LiHSO₄/SiO₂ as a New, Efficient and Reusable Catalytic System for the Chemoselective Conversion of Aldehydes to Acylals under Solvent-Free Conditions

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Abstract: A highly efficient, green and expeditious solvent-free method is described for the chemoselective conversion of aldehydes to the corresponding acylals in excellent yields, using acetic anhydride in the presence of catalytic amount (20 mol%) of silica-supported LiHSO₄. Ketones does not react under these reaction conditions. LiHSO₄/SiO₂ can be recovered and reused without any significant loss of its catalytic activity.

Keywords: LiHSO₄/SiO₂, Aldehyde, Acylal, Solvent-free, Acetic anhydride and Green chemistry.

Introduction

Selective protection of carbonyl function as acylals is an important transformation in organic chemistry because of their stability under neutral and basic conditions as well as under critically controlled acidic conditions¹⁻³. Acylals have been also used as substrates for nucleophilic substitution reactions^{4,5}. As synthons, they have been exploited in well-known reactions of organic chemistry, like Grignard⁶, Barbier⁷, Knoevenagel⁸, and benzoin type reactions⁹, and have been also used in the total syntheses of sphingofungins E and F¹⁰. Their utility in the cotton¹¹ and other industries have been also well established¹². Because of their

unique properties as protective groups as well as important synthons, search for new and efficient preparation of acylals is of current interest. The most common method for the preparation of acylals is acylation of carbonyl compounds with acetic anhydride catalyzed by protic or Lewis acids, such as Nafion-H¹³, H₆P₂W₁₈O₆₂·24H₂O¹⁴, supported H₃PMo₁₂O₄₀¹⁵, In(OTf)₃¹⁶, AlPW₁₂O₄₀¹⁷, Ce(OTf)₄·xH₂O¹⁸, RuCl₃·xH₂O¹⁹, P₂O₅/montmorillonite K-10²⁰, ZrCl₄²¹, P₂O₅/Al₂O₃²², Bi(OTf)₃·xH₂O²³, HClO₄/SiO₂²⁴, Sc(OTf)₃²⁵, Er(OTf)₃²⁶, and WCl₆²⁷. However, most of the reported methods are associated with one or more of the following drawbacks: (i) lack of substrate tolerance and generality, (ii) long reaction time, (iii) low yield and selectivity, (iv) the use of large amount of reagent, (v) the use of harmful and volatile organic solvents, and subsequently no agreement with the green chemistry protocols, (vi) rigorous reaction conditions, and (vii) application of expensive, non-recoverable, non-available, corrosive as well as moisture and air-sensitive reagents. Therefore, search for finding a protocol for the synthesis of acylals that are not associated with the above disadvantages is still relevant.

Recently, the use of catalysts and reagents supported on solid supports as well as solvent-free conditions has been developed because such reagents not only cause to simplify the purification processes but also help to prevent the releasing of toxic reaction residues into the environment²⁸⁻³⁹. Moreover, due to moisture sensitivity of some reagents; application of them in organic reactions is difficult. This problem can be solved by supporting of them on solid supports²⁸⁻³⁹. Handling of solid-supported reagents is also easy. In addition, these reagents can be removed from the reaction mixture by simple filtration. Silica gel is one of the most interesting solid supports and is inexpensive, reusable, commercially available and environmentally benign that has been used in various organic transformations³³⁻³⁹. More recently, we introduced silica-supported LiHSO₄ as a new, highly efficient, non-toxic, green, readily producible, heterogeneous and reusable catalyst for the synthesis of bis(indolyl)methanes³⁵. In this catalyst, the strong oxophilicity of Li⁺ as well as H⁺ of HSO₄⁻ powerfully activates oxygen-containing electrophiles for nucleophilic attack^{35,40,41}.

In this paper, we wish to extend application of our catalyst, LiHSO₄/SiO₂, in organic synthesis. Herein, we report our results on the synthesis of acylals from aldehydes and acetic anhydride in the presence of catalytic amount of silica-supported LiHSO₄ under solvent-free conditions at room temperature (Scheme 1). It is noteworthy that this method has none of the above-mentioned drawbacks at all.

Scheme 1

Experimental

All chemicals were purchased from Merck or Fluka Chemical Companies. H₂SO₄ 98% was used for the preparation of LiHSO₄. Silica gel 60, 0.063-0.200 mm (7-230 mesh ASTM) was applied as support. All products are known and their structures were identified by comparison of their IR and ¹H NMR data and melting points with those in the authentic samples. IR spectra were run on a Shimadzu FTIR-8300 spectrophotometer. The ¹H NMR (250 MHz) was run on a Bruker Avance DPX-250 FT-NMR spectrometer. Microanalyses were performed on a Perkin-Elmer 240-B microanalyzer. Melting points were recorded on a Stuart Scientific Apparatus SMP3 (UK) in open capillary tubes.

Preparation of LiHSO₄

A mixture of LiCl (0.848 g, 20 mmol) and H₂SO₄ (2.002 g, 20 mmol) was stirred under N₂ gas for 120 min to give LiHSO₄ (2.080 g) as a white powder. The HCl gas produced was trapped with NaOH solution³⁵.

Preparation of LiHSO₄/SiO₂ catalytic system

A mixture of LiHSO₄ (2 g) and SiO₂ (2 g) was ground vigorously in a mortar to give LiHSO₄/SiO₂ catalytic system as a white powder (4 g)³⁵.

General procedure for the chemoselective conversion of aldehydes to acylals

To a mixture of acetic anhydride (0.817 g, 8 mmol) and LiHSO₄/SiO₂ (0.083 g, 0.4 mmol) in a 10 mL round-bottomed flask was added aldehyde (2 mmol), and the resulting mixture was stirred at room temperature. After completion of the reaction, as monitored by TLC, to it was added EtOAc (30 mL), stirred for 1 min and filtered to separate the catalyst. The filtrate was washed with saturated solution of NaHCO₃ (2×20 mL), and then with saturated brine (2×20 mL). The organic layer was dried with Na₂SO₄ and the solvent was evaporated to afford the pure product or chromatographed on silica gel (petroleum ether/EtOAc) where necessary. The recycled catalyst was washed by EtOAc, dried and reused.

Selected spectral data of the products

Table 3, Entry 1

IR (KBr): 3067, 2952, 1754, 1503, 1441, 1242, 1010, 951 cm⁻¹; ¹H NMR (CDCl₃): δ 2.09 (s, 6H), 7.36-7.40 (m, 3H), 7.50-7.53 (m, 2H), 7.65 (s, 1H); Anal. calcd. for C₁₁H₁₂O₄: C, 63.45; H, 5.81. Found: C, 63.68; H, 5.69.

Table 3, Entry 3

IR (KBr): 2961, 1757, 1625, 1536, 1349, 1234, 995 cm⁻¹; ¹H NMR (CDCl₃): δ 2.13 (s, 6H), 7.76 (d, 2H, *J* = 7.9 Hz), 8.25 (d, 2H, *J* = 7.9 Hz), 7.71 (s, 1H); Anal. calcd. for C₁₁H₁₁NO₆: C, 52.18; H, 4.38; N, 5.53. Found: C, 51.99; H, 4.51; N, 5.44.

Table 3, Entry 16

IR (KBr): 3114, 1751, 1609, 1501, 1374, 1140, 960 cm⁻¹; ¹H NMR (CDCl₃): δ 2.15 (s, 6H), 6.42 (m, 1H), 6.59 (m, 1H), 7.38 (m, 1H), 7.76 (s, 1H); Anal. calcd. for C₉H₁₀O₅: C, 54.55; H, 5.09. Found: C, 54.81; H, 5.23.

Results and Discussion

Initially the catalytic system, LiHSO₄/SiO₂ (50% W/W), was prepared by grinding LiHSO₄ and SiO₂ in a mortar. Afterward, the effect of different molar ratios of the catalyst on acylation of benzaldehyde with acetic anhydride under solvent-free conditions at room temperature was studied. The results are summarized in Table 1. As Table 1 indicates, the reasonable results were observed when the reaction was performed in the presence of 20 mol% of LiHSO₄/SiO₂.

Table 1. Effect of different molar ratios of LiHSO₄/SiO₂ on the acylation of benzaldehyde with acetic anhydride.

Entry	Molar ratio of LiHSO ₄ /SiO ₂ , %	Time, min	Yield ^a , %
1	5	20	73
2	15	15	95
3	20	12	97
4	30	10	97

^aIsolated yield.

To prove the better catalytic activity of the supported catalyst over LiHSO₄, the reaction of benzaldehyde with acetic anhydride was examined using LiHSO₄ and SiO₂ separately (Table 2). As Table 2 demonstrates, silica-supported LiHSO₄ was more efficient than LiHSO₄ and SiO₂ separately.

Table 2. The reaction of benzaldehyde with acetic anhydride using LiHSO₄ and SiO₂ separately.

Entry	Catalyst	Time, min	Yield ^a , %
1	No catalyst	720	-
2	LiHSO ₄	15	91
3	SiO ₂	720	39
4	LiHSO ₄ /SiO ₂	12	97

^aIsolated yield

To assess the scope and the efficiency of the method, different aromatic and aliphatic aldehydes were acylated with acetic anhydride in the presence of LiHSO₄/SiO₂ under solvent-free conditions at room temperature to furnish the corresponding acylals. The results are displayed in Table 3.

Table 3. Conversion of aldehydes to acylals using LiHSO₄/SiO₂ under solvent-free conditions at room temperature.

Entry	Product	Time, min	Yield ^a , %	M.p. °C (Lit.)
1		12	97	44-46 (42-43) ²²
2		12	94	98-100 (101) ²⁴
3		10	97	123-125 (125) ²⁴
4		10	98	60-62 (64-66) ¹⁶
5		15	90	87-89 (85-86) ¹⁶
6		10	96	78-80 (80) ²⁴
7		10	98	60-62 (65-66) ²²
8		12	90	97-99 (100-102) ²⁴
9		10	94	83-85 (84) ²⁴
10		20	86	Oil (Oil) ²²
11		15	92	55-57 (57) ²⁴
12		15	90	55-57 (57) ²⁴

Contd...

Table 3. Continued.

Entry	Product	Time, min	Yield ^a , %	M.p. °C (Lit.)
13		600	-	-
14		12	93	83-85 (81-82) ¹⁹
15		12	92	124-126 (128-130) ²¹
16 ^b		20	84	50-52 (51-52) ²²
17 ^c		20	89	169-171 (174-175) ²⁴
18		20	86	Oil (Oil) ²²

^aIsolated yield. ^bThis reaction was carried out using 15 mol% of the catalyst in CH₂Cl₂. ^cIn this reaction, the aldehyde/Ac₂O ratio (mol/mol) was 1/8, and 30 mol% of the catalyst was applied.

As can be seen from Table 3, benzaldehyde, 2-naphthaldehyde and aromatic aldehydes possessing electron-withdrawing substituents, halogens and electron-releasing substituents on the aromatic ring afforded the corresponding acylals in excellent yields and in short reaction times (Table 3, entries 1-9, 11, 12, 14 and 15). Nevertheless, the powerful electron-releasing substituent OMe slightly decreased the yield and increased the reaction time (Table 3, entry 10). It is noteworthy that *p*-hydroxybenzaldehyde gave the corresponding triacetate (Table 3, entry 11). The acylation reaction was not carried out when *p*-(dimethylamino)benzaldehyde was used (Table 3, entry 13). The conversion of aldehydes to acylals was also performed successfully in the case of acid-sensitive aldehyde furfural, terephthalaldehyde and aliphatic aldehydes (Table 3, entries 16-18).

In order to show the high selectivity of the method, we studied competitive reactions for the acylation of aldehydes in the presence of ketones using LiHSO₄/SiO₂ as catalyst. Using this catalytic system, the highly selective conversion of an aldehyde in the presence of a ketone was observed (Scheme 2).

Ease of recycling of the catalyst is one of the most advantages of our method. For the reaction of benzaldehyde with acetic anhydride no significant loss of the product yield was observed when LiHSO₄/SiO₂ was reused even after three times recycling (Table 4).

Table 4. The synthesis of acylal from benzaldehyde and acetic anhydride in the presence of recycled LiHSO₄/SiO₂.

Entry	Cycle	Time, min	Yield ^a , %
1	1 st use	12	97
2	2 nd use	14	96
3	3 rd use	18	93
5	4 th use	25	89

^aIsolated yield.

Conclusions

In summary, we have developed a new method for the chemoselective conversion of aldehydes to acylals. The advantages of this method are efficiency, generality, high yield, short reaction time, low cost, cleaner reaction profile, simplicity, ease of preparation of the catalyst, ease of product isolation, and compliance with the green chemistry protocols.

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