Selective trimethylsilylation of alcohols and phenols with hexamethyldisilazane catalyzed by LaCoO₃ perovskite

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Abstract

Trimethylsilylation of alcohols and phenols were carried out under solvent-free conditions with hexamethyldisilazane (HMDS) using LaCoO₃ perovskite. LaCoO₃ as an efficient catalyst accelerated this reaction under milder condition. The advantages of this method are evident regarding, easy separation, low cost and low catalyst loading, lack of pollution, easy work-up, and selective protection of primary and secondary alcohols.

Keywords: Protection; trimethylsilylation; trimethylsilyl ether; hxamethyldisilazane; heterogeneous catalyst.

Introduction

Silyl ethers are the most widely used protecting groups for hydroxyl groups such as alcohols and phenols in the multi-step synthetic organic chemistry [1]. Several methods have been reported for the preparation of silyl ethers using various types of silylating agents [2-5]. 1,1,1,3,3,3-hexamethyldisilazane (HMDS), as a stable and inexpensive reagent, is used for the synthesis of silyl ethers. However, the use of HMDS has limitations such as its low silylating power, forceful condition and long reaction times. Therefore, to activate this reagent, an appropriate catalytic system is required [6]. For its efficiency, a variety of catalysts have been used [6-12]. Although these catalytic systems provide an improvement, in most cases, they are

characterized by various limitations such as low selectivity, tedious reaction procedure, moisture sensitive, and toxic or expensive of the catalyst [12]. Hence, the development of new procedures to circumvent these problems is still in demand.

In recent years, perovskite-type oxides have been made in the chemical reactions due to their outstanding properties of good thermal stability, high activity, and non-toxicity [13]. Among perovskite-type oxides, the extensive use of LaCoO₃ as a catalyst and oxidant reagent is due to many characteristic features such as interesting electrical and electrocatalytic properties, very high electronic conductivity and good ionic conductivity [14]. LaCoO₃ presents high catalytic activity in the oxidation of organic compounds [15], the

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production of lactic acid from cellulosic biomass [16], and photocatalytic water oxidation [17].

A number of different analytical methods have been developed for the successful identification of various organic samples. Gas chromatography-mass spectrometry (GC-MS) is an analytical technique that combines the features of gas-chromatography and mass spectrometry to identify different substances within a test sample. GC-

MS method is used in explosives investigation, drug detection, fire investigation, environmental analysis, and identification of unknown samples [18-20].

Here, we disclose a clean and mild procedure for the protection of alcohols and phenols using HMDS in the presence of $LaCoO_3$ under green solvent-free conditions with good to excellent yields (Scheme 1).

$$2ROH + SiMe_3-\underset{\underset{H}{|}}{N}-SiMe_3 \xrightarrow[\text{solvent-free, 40 °C}]{LaCoO_3} 2ROSiMe_3 + NH_3$$
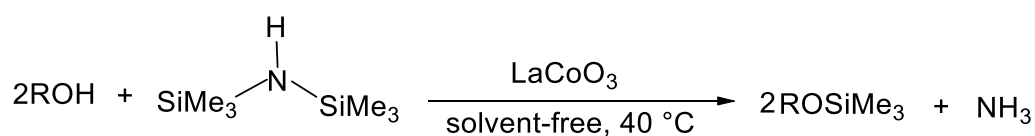
Scheme 1. Trimethylsilylation of alcohols and phenols with HMDS catalyzed by $LaCoO_3$

Experimental

General

All chemicals were purchased from Fluka, Merck, or Aldrich chemical companies. The $LaCoO_3$ catalyst was prepared as reported previously [14]. The used domestic microwave oven was LG-30L, 900W, MW frequency 2.45GHz. GC-Mass measurement was recorded using a Shimadzu GCMS-QP 505 A with DB5 column. Helium gas with the purity of 99.999% was used as the carrier at 1.2 ml min^{-1}. The software used for the data acquirement and processing was Lab solution. The temperatures of injector and interface were maintained at 250 ºC and 280 ºC, respectively. The temperature program for the column oven was as follows: 70 ºC for 2 min, a linear ramp to 250 ºC at 10 ºC/min and a 5 min held. The electron impact (EI)-ionization was performed at 70 eV.

Preparation of LaCoO₃ perovskite

To prepare $LaCoO_3$ perovskite, $La[Co(CN)_6].5H_2O$ powder was pressed into pellets with a pressure of 200MPa and was put in a porcelain crucible. The crucible was placed in another larger porcelain crucible in the presence of CuO powder. This assembly was placed in a microwave oven and irradiated at the highest power level of 900W in the air for 10 min. After this time, the CuO powder became fully red hot, the complete decomposition of the precursor pellet occurred. The product was cooled to room temperature and collected for catalytic applications [14].

Trimethylsilylation of alcohols and phenols

A mixture of alcohol or phenol (10 mmol), LaCoO3 (0.01 g) and HMDS (7.5 mmol) was prepared and stirred at 40 °C under solvent-free conditions for an appropriate time. The progress of the reaction was monitored by GC. After completion of the reaction, the n-hexane was added to the residual mixture and the catalyst was filtered. The evaporation of the solvent under reduced pressure afforded the silylated product.
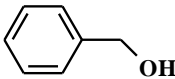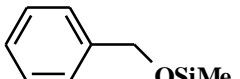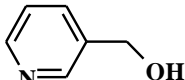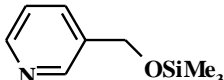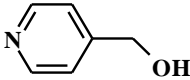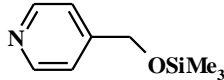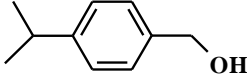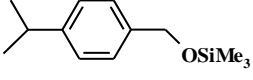
Results and discussion
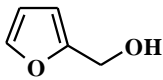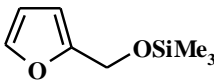
In the present work, we disclose a green and mild method for the protection of alcohols and phenols with HMDS using catalytic amounts of $LaCoO_3$ under solvent-free heterogeneous reaction conditions at 40 °C with good to excellent yields. The organic solvent such as CH_3CN and CH_2Cl_2 was not used. A solvent-free condition is more environmentally benign and economically feasible. In comparison to a reaction in organic solvents, the advantages of solvent-free condition include cost-effective, environmentally friendly and easy workup procedures, energy storage, and high yields.
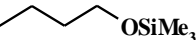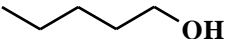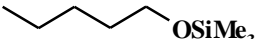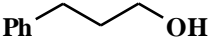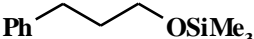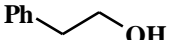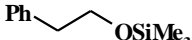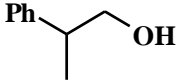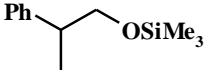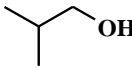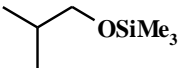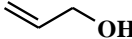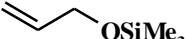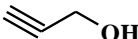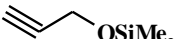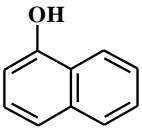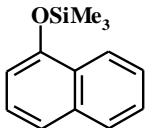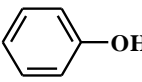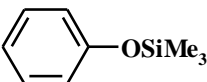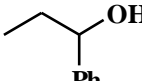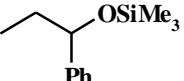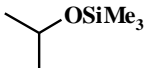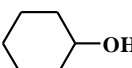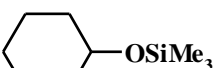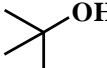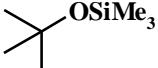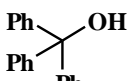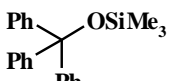
At the beginning of this research, the protection of benzyl alcohol with HMDS as a model reaction in the presence of $LaCoO_3$ as the catalyst was carried out to optimize the reaction conditions. After various experiments, 7.5 mmol of HMDS (for 10 mmol of the substrate) and $LaCoO_3$ loading of 0.01 g at 40 °C under solvent-free conditions were selected as the optimized reaction conditions. In the absence of $LaCoO_3$, only the small amounts of corresponding products were produced.

Encouraged by the obtained results, the various alcohols and phenols were applied for the synthesis of silyl ethers. The results have been shown in Table 1. Trimethylsilylation of primary alcohols proceeded efficiently with good to excellent yields (60-99%). No elimination and rearrangement by-products were observed at all. Phenols also underwent silylation using this method to give silylation products in high yields (98-99%). Secondary alcohols were resistant to this method and gave low yeilds or no conversion under the selected conditions. Cyclohexanol was easily protected with HMDS in good yields despite being secondary alcohol, presumably because its cyclic 2° alkyl group presents less steric hindrance than an acyclic 2° alkyl group. The silylation of tertiary alcohols such as tert-butyl alcohol and triphenylmethanol did not occur.

Table 1. Trimethylsilylation of alcohols and phenols with HMDS catalyzed by $LaCoO_3$ at 40 °C

Entry	Hydroxy compound	Trimethylsilyl ether	Time (min)	Yeild (%)[a]
1			50	96
2			95	84
3			120	61
4			120	99
5			120	93

Entry	Substrate	Product	Time	Yield[a]
6	CH₃CH₂CH₂CH₂OH	CH₃CH₂CH₂CH₂OSiMe₃	90	78
7	n-pentyl-OH	n-pentyl-OSiMe₃	100	78
8	Ph(CH₂)₃OH	Ph(CH₂)₃OSiMe₃	120	56
9	PhCH₂CH₂OH	PhCH₂CH₂OSiMe₃	120	89
10	PhCH(CH₃)CH₂OH	PhCH(CH₃)CH₂OSiMe₃	120	97
11	(CH₃)₂CHCH₂OH	(CH₃)₂CHCH₂OSiMe₃	90	61
12	CH₂=CHCH₂OH	CH₂=CHCH₂OSiMe₃	60	98
13	HC≡CCH₂OH	HC≡CCH₂OSiMe₃	90	79
14	1-naphthol (OH)	1-naphthyl-OSiMe₃	20	98
15	Ph-OH	Ph-OSiMe₃	20	99
15	CH₃CH₂CH(Ph)OH	CH₃CH₂CH(Ph)OSiMe₃	120	-
16	(CH₃)₂CHOH	(CH₃)₂CHOSiMe₃	120	23
17	cyclohexyl-OH	cyclohexyl-OSiMe₃	120	82
18	(CH₃)₃COH	(CH₃)₃COSiMe₃	120	-
19	Ph₃COH	Ph₃COSiMe₃	120	-

[a]GC yield

We also explored the ability of LaCoO₃ and HMDS to discriminate between different kinds of hydroxy groups of alcohols and the selectivity is outlined in Scheme 2. The results showed that secondary alcohols are more reactive than tertiary alcohols, while, primary alcohols are more reactive than the secondary alcohols. It seems that the higher reactivity of primary alcohols in comparison with secondary and tertiary alcohols is due

to their less steric hindrance for attacking to HMDS. Figure 1 shows the GC-Mass results in a binary mixture of benzyl alcohol and cyclohexanol, the benzyl alcohol was converted to the silyl ether product in 82% yield, while only 18% of the corresponding trimethylsilyl ether was observed for the cyclohexanol. A and C are related to the benzyloxy(trimethyl)silane and cyclohexyloxy(trimethyl)silane, respectively.
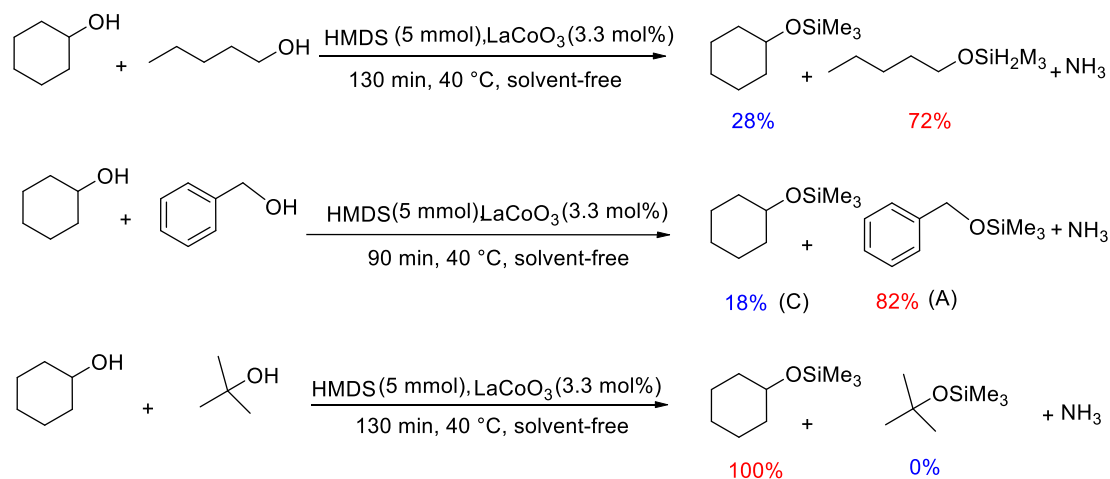
Scheme 2. Comparison of reactivity of between hydroxy groups of alcohols (alcohol: 10 mmol)
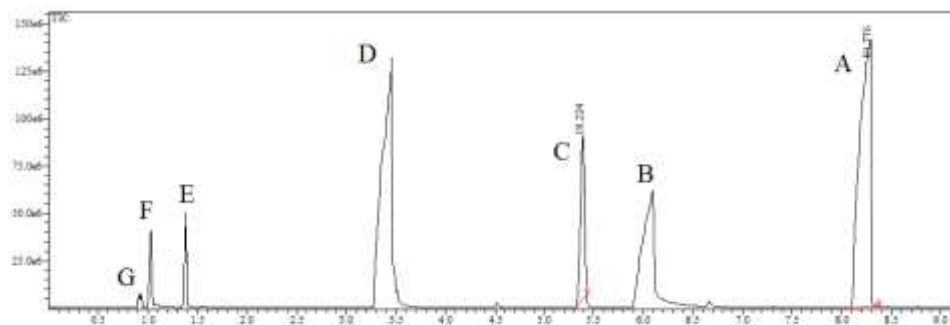
Figure 1. GC chromatogram related the mixture of reaction for trimethylsilylation of benzyl alcohol and cyclohexanol by the catalyst. A: benzyloxy(trimethyl)silane, B: benzyl alcohol, C: cyclohexyloxy(trimethyl)silane, D: cyclohexanol, E: impurity, F: impurity, and G: acetone

GC-Mass results for trimethylsilylation of α-naphtol and mass spectrum of trimethyl(1-naphthyloxy)silane are shown in Figure 2. In the mass spectrum of trimethyl(1-naphthyloxy)silane, the intense molecular ion peak is at $m/z = 216$ and the intense peak at $m/z = 201$ is due to loss of a methyl group.

A plausible mechanism for catalytic trimethylsilylation of alcohols by LaCoO$_3$ is shown in Scheme 3. The La and Co cationic sites as Lewis acids polarizing the Si-N bonds in HMDS and converts it to a reactive silylating agent. Finally, the hydroxyl group of alcohols and phenols are silylated and ammonia gas is released as a by-product [10].

(a)

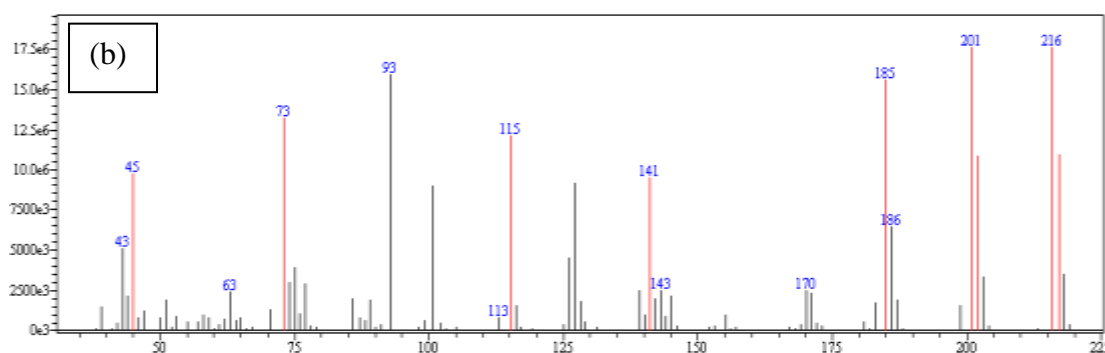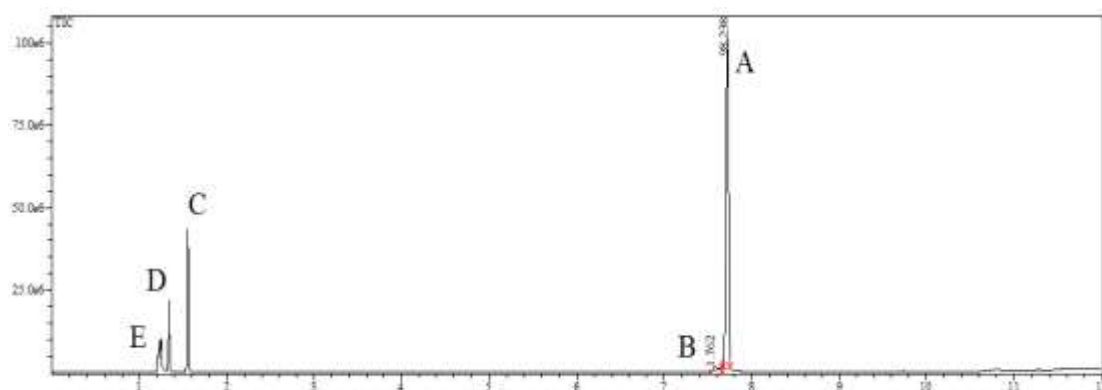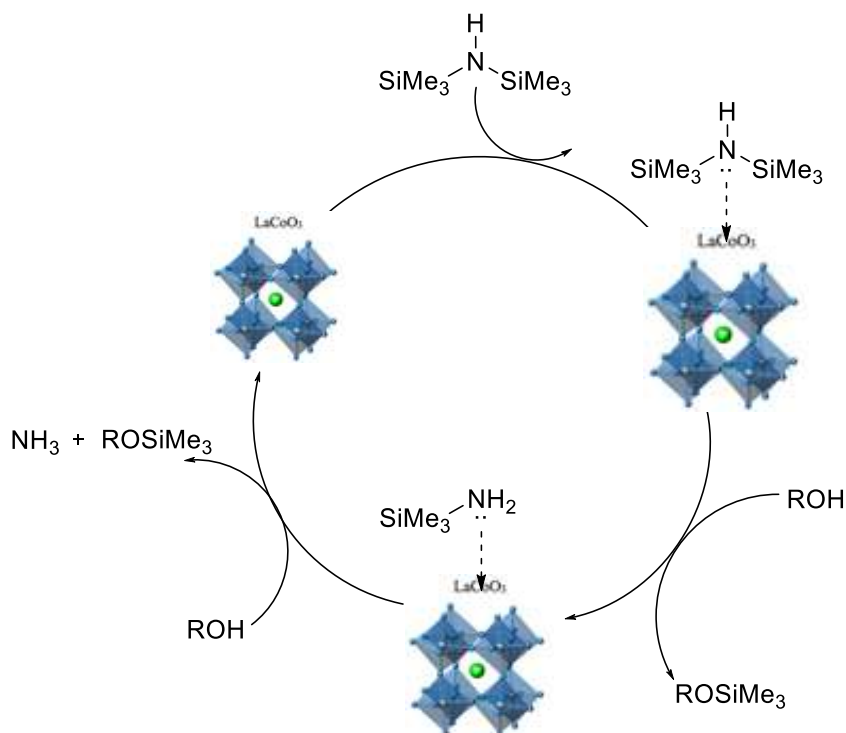**Figure 2.** (a) GC chromatogram related the mixture of reaction for trimethylsilylation of α-naphtol (A: trimethyl(1-naphthyloxy)silane, B: α-naphtol, (C) HMDS, (D) impurity, and (E) acetone.) and (b) mass spectrum of trimethyl(1-naphthyloxy)silane

Scheme 3. Proposed mechanism for trimethylsilylation of alcohols with HMDS catalyzed by $LaCoO_3$

The catalytic role of $LaCoO_3$ for the trimethylsilylation of α-naphtol has been compared with previously reported catalysts and the results are summarized in Table 2. This catalytic method offers several advantages, in comparison with other previously reported procedures, including high-efficiency product, trace amounts of catalyst to the substrate, inexpensive and non-toxic catalyst, and easy and clean reaction process.

Table 2. Comparison of the activity of various catalysts in the silylation of α-naphtol with HMDS

Entry	Catalyst	Condition	Time (min)	Yeild (%)	Ref.
1	$LiClO_4$-SiO_2	CH_2Cl_2, RT	120	90	21
2	MMT-K10	CH_2Cl_2, RT	-	92	22
3	I_2	CH_2Cl_2, RT	-	-	7
4	NBS	CH_2Cl_2, RT	180	93	8
5	$CuSO_4.5H_2O$	CH_3CN, reflux	38h	50	9
6	KBr	CH_3CN, RT	7-8	85	23
7	$Si(CH_3)_3Cl$	Solvent-free, 125°C	-	-	24
8	$LaCoO_3$	Solvent-free, 40 °C	20	98	This work

Conclusion

We have reported a new catalytic protocol for the efficient and selective trimethylsilylation of alcohol and phenols in the presence of $LaCoO_3$ under solvent-free and ambient conditions. This clean methodology offers non-toxic conditions, high selectivity, cost-effective reagents and catalyst, and an easy workup.

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