



Mg-Al-O-Bu^t-Hydrotalcite:

a mild and ecofriendly catalyst for the cyanoethylation of alcohols and thiols†

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Summary

Mg-Al-O-Bu^t-Hydrotalcite is found to be a mild and efficient catalyst for the cyanoethylation of alcohols and thiols in quantitative yields. Exclusive synthesis of 3-alkoxypropionitriles or 3-alkylmercaptopyropionitriles is realised by compatible basic sites of Mg-Al-O-Bu^t-hydrotalcite. The present ecofriendly catalytic system is a potential alternative to soluble bases.

Introduction

Stringent environment protection laws, public and corporate pressure to reduce the amount of toxic waste and by-products arising from the chemical processes have prompted the development of innovative and environment-friendly new technologies¹ by solid acid–base catalysts. Therefore, enviro-economics has become the focused theme for the development of new processes for existing products and new products.² The use of heterogeneous catalysts has made significant advancement in the development of new methodologies in organic synthesis targeted to dispense the conventional and waste generating reagents and achieve high atom economy to be applied in the fine chemical sector.³

Cyanoethylation is one of the important reactions for the synthesis of drug intermediates, plasticizers, insecticides, emulsifiers, additives for synthetic rubber and physiologically active compounds.⁴ Acrylonitriles undergo cyanoethylation with compounds containing an active hydrogen to form β-alkoxy nitriles which are in turn converted to carboxylic acids by hydrolysis or to amines by reduction. Generally cyanoethylation proceeds in the presence of soluble base catalysts^{4,5} such as alkali hydroxides,⁶ alkali alkoxides,⁷ tetraalkylammonium hydroxides,⁷ alkali metal or tetraalkylammonium salts of partial phosphate esters, alkyl mercaptans, cresols, and partial pyrophosphate esters.⁸ However, these catalysts need to be neutralised before purification of the product, thus resulting in the generation of waste, loss of catalyst and reduced product yields. Heterogeneous anion exchange resin catalysts are also used for this reaction^{9–11} but the resins become inactive after a few runs possibly due to the formation of a film of polyacrylonitrile on the surface of the resin. Recently, Hattori and Kabashima^{12,13} have reported the use of alkaline metal oxides, carbonates, hydroxides and alumina supported KF and potassium hydroxide catalysts and found MgO to be very active for cyanoethylation of alcohols. The calcination protocol seems to play a key role in evolving a very active MgO catalyst. Various fluorides supported on basic alumina, MgO, CaO, BaO, silica gel, or Celite are explored¹⁴ in the cyanoethylation of polytetrahydrofuran (hydroxy number 169) and cesium

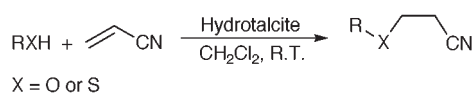
and potassium fluorides supported on basic material have effected the reaction.

Solid bases in the form of layered double hydroxides (LDHs) or hydrotalcite like compounds (HTLCs) are used extensively as adsorbents, anion exchangers and most importantly as basic catalysts.¹⁵ Earlier, we had designed and developed Mg-Al-O-Bu^t-hydrotalcite by incorporation of *tert*-butoxide by an exchange process to tune up the hydrotalcites for higher basicity and found them to be excellent catalysts for aldol condensations¹⁶ and the epoxidation of olefins.¹⁷

Results and discussion

Here we describe cyanoethylation of alcohols and thiols catalysed by Mg-Al-O-Bu^t-hydrotalcite affording high yields and selectivities. This is the first report on the cyanoethylation of thiols catalysed by solid base catalysts.

The general reaction scheme for the cyanoethylation is shown in Scheme 1. The reaction of acrylonitrile with alcohols or thiols



Scheme 1

is fast and forms the addition product generally in high conversion and yield. The catalyst was found to be highly active for alcohols and thiols. The selectivity for the corresponding 3-alkoxypropionitriles and 3-alkylmercaptopyropionitriles was quantitative (Table 1). It is interesting to note that the 3-alkylmer-

Green Context

Cyanoethylation is a widely used reaction in organic chemistry with areas of application including pharmaceutical intermediates, emulsifiers, plasticizers and additives for synthetic rubber. Traditionally the reaction is carried out in the presence of soluble bases such as metal hydroxides but an aqueous quench step is employed to separate the resulting organic products leading to the destruction of the base (by subsequent neutralisation) and the production of an aqueous salt waste stream. Previous attempts to use solid bases in this reaction have had limited success but in this article a high-yielding very selective procedure for the cyanoethylation of alcohols and thiols based on a basic hydrotalcite is described. This environmentally friendly procedure leads to minimal waste and gives high process efficiency. JHC

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Table 1 Cyanoethylation catalysed by Mg-Al-O-Bu^t-hydrotalcite

Entry	Alcohol or thiol	<i>t</i> /h	Product	Yield ^a (%)
1	MeOH	0.6		92 ^b
2	EtOH	1.5		96 ^b
3		4.0		90 ^b
4	Ph-CH ₂ OH	1.5		100
5		2.0		100
6		4.0		87
7		2.5		89
8		2.0		80
9		3.0		100
10		2.0		98
11		0.5		90
12		0.6		100
13		1.5		90
14	Me-[CH ₂] ₁₁ -SH	0.5		94

^a Yields based on ¹H NMR. ^b Isolated yields.

captropionitriles, valuable intermediates for dyes, drugs and insecticides,¹⁸ are realised by employing solid bases. However, the catalyst is inert for the cyanoethylation of amines, and utilising this opportunity we have successfully prepared alkoxy nitriles bearing amino groups for the first time (entry 10).

We compared the activity of the Mg-Al-O-Bu^t-hydrotalcite catalyst to a variety of soluble and solid bases such as metal oxides, γ -alumina,¹² KF-alumina,¹² KOH-alumina,¹³ hydrotalcites¹⁹ and rehydrated Mg-Al-hydrotalcite¹⁹ in the cyanoethylation reaction of acrylonitrile with methanol as a model reaction in order to demonstrate the efficacy of our catalyst (Table 2). Although the reaction of acrylonitrile with methanol using basic alkali earth metal oxides as catalysts afforded good yields, these

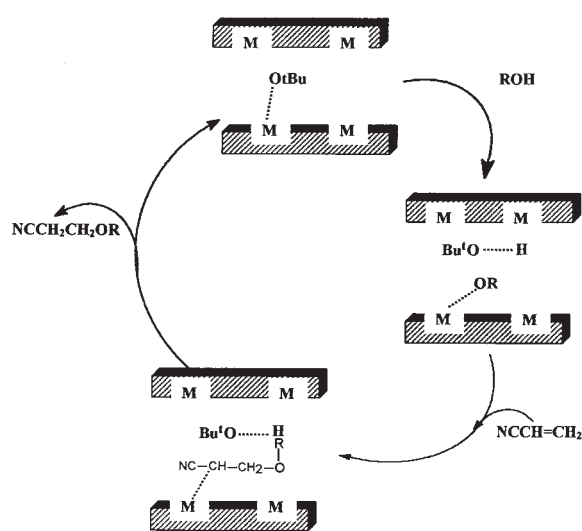
catalysts require longer reaction times and high temperature. There is no cyanoethylation reaction with γ -alumina, but the catalysts, KF, KOH doped on alumina gave moderate to good yields. The samples of hydrotalcites as synthesised and calcined showed poor activity. On rehydration, Mg-Al-hydrotalcite offers excellent yields. The present modified hydrotalcite developed through the exchange of Bu^tO displayed superior activity, two to ten times that over the reported hydrotalcites, basic oxides, and potassium fluoride and hydroxide doped catalysts.

A plausible mechanism for the cyanoethylation of alcohols with acrylonitrile is illustrated in Scheme 2. The incorporated *tert*-butoxide of the hydrotalcite reacts with alcohol to form the respective alkoxide on the basic sites of the catalyst. The alkox-

Table 2 Cyanoethylation reaction between acrylonitrile with methanol using various base catalysts.^a

Entry	Catalyst	t/min	Conversion(%) ^b	Specific activity/ mmol g ⁻¹ h ^{-1d}
1	Mg-Al-O-Bu ^t -hydrotalcite	40	92 ^c	110.4
2	γ-Alumina	120	0	0
3	KF/Alumina	120	52.3	10.5
4	KOH/Alumina	120	85.3	17.1
5	MgO	120	98.7	19.7
6	CaO	120	94.7	18.9
7	BaO	120	78.2	15.6
8	Rehydrated Mg-Al hydrotalcite	45	99.8	53.2
9	Hydrotalcite (uncalcined)	120	2.5	0.5
10	Hydrotalcite (calcined)	120	20	4.0

^a Reaction temp., 323 K, catalyst 0.100 g, unless otherwise stated. ^b Conversion was calculated by the decrease in acrylonitrile percentage. ^c Reaction temp., room temp. using 0.050 g catalyst, isolated yield. ^d Specific activity = mmol of 3-methoxypropionitriles obtained per gram of catalyst per hour.

**Scheme 2**

ide anion is stabilised with the surface metal cationic charge and further reacts with acrylonitrile to form the 3-alkoxypropanenitrile anion, which on interaction with alcohol yields 3-alkoxypropanenitrile.

The present Mg-Al-O-Bu^t-hydrotalcite catalyst is much more active than hydrotalcites and rehydrated hydrotalcite in cyanoethylation reactions. The process of hydration generates hydroxy groups in the interlayers of hydrated hydrotalcites.¹⁹ Understandably, the Bu^tO anion incorporated hydrotalcite is more basic than the hydrated hydrotalcite and facilitated easy formation of alkoxide in the hydrotalcite discussed in the mechanism.

An attempt was made to check the reusability of the catalyst in the following manner. The substrates, catalyst and solvent were taken and the reaction was performed as usual for the specified time. Then stirring was stopped and the reaction mixture was withdrawn with a syringe. Fresh substrate and solvent were added to the residual catalyst and the reaction performed in the usual manner. The activity of the catalyst was found to be the same.

In the cyanoethylation reaction catalysed by soluble base (NaOH),⁵ each tonne of the substrate requires 50 kg of the base (calculated based on 5 wt% of the base, NaOH employed in the reaction) which has to be neutralised with an acid to generate 72

kg of total dissolved salt (NaCl). The organic waste generated depends upon conversion and selectivity of the specific reaction. The present catalyst can be recycled several times, if proper care is taken. Assuming that our catalyst lasts for 20 recycles, 5–6 kg catalyst per tonne of product has to be disposed as solid waste. Since selectivity is very high, there is no substantial amount of organic waste to be disposed of.

Thus, compatible basic sites present in the Mg-Al-O-Bu^t-hydrotalcite can promote the cyanoethylation reaction with excellent yields in shorter times. The advantages are high catalytic activity under very mild liquid phase conditions, easy separation of the catalyst by simple filtration, excellent yields and 100% selectivity of 3-alkoxypropanitriles at faster rates of reaction, involvement of non-toxic and inexpensive materials, and zero emission of pollutants. The present catalytic system is a potential alternative to soluble bases.

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- 20 *Representative procedure*: a 100 ml two-necked round bottomed flask was charged with Mg-Al-O-Bu¹-HT (0.05 g) and acrylonitrile (4 mmol) in dry CH₂Cl₂ under nitrogen atmosphere. Alcohols or thiols (4 mmol) were then added to the reaction mixture which was then stirred at room temperature and monitored by TLC. After completion, the catalyst was filtered off and the filtrate was concentrated under reduced pressure. The product was analysed by ¹H NMR and mass spectrometry.

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