



Lanthanum nitrate hexahydrate ($\text{La}(\text{NO}_3)_3 \cdot 6\text{H}_2\text{O}$). An efficient and highly selective catalyst for solventless acetylation of alcohols and phenols with acetyl chloride

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Abstract

Acetylation of alcohols and phenols with acetyl chloride using lanthanum nitrate hexahydrate ($\text{La}(\text{NO}_3)_3 \cdot 6\text{H}_2\text{O}$) as a catalyst is described. The remarkable selectivity under mild and neutral conditions of the catalyst is advantages.

Keywords: Alcohols; phenols; acetylation; acetyl chloride; solventless acetylation; lanthanum nitrate hexahydrate ($\text{La}(\text{NO}_3)_3 \cdot 6\text{H}_2\text{O}$).

1. Introduction

Acetylation of hydroxyl groups is a frequently used transformation method in organic synthesis. Among the various protecting groups used for the hydroxyl function, acetyl is the most convenient group in view of its easy introduction, being stable to the acidic reaction conditions, and also easily removable by mild alkaline hydrolysis [1]. Generally, acylation of alcohols and phenols is carried out with carboxylic acids and more conveniently anhydrides or acyl chlorides in the presence of basic catalysts, Brønsted or Lewis acids and metal salts [2b]. Amongst the catalysts used for activation of anhydrides and acyl chlorides, pyridine [2], Et_3N [1], 4-(dimethylamino) pyridine (DMAP) [3], Bu_3P [4], $\text{MgBr}_2\text{-Et}_3\text{N}$ [5] and $\text{KF-Al}_2\text{O}_3$ [6] are the most significant, whereas H_2SO_4 [7], P-TsOH [8] and $\text{NH}_2\text{SO}_3\text{H}$ [9] are acidic catalysts.

Recently, beside mineral oxides which have proved to be useful to chemists in the laboratory and industry due to the good activation of adsorbed compounds and reaction rate enhancement, selectivity, easier work-up and recyclability of the supports and the eco-friendly, green, reaction conditions [10, 11], other reagents such as distannoxane [12], metal triflates [13-15], $\text{AlPW}_{12}\text{O}_{40}$ [16], ZrCl_4 [17], $\text{Cu}(\text{BF}_4)_2 \cdot 6\text{H}_2\text{O}$ [18], LiClO_4 [19], $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ [20], CeCl_3 [21], $\text{BiOClO}_4 \cdot \text{XH}_2\text{O}$ [22], MgBr_2 [23], LiCl [24], I_2 , NBS [25], metal triflates in ionic liquids [15], twisted amides [26], solid supported reagents [27] and Lipase enzymes [28] have been applied for acylation of alcohols and phenols. However, there is always the need for better methods.

Recently, $\text{La}(\text{NO}_3)_3 \cdot 6\text{H}_2\text{O}$ has been used as a Lewis acid catalyst for various organic transformations [29, 30]. It is an inexpensive, available and extremely safe reagent to be used in

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chemical reactions. We are interested in catalytic reactions in eco-friendly and solventless conditions [31, 32]. We describe herein an efficient and convenient procedure for acetylation of alcohols and phenols under solvent-free conditions in the presence of a catalytic amount of lanthanum nitrate hexahydrate with acetyl chloride at room temperature.

2. Experimental

2.1. Apparatus

The products were purified by column chromatography and the purity determinations of the products were accomplished by GLC on a Shimadzu model GC- 10A instrument or by TLC on silica- gel polygram STL G/UV 254 plates. FT- IR spectra were recorded on a Perkin Elmer RXI spectrometer. NMR Spectra were recorded on a Bruker Avance DPX 250 MHz instrument.

2.2. Typical procedure for acetylation of benzyl alcohol

Benzyl alcohol (1 mmol, 0.108 gr) and acetyl chloride (3 mmol, 0.2355 gr) were added to $\text{La}(\text{NO}_3)_3 \cdot 6\text{H}_2\text{O}$ (0.01 mmol, 0.00004 gr). The homogeneous mixture was stirred at room temperature. GC analysis showed that the reaction was completed immediately. The reaction mixture was filtered. Column chromatography of the filtrate on silica- gel using *n*-hexane as eluent gave benzyl acetate in 98% yield

3. Results and discussion

We are especially interested in exploring the potential use of neutral or nearly neutral catalyst. Herein, we wish to describe a new protocol for the mild and rapid protection of a wide variety of alcohols and phenols using acetyl chloride and a catalytic amount of lanthanum nitrate hexahydrate.

Initially a systematic study was carried out for the catalytic evaluation of lanthanum nitrate hexahydrate for acetylation of benzyl alcohol. The reaction could not be carried out in acetic acid with catalytic amount of catalyst. Also the reaction could not be completed in acetyl chloride and acetic anhydride in the absence of catalyst. Different molar ratios of ROH/acetylating agent, solvents and temperature were examined (Table 1).

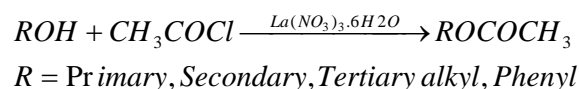
Table 1

Reaction of benzyl alcohol with different acetylating agents in the presence of $\text{La}(\text{NO}_3)_3 \cdot 6\text{H}_2\text{O}$

Entry	Acylating agent	Molar Ratio ROH/Acetylating agent	Solvent	T / °C	Time/ h	Conversion / % *
1	CH_3COCl	1/1	CH_2Cl_2	rt/reflux	24/16	100/100
2	CH_3COCl	1/1	CH_3CN	rt/reflux	20/14	100/100
3	CH_3COCl	1/2	CH_3CN	rt	3	100
4	CH_3COCl	1/3	solvent free	rt	immediately	100
5	$(\text{CH}_3\text{CO})_2\text{O}$	1/1	CH_2Cl_2	rt/reflux	24/19	70/100
6	$(\text{CH}_3\text{CO})_2\text{O}$	1/1	CH_3CN	rt/reflux	24/18	80/100
7	$(\text{CH}_3\text{CO})_2\text{O}$	excess of acetylating agent	solvent free	rt	96	60
8	$\text{CH}_3\text{CO}_2\text{H}$	1/1	CH_2Cl_2	rt/reflux	24/24	no reaction
9	$\text{CH}_3\text{CO}_2\text{H}$	1/1	CH_3CN	rt/reflux	24/24	no reaction
10	$\text{CH}_3\text{CO}_2\text{H}$	excess of acetylating agent	solvent free	rt	120	95

* GC Yield Using Internal Standard.

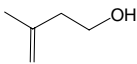
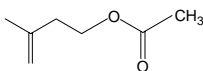
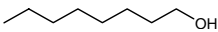
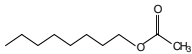


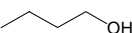
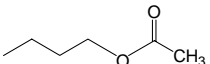
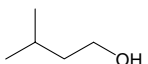
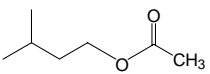
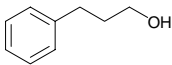
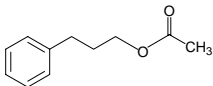
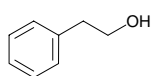
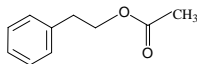
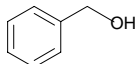
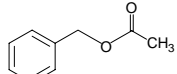
Benzyl acetate was produced immediately in solvent free condition at room temperature in quantitative yield.



The efficiency of this reaction is evident from the variety of hydroxy compounds including primary, secondary, tertiary, benzylic and allylic alcohols and phenols, to give the products in mild conditions and excellent yields. This method works well with a 1: 3 molar ratio of alcohol or phenol to acetyl chloride in the presence of a catalytic amount of La (NO₃)₃.6H₂O (0.01mmol) without solvent (Table 2).

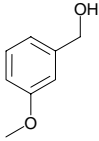
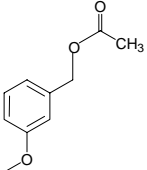
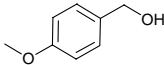
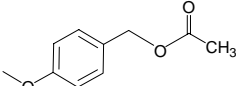
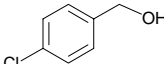
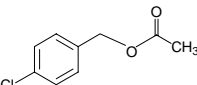
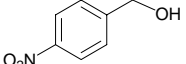
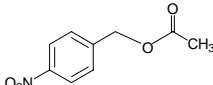
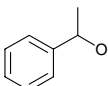
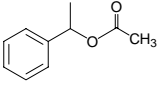
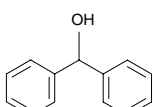
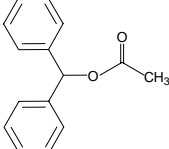

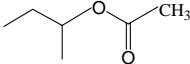

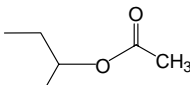
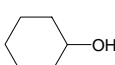
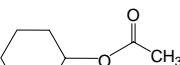
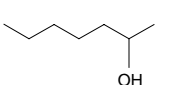
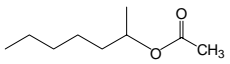
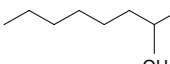
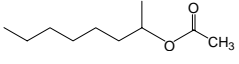
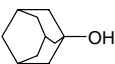
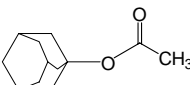
Table 2

Acetylation of different structually alcohols and phenols under catalytic effect of La (NO₃)₃.6H₂O.

Entry	ROH	Product	Time / h	Conversion % [*]	Isolated yield %
1			4	100	98
2			4	100	95
3			4	100	97
4			6	100	96
5			5	100	98
6			immediately	100	95
7			immediately	100	94
8			immediately	100	98

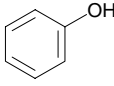
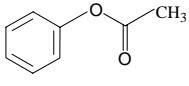
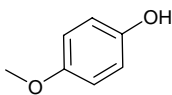
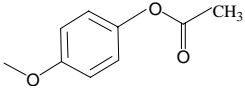
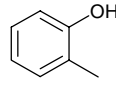
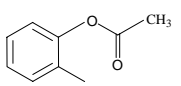
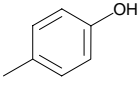
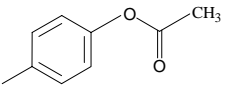
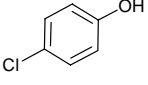
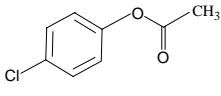
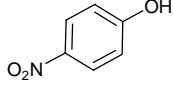
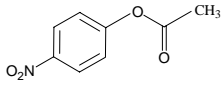
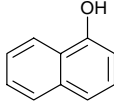
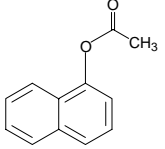
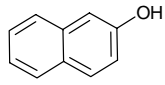
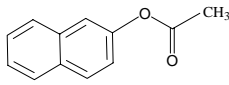
* GC yield using internal standard.

Table 2 (continuation)

Entry	ROH	Product	Time / h	Conversion % [*]	Isolated yield %
9			immediately	100	98
10			immediately	100	97
11			12.5	100	96
12			21	100	95
13			immediately	100	98
14			19	80	74
15			17	100	93
16			21	100	98
17			20	100	95
18			17	100	94
19			23	100	96
20			58	100	95

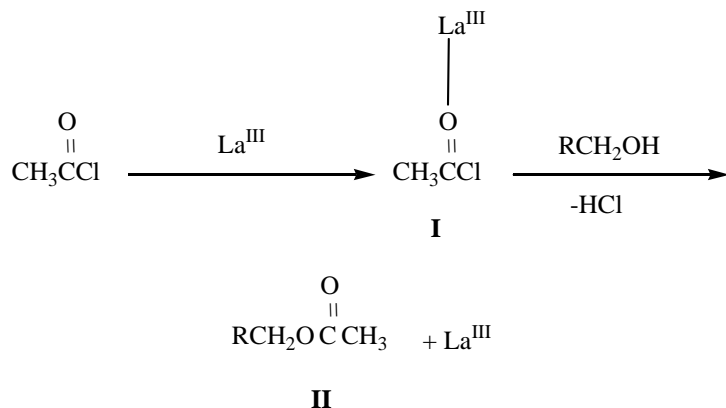
* GC yield using internal standard.

Table 2 (continuation)

Entry	ROH	Product	Time / h	Conversion % [*]	Isolated yield %
21			1.5	100	96
22			3	100	98
23			3.5	100	96
24			immediately	100	96
25			6	100	97
26			22	100	97
27			5.5	100	94
28			10	100	93

* GC yield using internal standard.

The mechanism for these transformations is unclear. One idea may be that $\text{La}(\text{NO}_3)_3 \cdot 6\text{H}_2\text{O}$ acts as a Lewis acid which may activate the carbonyl group to produce the acetylating agent **I** (Scheme 2).

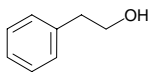
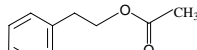
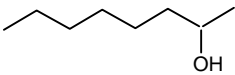
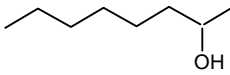
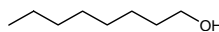
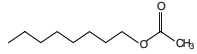
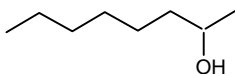
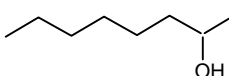
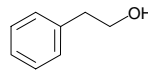
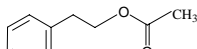
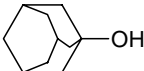
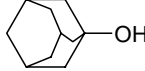
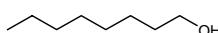
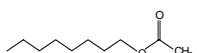
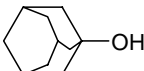
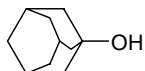
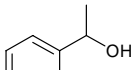
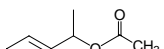
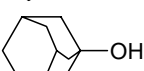
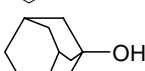
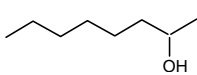
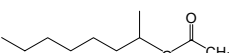
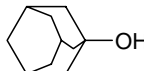
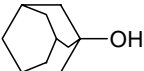
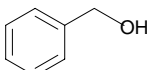
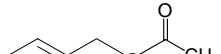
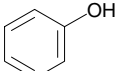
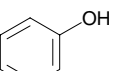


Scheme 1

A rapid reaction with alcohol then ensues, leading to **II** and concomitant release of HCl. This is followed by the formation of the acetyl chloride-La^{III} complex **I** again. Nevertheless, at this time there is no experimental evidence for this feature of **I**, and the actual role of this reagent should be further studied in detail.

Table 3

Selective reaction of different binary mixtures.

Entry	Binary mixture	Products ^a	Time / h	Conversion % ^b
1			immediately	98
				100
2			4	100
				100
3			immediately	100
				100
4			4	98
				100
5			immediately	100
				100
6			23.5	100
				100
7			immediately	100
				100

^a The product was identified by the comparison of its physical constants and IR and NMR spectral data with those of an authentic sample

^b GC yield using internal standard .

In order to establish the scope of La(NO₃)₃.6H₂O in the chemoselective protection of primary alcohols in the presence of secondary alcohols, we reacted acetyl chloride with binary mixture of 2- phenylethanol and 2- octanol at room temperature using La(NO₃)₃.6H₂O to

produce 2- phenylethyl acetate in 98% yield while 2-octanol remains intact. Encouraged by the success of this reaction, various binary mixtures of alcohols were subjected to the protection with excellent selectivity (Table 3).

4. Conclusion

In conclusion, we have developed a simple, efficient, mild and highly selective process for acetylation of alcohols using lanthanum nitrate as a catalyst. The mild, environmentally clean reaction conditions and short reaction times with high yields are advantages of the present method. We believe that the present protocol will find useful application for the protection of alcohols in modern synthetic methodology.

Acknowledgements

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