Acylation of alcohols, thiols and amines with carboxylic acids catalyzed by yttria–zirconia-based Lewis acid

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Abstract

A simple and efficient method has been developed for the acylation of alcohols, amines and thiols using yttria–zirconia-based Lewis acid as catalyst and carboxylic acids as acylating agent. The reaction was found to be chemoselective for the amino alcohol, 2-mercapto ethanol and 1,2-diol. Thus, using this method, acylation of an amino group in the presence of OH group, of OH group in the presence of SH, and of a primary OH group in the presence of secondary OH group has been achieved with excellent selectivity. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Yttria–zirconia-based Lewis acid; Carboxylic acids; Acylation reaction; Heterogeneous catalysis; Chemoselectivity

1. Introduction

The acylation of alcohols, thiols and amines is one of the most frequently used transformations in organic synthesis as it provides an efficient and inexpensive means for protecting hydroxy, thiol and amino groups in a multistep synthetic process [1]. Acylation is usually performed employing acid anhydrides or acid chlorides in the presence of stoichiometric amounts of bases such as 4-(dimethylamino)pyridine or 4-pyrrolidinopyridine (4-PPY) [2,21], *tertiary* amine [3,22] and tributylphosphine [4]. The Lewis acid catalyzed acylation of alcohols and amines is a mild, strategic alternative to basic and nucleophilic catalysts. Some procedures have been developed wherein Lewis acid catalysts such as $Cu(OTf)_2$ [5], $TaCl_5$ [6], TMSOTf [7], $Sc(OTf)_3$ [8,23–25], $In(OTf)_3$

[9], $CoCl_2$ [10] are known to catalyze the acylation of alcohols and phenols in the presence of acetic anhydride. However, most of these methods either suffer from problem in recovery of the large amount of soluble bases or acids or from the excessive use of acetic anhydride or acid chloride as acylating agent. These drawbacks have a negative impact on the environment. Therefore, there is a genuine need to develop a reusable solid catalyst for acylation reaction using carboxylic acids so as to achieve high atom efficiency. More recently, the use of montmorillonite K-10 and KSF [11,26,27] and zeolite [12] as heterogeneous catalysts has been reported to effect acylation reaction.

As part of a research program aimed at developing a new solid catalyst and its subsequent application for various organic transformations, the yttria–zirconia-based Lewis acid was found to be an extremely efficient catalyst for the Diels–Alder reaction [13,28], synthesis of acetals from carbonyl compounds [14], silylation of alcohols with HMDS [15], and transesterification of β-keto esters [16]. This

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prompted us to use this catalyst for acylation reaction and herein, we report that yttria–zirconia-based Lewis acid serves as an excellent catalyst for acylation of alcohols, thiols and amines with carboxylic acids:
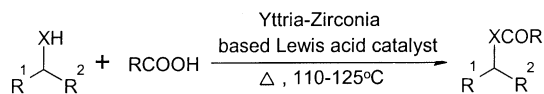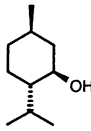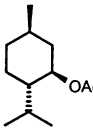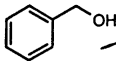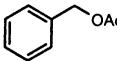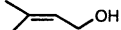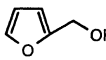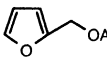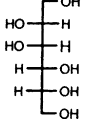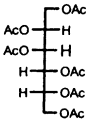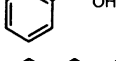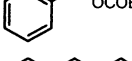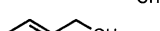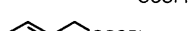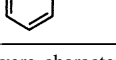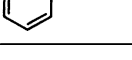

$X = O, NH, S$ $R = Me, Et, Ph$

2. Experimental

2.1. Materials and equipment

Solvents were purified and dried by standard procedures before use according to reported procedure [17]; petroleum ether of boiling range 60–80 °C was used. The acids and alcohols were obtained from commercial sources and were purified by

Table 1
The yttria–zirconia-based Lewis acid catalyzed acylation of alcohols

Entry	Alcohol	Acid	Reaction time (h)	Product[a]	Yield[b] (%)
1		AcOH	3		89
2		AcOH	4.5		94
3		AcOH	3		91
4		AcOH	15		77
5		AcOH	4		94
6		AcOH	8		85
7		AcOH	7		88
8		AcOH	8		92
9		AcOH[c]	9		92
10		EtCOOH	3		89
11		EtCOOH	3.5		90
12		C_6H_5COOH[d]	9		83
13		C_6H_5COOH[d]	13.5		79

[a] Products were characterized by usual spectral analyses.
[b] Isolated yield.
[c] 10 equivalents of acid was used.
[d] 1.1 equivalent of acid was used.

distillation/recrystallization before the experiment. Infrared spectra were recorded with ATI MATT-SON RS-1 FTIR spectrometer. Proton NMR spectra were recorded on Bruker AC-200 machine in $CDCl_3$ with TMS as internal standard. Mass spectra were obtained with Finningen MAT mass spectrometer. Elemental analyses were carried out with a Carlo Erba CHNS-O analyzer. The diffractogram of X-ray powder diffraction pattern was recorded on a Rigaku diffractometer model D/Max. IIIVC with N-filtered Cu Kα radiation. FTIR spectrum of pyridine adsorbed on the yttrium-based catalyst was recorded on a Nicolet 60 SXB FTIR spectrometer. TPD profile (ammonia) of the yttrium-based catalyst was recorded on a Sorbstar apparatus. Determination of specific surface area was carried out by BET (Brunner–Emmett–Teller) N_2 adsorption using a Omnisorp 100CX apparatus.

2.2. Synthesis of the catalyst

The catalyst was prepared by mixing aqueous solutions of yttrium nitrate and zirconyl nitrate in the mole ratio 16:84, to which aqueous ammonia (28%) was added under vigorous stirring until a pH of 8.5 was achieved and precipitate was formed. Washing with deionized water, drying at $110\,^\circ C$ for 24 h, treating with sulfuric acid (4 M), drying at $120\,^\circ C$ and subsequent programmed calcination at $500\,^\circ C$ for 3 h at a heating rate of $2\,^\circ C\,min^{-1}$ resulted in a highly acidic material. The chemical composition of the final catalyst (determined by XRF technique) was found to be 82.6 mol% Zr, 15.6 mol% Y and 1.8 mol% S. The physicochemical characterization of the catalyst was carried out by titration, temperature programmed desorption (TPD), scanning electron microscopy (SEM) and N_2 adsorption techniques.

2.3. A typical procedure for acylation reaction

Alcohol/amine/thiol (10 mmol) was added to acid (50 mmol) containing (20%, w/w with respect to substrate) and mixture was heated to $110\,^\circ C$ ($125\,^\circ C$ in the case of benzoic acid) for the indicated length of time (Tables 1–3). The reaction was monitored by TLC. After completion of reaction, the catalyst was filtered; filtrate was concentrated, diluted with water (15 ml) and extracted with CH_2Cl_2 (2×20 ml).

The organic layer was separated, washed with 10% aqueous $NaHCO_3$, brine, water and dried over Na_2SO_4. The solvent was removed and the crude product was chromatographed on silica gel column (3% EtOAc in light petrolum ether) to afford the product in high yield. The structure was confirmed by ^{1}H NMR, mass spectroscopy and also by comparison with authentic sample. After the reaction, the catalyst is recovered with retention of its catalytic activity. It can be further reactivated for reuse by heating it at $500\,^\circ C$ in the presence of air.

Table 2
The yttria–zirconia-based Lewis acid catalyzed acetylation of amines and thiols

Entry	Substrate	Reaction time (h)	Product[a]	Yield[b] (%)
1	⌬–NH₂	2	⌬–NHAc	93
2	⌬–CH₂NH₂	2	⌬–CH₂NHAc	92
3	⌬–SH	8	⌬–SAc	94
4	H₃C–⌬–SH	4	H₃C–⌬–SAc	92

[a] Products were characterized by usual spectral analyses.
[b] Isolated yield.

Table 3
Chemoselective acetylation of amino alcohol, mercapto alcohol and diol catalyzed by yttria–zirconia-based Lewis acid catalyst

Entry	Substrate	Reaction time (h)	Product[a]	Yield[b] (%)
1	OH NH₂	24[c]	HO NHAc	94
2	SH OH	24[d]	HS OAc	65
3	OH OH	20[e]	HO OAc	8
			AcO OAc	72

[a] Products were characterized by usual spectral analyses.
[b] Isolated yield.
[c] Reaction was performed at $60\,^\circ C$.
[d] Reaction was carried out at $85\,^\circ C$.
[e] Reaction was performed at $75\,^\circ C$.

3. Results and discussion

3.1. Characterization of the catalyst

The physicochemical characterization of the catalyst was carried out by titration, TPD, SEM and N_2 adsorption techniques. The X-ray powder diffraction profile of the catalyst shows the formation of a cubic phase (Fig. 1). The IR spectra of pyridine adsorbed on the catalyst show absorption bands at 1640, 1605, 1577, 1542, 1490 and 1444 cm^{-1} (Fig. 2). The strong absorption bands at 1605 and 1444 cm^{-1} indicate the presence of coordinated pyridine at the Lewis acid sites of the catalyst. The weak absorption at 1542 cm^{-1}, attributed to the pyridinium ion [18] indicates the presence of a few Brönsted acid sites. The potentiometric titration of the acid sites with *n*-butylamine in non-aqueous medium (Fig. 3) shows the influence of yttrium in enhancing the number of acid sites [19]. The amount of *n*-butylamine consumed was 7.7 mol equiv. g^{-1} for the yttrium-based catalyst compared to 5.8 mol equiv. g^{-1} for the yttrium-free catalyst. The presence of very strong acid sites in the catalyst is indicated by the peak maxima at 530 °C in the TPD profile (Fig. 4) [20]. The scanning electron micrograph of the sample shows the presence of uniform-sized (around 0.3 μm) particles (Fig. 5). The
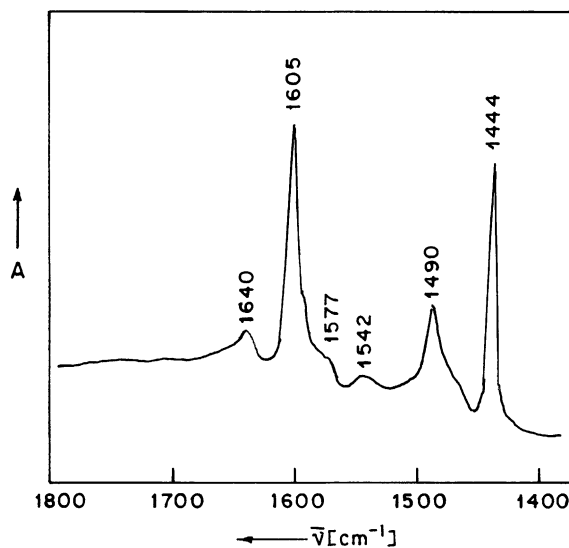
Fig. 2. FTIR spectrum of pyridine adsorbed on the yttrium-based catalyst, recorded on a Nicolet 60 SXB FTIR spectrometer; A: absorption (arbitrary units).

surface area of the sample determined by the BET method was 150 $m^2\,g^{-1}$. The lattice defects caused by the incorporation of yttrium in the Zr^{4+} sites appear to enhance the number and strength of the Lewis acid sites of the catalyst.

Fig. 1. X-ray powder diffraction pattern of the yttrium-based catalyst prior to (a) and after (b) sulfation. The diffractogram was recorded on a Rigaku diffractometer, model D/Max. IIIVC with Ni-filtered Ca Kα radiation; I: intensity (arbitrary units).

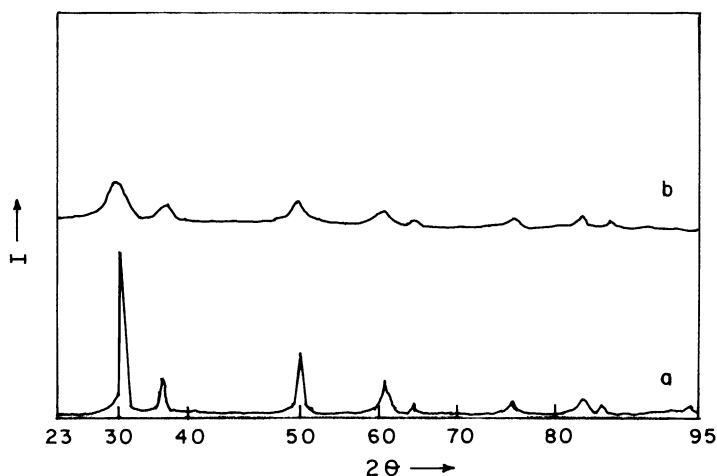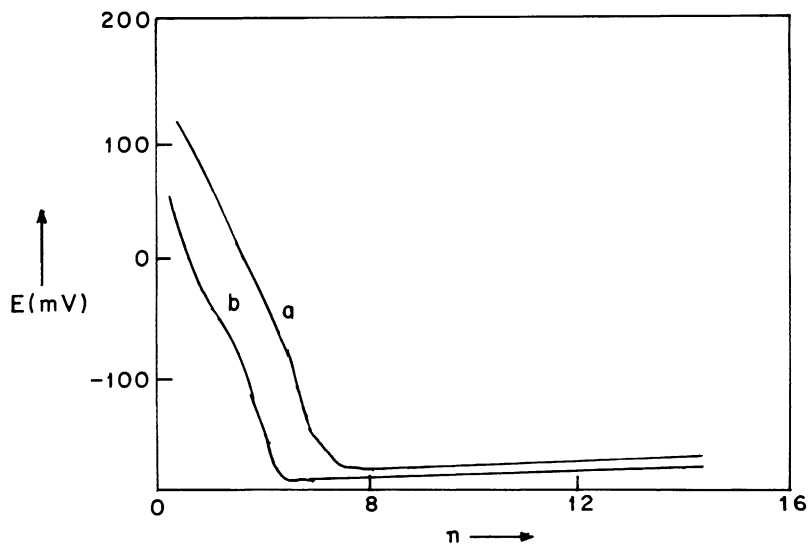Fig. 3. Potentiometric titration curves of the sulfated catalyst with yttrium (curve a) and without yttrium (curve b) in CH$_3$CN. For details, see Ref. [19]. *N*: number of molar equivalents of *n*-butylamine per gram.
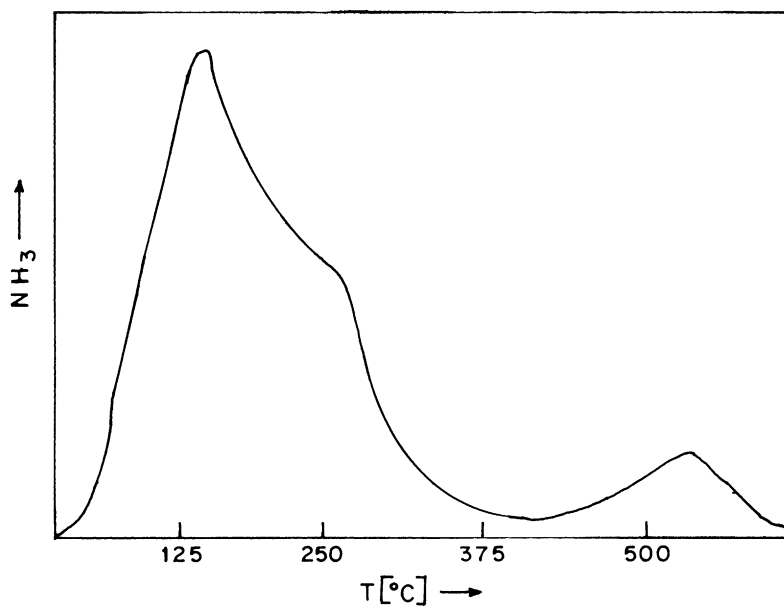
Fig. 4. TPD profile (ammonia) of the yttrium-based catalyst, recorded on a Sorbstar apparatus, Institute of Isotopes, Hungary, with He as the carrier gas, a flow rate of 50 ml min^{-1}, and a heating rate of 10 K min^{-1} from room temperature to 625 °C; NH$_3$: amount of ammonia desorbed (arbitrary units).

Fig. 5. Scanning electron micrograph of the catalyst.

3.2. Acylation reaction

A wide range of structurally varied alcohols, amines and thiols were subjected to acylation with carboxylic acid by this procedure. The present methodology demonstrates a simple acylation procedure under environmentally safe, heterogeneous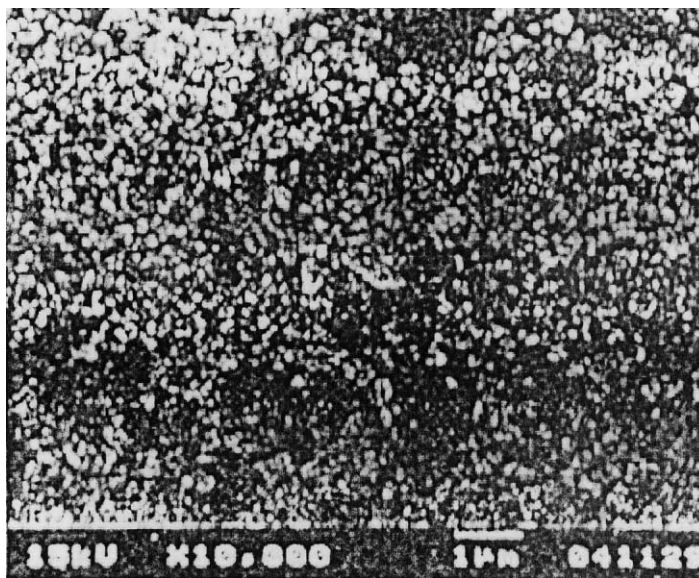 reaction conditions and has wide applicability, extending the scope to primary, secondary, allylic, cyclic and heterocyclic alcohols (Table 1). However, the acylation reaction with phenol is found to be sluggish and hence a little longer time is required to complete the reaction affording relatively low yield of the products (Table 1, entry 4). The reaction conditions are mild enough not to induce any isomerization of the double bond in allylic alcohol (Table 1, entry 6). Another notable feature of this method is that optically active alcohol underwent acylation without any racemization (Table 1, entry 3) and also the polyhydroxy compounds such as ethylene glycol and D-mannitol underwent exhaustive acylation to afford the corresponding products in excellent yields (Table 1, entries 8 and 9). Even a wide variety of other alcohols could be acylated using propionic or benzoic acid as acylating agent under the present reaction conditions (Table 1, entries 10–13).

In order to explore the generality and scope of the yttria–zirconia-based Lewis acid catalyzed reaction, the procedure has been extended to a variety of other substrates such as amines and thiols. Thus aromatic and benzylic amines were successfully acylated in the presence of a yttria–zirconia-based Lewis acid catalyst (Table 2, entries 1 and 2). Similarly, acylation of thiols was also achieved by this procedure in excellent yields (Table 2, entries 3 and 4). More significantly, it was observed that the reaction is chemoselective for the amino alcohols, mercapto alcohols and diols. The acylation of amino alcohol produced the corresponding acetamide only (Table 3, entry 1); the hydroxy moiety remained untouched. The selective acylation of a primary NH_2 over a primary OH by this process is of considerable synthetic importance and is difficult to achieve with many other reagents [2,4,8,10,21,23–25]. Similarly, the hydroxyl group of 2-mercapto ethanol reacted preferentially over the thiol affording the corresponding acetate in high yield (Table 3, entry 2). In the case of 1,2-diol, we observed preference in the acylation for primary alcohol over secondary; however, a mixture of mono and di-acylated products was obtained (Table 3, entry 3). The chemoselectivity in acylation reaction with respect to different functional groups is in accordance

with those observed by us in the transesterification reaction [16].

4. Conclusion

We have described a mild, highly efficient and selective procedure for acylation of alcohols, thiols and amines using acetic, propionic and benzoic acids as acylating agent in the presence of catalytic amount of yttria–zirconia-based Lewis acid catalyst. The obvious advantages of heterogeneous catalysis in terms of simple operation coupled with the ease of work-up and recyclability of the catalyst are noteworthy. We believe this will present a better, more practical and environmentally safer alternative to the existing methodologies and should find widespread applications in organic synthesis.

Acknowledgements

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