0	70 ^d	1.169
5	Diamino-functionalised MCM-41	3.0	97 ^e	1.079
6	Rehydrated Mg–Al hydrotalcite	0.5	95	6.346

^a Determined by ¹H NMR based on starting aldehyde, unless otherwise stated.

^b Space time yield (g) of product obtained per gram of catalyst per hour.

^c Using 50 mg catalyst.

^d Isolated yield, using sodium hydroxide with surfactant.

^e Using diamino-functionalised MCM-41, nitroalkene being the sole product.

than that of aluminium oxide, 123 times the activity of magnesium oxide, 22 times more active than sodium hydroxide with PTC, 24 times the activity displayed by diamino-functionalised MCM-41 and 4 times more active than rehydrated Mg–Al hydrotalcite. Having found to be a superior catalyst, the Mg–Al–O-*t*-Bu hydrotalcite was tested for other Henry reactions involving variety of aldehydes with nitroalkanes. The results of Henry reaction are presented in Table 2. Mg–Al–O-*t*-Bu hydrotalcite preferred the best catalytic methodology in solid base chemistry. No dehydrated product was observed even after continuing the reaction for prolonged period.


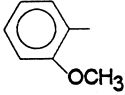
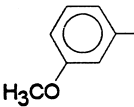
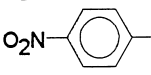
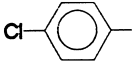

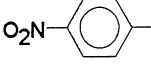

The Henry reaction with Mg–Al–O-*t*-Bu hydrotalcite shows several advantages over the recently reported rehydrated Mg–Al hydrotalcite [29], viz. low catalyst loading, shorter reaction time and activity for secondary nitroalkanes. The basic strength of rehydrated catalyst is not adequate to abstract the proton from secondary nitroalkane, viz. 2-nitro propane and eventually there is no reaction with this substrate. On the other hand, Brönsted hydroxyl anions intercalated in rehydrated hydrotalcite are too sluggish to react with weak acids like 2-nitro propane, whereas in the case of Mg–Al–O-*t*-Bu-hydrotalcite, the *t*-butoxide anions are strongly basic to coax the weakly activated secondary nitroalkanes.

4. Mechanism

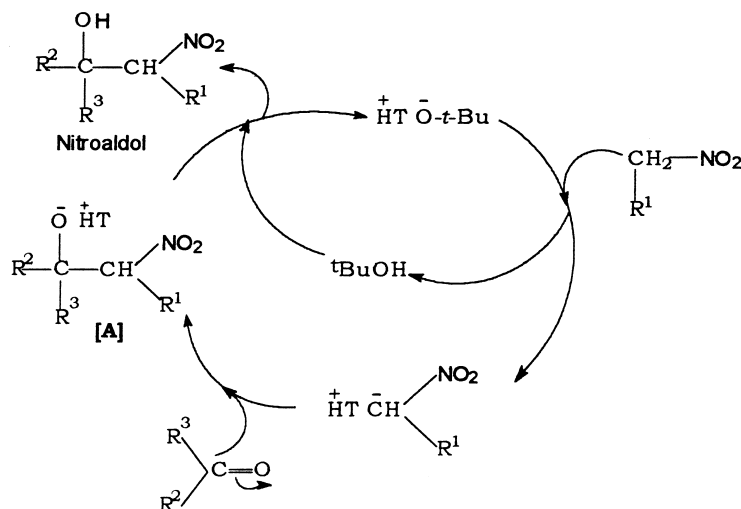
The classical mechanism of the Henry [9] reaction can be applied here. The abstraction of a proton from the active methylene of the nitro compound gives a car-

banion, which can be stabilised by the cationic charge of aluminium in the lattice of hydrotalcite as suggested in Scheme 2. It is proposed that this carbanion further adds to the carbonyl compound to form an intermedi-

Table 2
Henry reactions between aldehydes and nitroalkanes catalysed by Mg–Al–O-*t*-Bu hydrotalcite (Scheme 1)

Entry	R ¹	R ²	<i>T</i>	Yields (%) ^a
1		H	15 min	98
2		H	30 min	96
3		H	60 min	63
4		H	30 min	92
5		H	60 min	95
6	CH ₃ CH ₂ ⁻	H	30 min	92
7	(CH ₃) ₂ CH ₂ ⁻	H	40 min	94
8		H	30 min	73
9	CH ₃ CH ₂ ⁻	CH ₃	2 h	92
10	(CH ₃) ₂ CH ₂ ⁻	CH ₃	2 h	96
11		CH ₃	1.5 h	93
12		CH ₃	2 h	82

^a Determined by ¹H NMR, based on aldehyde.



Scheme 2.

ate **A**, which, in turn, abstracts a proton from *t*-butanol and gives the final nitroaldol product.

5. Conclusion

Thus, compatible basic sites present in Mg–Al–O–*t*-Bu hydrotalcite can coax the selective nitroaldol reaction with excellent yields in shorter times which is superior than the methodologies described earlier. The advantages are: (a) superior catalytic activity under very mild liquid phase conditions; (b) easy separation of the catalyst by simple filtration; (c) excellent yields and 100% selectivity of β -nitroalkanol at faster rates of reaction; (d) reaction involves non-toxic and inexpensive materials; and (e) zero emission of pollutants. The present catalytic system is a potential alternative to soluble bases.

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References

- [1] A.W.A. Brown, D.B.W. Robinson, H. Hurtig, B.J. Wenner, *Can. J. Res.* 26D (1948) 177.
- [2] P.W. Brian, J.F. Grove, J.C. McGowan, *Nature* 158 (1949) 876.
- [3] F.C. Bocobo, A.C. Curtis, W.B. Block, E.R. Harrell, E.E. Evans, R.F. Haines, *Antibiot. Chemother.* 6 (1956) 385.
- [4] O. Schales, H.A. Graefe, *J. Am. Chem. Soc.* 74 (1952) 4486.
- [5] K. Zeecheng, C. Cheng, *J. Med. Chem.* 12 (1969) 157.
- [6] A.G.W. Barrett, G.G. Graboski, *Chem. Rev.* 86 (1986) 751.
- [7] G.W. Kabalka, R.S. Varma, *Org. Prep. Proc. Int.* 19 (1987) 283.
- [8] A.G.W. Barrett, *Chem. Soc., Rev.* 20 (1991) 95.
- [9] G. Rosini, in: C.H. Heathcock, B.M. Trost, I. Fleming (Eds.), *Comprehensive Organic Synthesis*, Vol. 2, Chapter 1.10, Pergamon Press, Oxford, 1991, p. 321, and references cited therein.
- [10] R. Ballini, R. Castagnani, M. Petrini, *J. Org. Chem.* 57 (1992) 2160.
- [11] G. Rosini, R. Ballini, P. Sorrenti, *Synthesis*, 1983, p. 1014.
- [12] J.-M. Melot, F. Texier-Boulet, A. Foucaud, *Tetrahedron Lett.* 27 (1986) 493.
- [13] R. Ballini, G. Bosica, P. Forconi, *Tetrahedron* 52 (1996) 1677.
- [14] R. Ballini, G. Bosica, *J. Org. Chem.* 62 (1997) 425.
- [15] K.R. Kloetstra, H. Van Bekkum, *J. Chem. Soc., Chem. Commun.* (1995) 1005.
- [16] Y.V. Subba Rao, D.V. De Vos, P.A. Jacobs, *Angew. Chem. Int. Ed. Engl.* 36 (1997) 2661.
- [17] K. Koteswara Rao, M. Gravelle, J. Sanchez, F. Figueras, *J. Catal.* 173 (1998) 115.
- [18] W.T. Reichle, *J. Catal.* 94 (1985) 547.
- [19] J.G. Nunan, P.B. Himelfarb, R.G. Herman, K. Klier, C.E. Bogdan, G.W. Simmons, *Inorg. Chem.* 28 (1989) 3868.
- [20] C. Busetto, G. Delpiero, G. Manara, F. Trifiro, A. Vaccari, *J. Catal.* 85 (1984) 260.
- [21] F. Cavani, F. Trifiro, A. Vaccari, *Catal. Today* 11 (1991) 173.
- [22] E. Suzuki, Y. Ono, *Bull. Chem. Soc., Jpn.* 61 (1988) 1008.

- [23] E. Suzuki, M. Okamoto, Y. Ono, *J. Mol. Catal.* 61 (1990) 283.
- [24] C. Cativiela, F. Figueras, J.I. Garcia, J.A. Mayoral, M. Zurbano, *Synth. Commun.* 25 (1995) 1745.
- [25] C. Cativiela, F. Figueras, J.M. Fraile, J.I. Garcia, J.A. Mayoral, *Tetrahedron Lett.* 36 (1995) 4125.
- [26] W.T. Reichle, US Patent 4, 458, 026, 1984 to Union Carbide.
- [27] B.M. Choudary, M. Lakshmi Kantam, B. Kavita, Ch. Venkat Reddy, K. Koteswara Rao, F. Figueras, *Tetrahedron Lett.* 39 (1998) 3555.
- [28] B.M. Choudary, M.L. Kantam, B. Bharathi, Ch. V. Reddy, *Synlett.* (1998) 1203.
- [29] B.M. Choudary, M.L. Kantam, Ch. V. Reddy, K.K. Rao, F. Figueras, *Green Chem.* (1999) 187.