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H_2SO_4-silica as an efficient and chemoselective catalyst for the synthesis of acylal from aldehydes under solvent-free conditions

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A variety of aldehydes react with acetic anhydride in the presence of a catalytic amount of H_2SO_4-silica to afford the corresponding 1,1-diacetates (acylals) in excellent yields. Ketones are not affected under the reaction conditions. The advantages are the simplicity of the acylation procedure, and the relatively non-toxic nature of the catalyst as well as its easy availability and low cost.

Key Words: Acylals, aldehydes, catalysis, solvent-free reactions, H_2SO_4-silica.

Introduction

The use of protecting groups is very important in organic synthesis, being often the key for the success of many synthetic enterprises. Acylals (geminal diesters) are frequently used as protecting groups for aldehydes because they are stable to both neutral and basic media as well as under acidic conditions.[1] Having masked aldehydic functionality, acylals have been used as a valuable intermediate in various organic syntheses.[2–4] In addition, they can be used as building blocks for the synthesis of dienes for Diels-Alder cycloaddition reactions.[5]

Generally, acylals are prepared by treating aldehydes with acetic anhydride in the presence of protonic acids, Lewis acids, heteropoly acids, or clays.[6] Some examples of the reagents and catalysts that have been developed for this purpose include LiOTf,[7] ceric ammonium nitrate,[8] $InCl_3$,[9] H_2NSO_3H,[10] $LiBF_4$,[11] H_2SO_4,[12] PCl_3,[13] NBS,[14] I_2,[15] TMSCl-NaI,[16] and $FeCl_3$.[17] Although some of these methods have convenient protocols with good to high yields, the majority of these methods suffer at least from one of the following disadvantages:

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reaction under oxidizing conditions, prolonged reaction time, high temperatures, use of moisture-sensitive and expensive catalysts, use of solvents, stringent conditions, difficulty in scaling up, etc. Therefore, development of catalysts working under mild reaction conditions is desirable.

Recently, the use of catalysts and reagents supported on solid supports and solvent-free conditions was developed because such reagents not only simplify the purification processes but also help to prevent the releasing of toxic reaction residues into the environment.[18–22]

Experimental

All yields refer to isolated products after purification. All the products were confirmed by comparison with authentic samples (mp, TLC, FTIR, and ^{1}H-NMR). FTIR spectra were recorded on a Perkin Elmer RXI spectrometer. NMR spectra were recorded on a Varian EM-390 NMR spectrometer operating at 300 MHz. The spectra were measured in $CDCl_3$ (unless otherwise stated) relative to TMS.

Preparation of H_2SO_4-silica

In a mortar silica gel (0.063-0.2 mm 2 g) and H_2SO_4 (98% 1 g 10 mmol) were ground with a pestle and the residue was heated at 100 °C for 12 h to furnish H_2SO_4-silica as a free flowing powder (3 mg = 0.01 mmol of H_2SO_4).

Typical procedure for acylal formation

A mixture of aldehyde (10 mmol), freshly distilled Ac_2O (40 mmol), and H_2SO_4-silica (3 mg, 1 mol%) was stirred at ambient temperature and the progress of the reaction was monitored by TLC. After completion of the reaction, the catalyst was filtered and washed with ethyl acetate. The combined organic layers were washed with saturated $NaHCO_3$ solution (3 × 10 mL) and water (10 mL) and then dried (Na_2SO_4). The solvents were removed on a rotary evaporator to give almost pure product, which was characterized by FT-IR and ^{1}H-NMR spectroscopy.

1,1-Diacetoxy-1- phenyl methane (Entry 1): mp 44 °C (Lit[29], 44-45 °C), ^{1}H-NMR δH = 2.10 (s, 6H), 7.40-7.42 (m, 3H), 7.52-7.55 (m, 2H), 7.69 (s, 1H) ppm; IR (KBr) ν = 1756, 1510, 1440, 1250, 1220, 1010 cm^{-1}.

1,1-Diacetoxy-1-(2-nitrophenyl) methane (Entry 2): mp. 87 °C (Lit.[29] 88 °C); ^{1}H-NMR ($CDCl_3$) δH = 2.15 (brs, 6H), 7.62 (m, 2H), 7.73 (m, 1H), 8.04 (d, 1H). 8.21 (s, 1H) ppm; IR ($CHCl_3$): 3019, 1763, 1534, 1374, 1216, 757, 669 cm^1.

1,1-Diacetoxy-1-(3-nitrophenyl) methane (Entry 3): mp 66 °C (Lit.[30] 65-66 °C); ^{1}H-NMR δH = 2.17 (s, 6H), 7.61 (t, J = 7.9 Hz, 1H), 7.74 (s, 1H), 7.84 (d, J= 7.7 Hz, 1H), 8.28 (dd, J= 1.1 and 8.2 Hz, 1H), 8.40 (s, 1H) ppm; IR (KBr): ν = 670, 680, 695, 740, 815, 1010, 1200, 1235, 1350, 1530, 1760, 3010, 3090 cm^{-1}.

1,1-Diacetoxy-1-(3,4-dimethoxyphenyl)methane (Entry 4): mp 64 °C, (Lit.[31] 65-66 °C) ^{1}H-NMR ($CDCl_3$): δH = 2.12 (s, 6H), 3.89 (s, 3H), 3.91 (s, 3H), 6.87 (d, 1H, J= 8.2 Hz), 7.00 (s, 1H), 7.10 (d, 1H, J = 8.2 Hz), 7.62 (s, 1H) ppm; IR (KBr) ν = 1750 cm^{-1}.

1,1-Diacetoxy-1-(2,4-dichlorophenyl) methane (Entry 5): mp 100 °C (Lit.[32])^{1}H-NMR ($CDCl_3$), δ H = 2.16 (s, 6H), 7.32-7.34 (m, 1H), 7.45-7.53 (m, 1H), 7.67 (s, 1H), 7.89-7.93 (m, 1H) pmm; IR (KBr) ν = 1763, 1541, 1473, 1233, 1199, 1012 cm^{-1}.

1,1-Diacetoxy-1-(3,4,5-trimethoxyphenyl)methane (Entry 6): mp 112-114 °C (Lit.[33] 114-116 °C) ^{1}H-NMR ($CDCl_3$), δH = 2.10 (s, 6H), 3.77 (s, 3H), 3.82 (s, 6H), 6.73 (s, 2H), 7.56 (s, 1H) ppm, IR (KBr) ν = 1750 cm^{-1}.

1,1-Diacetoxy-1-(4-flourophenyl) methane (Entry 7): mp 51 °C (Lit.[34] 50-51 °C) ^{1}H-NMR ($CDCl_3$) δH = 2.10 (s, 6H); 6.9-7.2 (m, 2H), 7.2-7.4 (m, 2H) 7.80 (s, 1H) ppm, IR (KBr) ν = 3014, 2913, 1764, 1749, 1609, 1477, 1370, 1237, 1201, 1037, 795, 675 cm^{-1}.

1,1-Diacetoxy-1-(4-chlorophenyl) methane (Entry 8): mp 83 °C (Lit.[30] 82-83 °C); ^{1}H-NMR ($CDCl_3$) δH = 2.10 (s, 6H); 7.33-7.46 (m, 4H), 7.62 (s, 1H) ppm, IR (KBr) ν = 3014, 2913, 1764, 1749, 1609, 1477, 1370, 1237, 1201, 1037, 795, 675 cm^{-1}.

1,1-Diacetoxy-1-(4-methoxyphenyl) methane (Entry 9): mp 64-65 °C (Lit.[30] 65-66 °C) ^{1}H-NMR ($CDCl_3$): δH = 2.11 (s, 6H), 3.81 (s, 3H), 6.95 (d, J= 8.5 Hz, 2H), 7.45 (d, J= 8.5 Hz, 2H), 7.56 (s, 1H) ppm; IR (KBr) ν = 1745 cm^{-1}.

1,1-Diacetoxy-1-(2-metoxyphenyl) methane (Entry 10): mp 69 °C (Lit.[30] 68-70 °C) ^{1}H-NMR ($CDCl_3$): δH = 2.11 (s, 6H), 3.85 (s, 3H), 6.91 (dd, J =8.1, 1.5 Hz, 1H), 6.99 (td, J =7.6, 1.8 Hz, 1H), 7.37 (td, J =8.1, 1H), 7.48 (dd, J =7.6, 1.8 Hz, 1H), 8.02 (s, 1H) ppm; IR (KBr) ν = 1760, 1244, 1203, 1000, 760 cm^{-1}.

1,1-Diacetoxy-1-(α-methylcinnamyl) methane (Entry 11): mp. 92-94 °C (Lit.[29]); ^{1}H-NMR ($CDCl_3$) δH = 1.95 (s, 3H), 2.18 (s, 6H), 6.75 (s, 1H), 7.21-7.53 (m, 5H). IR ($CHCl_3$) ν = 3020, 2975, 2876, 1765, 1610, 472, 1216, 1011, 768, 650 cm^{-1}.

1,1-Diacetoxy-1-(cinnamyl) methane (Entry 12): mp 83 °C (Lit.[30] 84-86 °C); ^{1}H-NMR ($CDCl_3$) δH = 2.11 (s, 6H), 6.15 (dd, J = 15 Hz, 6 Hz, 1H), 6.82 (d, J = 15 Hz, 1H), 7.28-7.34 (m, 5H), 7.38 (d, J = 6 Hz, 1H) ppm; IR ($CHCl_3$) ν = 3020, 2971, 2876, 1759, 1601, 472, 1216, 1011, 759, 669 cm^{-1}.

1,1-Diacetoxy-1-(furyl) methane (Entry 13): mp 52 °C (Lit.[30] 52-53 °C); ^{1}H-NMR ($CDCl_3$)) δH = 2.12 (s, 6H), 6.38 (d, J = 3 Hz, 1H), 6.51 (d, J = 2 Hz, 1H), 7.44 (brs, 1H), 7.70 (s, 1H) ppm; IR ($CHCl_3$) ν = 3021, 1763, 1372, 1218, 755, 668 cm^{-1}.

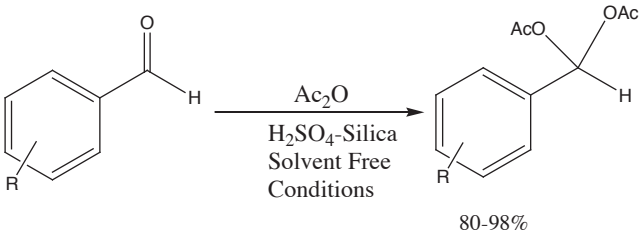
1,1-Diacetoxy-1-(5-methylfuryl) methane (Entry 14): mp 89-91 °C (Lit.[30] 90-92 °C), ^{1}H-NMR: δH = 2.15 (s, 6H), 2.35 (s, 3H), 6.0 (d, J= 3.1 Hz, 1H), 6.42 (d, J= 3.1 Hz, 1H), 7.6 (s, 1H) ppm; IR (KBr) ν = 3100, 2940, 1758, 1572, 1376, 1243, 1202, 1025, 955 cm^{-1}.

1,1-Diacetoxybuthane (Entry 16): Oil; (Lit.[29]), ^{1}H-NMR: δH = 0.94 (t, J= 5 Hz, 3H), 1.42-1.45 (m, 2H), 1.77-1.79 (m, 2H), 2.06 (s, 6H), 6.81 (t, J = 5.5 Hz, 1H) ppm; IR (KBr) ν = 2956, 2880, 1755, 1250, 1225, 1080 cm^{-1}.

Results and discussion

Noting recent reports on the use of silica–sulfuric acid[23–25] and sulfuric acid immobilized on silica (H_2SO_4-silica)[26–28] for various organic transformations, herein we wish to report an extremely convenient, mild, and

highly chemoselective procedure for the conversion of aldehydes to the corresponding acylals in the presence of acetic anhydride and catalytic amount of H_2SO_4-silica under solvent-free conditions (Scheme 1).



Scheme 1

Initially we attempted the acylation reaction of benzaldehyde with acetic anhydride in the presence of H_2SO_4-silica. The treatment of 1 equivalent of benzaldehyde with 4 equivalents of acetic anhydride in the presence of H_2SO_4-silica (1 mol%) afforded corresponding acylal in a short time in almost quantitative yield. In a control experiment, we observed that the reaction does not take place in the absence of H_2SO_4-silica. To optimize the reaction conditions, we tried to convert benzaldehyde to its corresponding acylal in various solvents and also under solvent-free conditions (Table 1).

Table 1. Conversion of benzaldehyde to its corresponding diacetate in different solvents and under solvent-free conditions in the presence of H_2SO_4-silica[a] at rt.

Entry	Solvent	Yield[b]	Time (min)
1	THF	65	1
2	Ethyl acetate	70	2
3	Methanol	90	10
4	Acetonitrile	75	1
5	Dichloromethane	85	3
6	Solvent-Free Conditions	98	1

[a] benzaldehyde/Ac_2O/H_2SO_4-silica (1:4:0.01 mmol). [b] The yields refer to isolated pure products.

As shown in Table 1, in comparison to conventional methods in solution the yield of the reaction under solvent-free conditions is higher and the reaction time is shorter. Therefore, we employed the above conditions for the conversion of various aldehydes to the corresponding acylals under solvent-free conditions (Table 2).

The results listed in Table 2 show that both aromatic and aliphatic aldehydes react smoothly with acetic anhydride to afford the corresponding geminal diacetates in good to excellent yields. Deactivated aldehydes such as *m*-nitrobenzaldehyde and *o*-nitrobenzaldehyde can also produce good yields. Moreover, it should be noted that steric hindrance seems to have no significant effects on the efficiency of this transformation considering that 2,4-dichlorobenzylaldehyde and 2-methoxy benzaldehyde afforded the corresponding acylals in high yields within a short reaction time (Table 2, entry 5 and 10). The tolerance of various functional groups under the present reaction conditions is also worthy of mention in those acid sensitive or oxidizable groups such as furfural derivatives, and the methoxy group and double bonds do survive under such conditions.

Table 2. Formation of acylals using H_2SO_4-silica under solvent-free conditions at room temperature.[a,b]

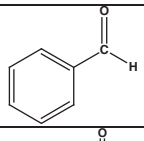
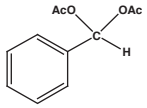
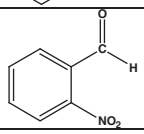
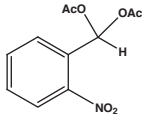
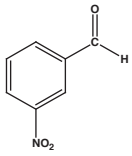
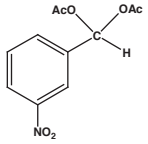
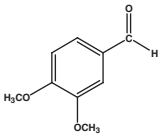
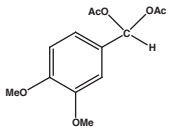
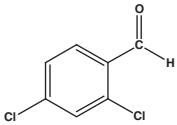
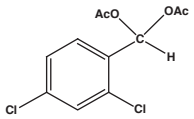
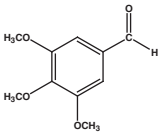
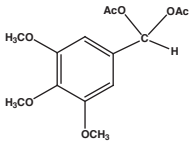
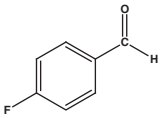
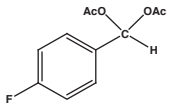
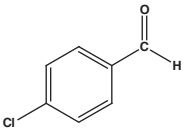
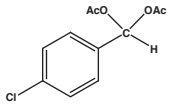
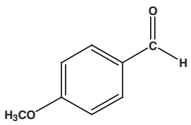
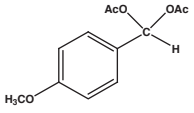
Entry	Substrate	Product	Time (min)	Yield
1			2	98
2			5	94
3			5	97
4			6	90
5			4	91
6			7	87
7			10	92
8			11	85
9			30	90

Table 2. Contunied.

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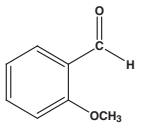
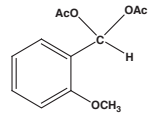
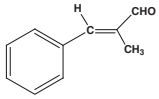
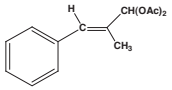
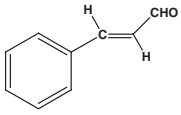
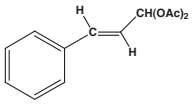
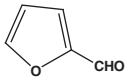
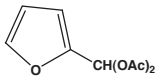
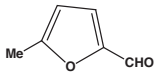
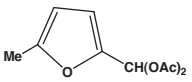
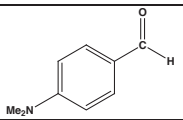
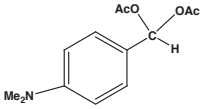
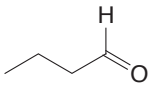
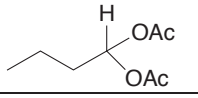
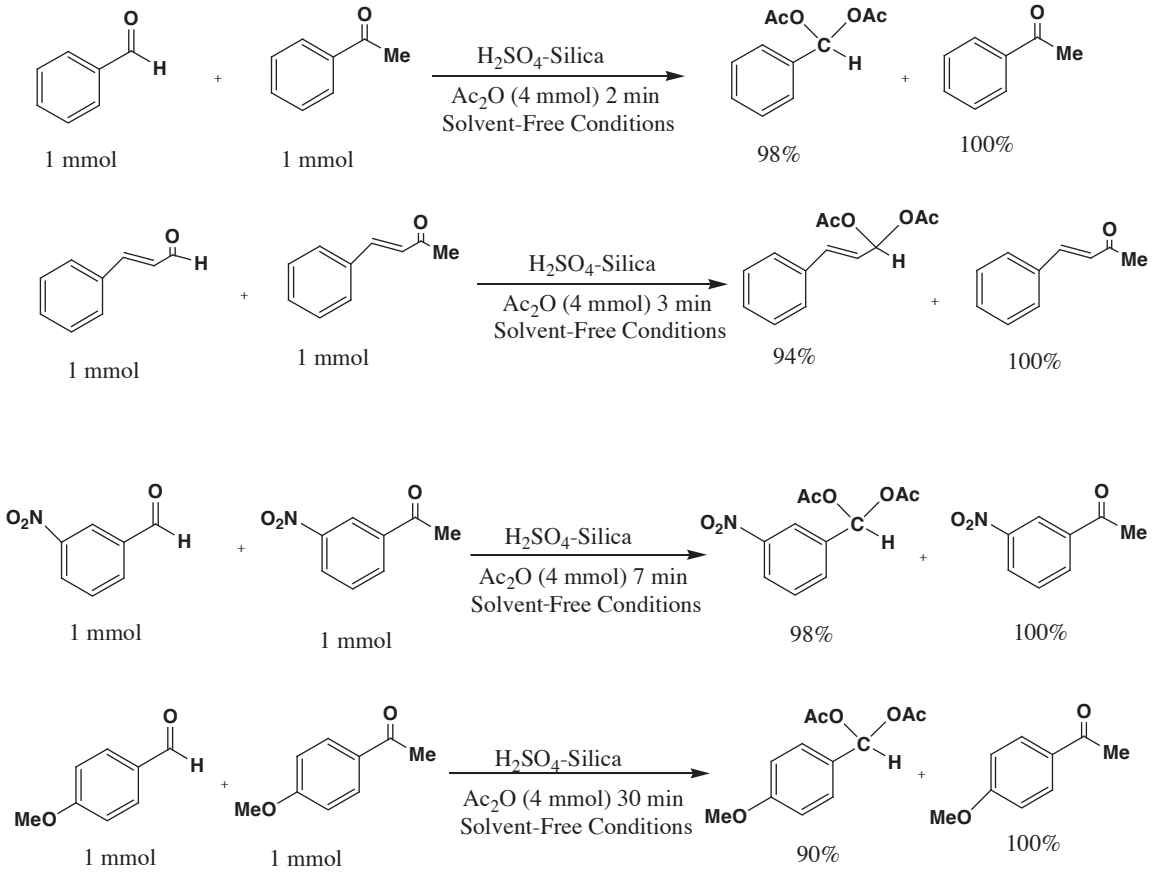
10			5	83
11			5	85
12			3	94
13			35	80 [c]
14			35	80 [c]
15			24 h	-[d]
16			10	85

[a] The yields refer to the isolated pure products. [b] The products were characterized from their spectral (IR and ^{1}H-NMR) and comparison to authentic samples. [c] The reaction was carried out at 0-5 °C. [d] No reaction.

Finally, to evaluate the selectivity of this method, we investigated competitive reactions for acylation of aldehydes in the presence of ketones using H_2SO_4-silica as catalyst. With this catalytic system the highly selective conversion of aldehydes in the presence of ketones was observed (Scheme 2).

In conclusion, H_2SO_4-silica is a chemoselective and highly efficient catalyst for acylal formation from aldehydes. The advantages of this methodology over the reported methods is the availability of the starting materials, simplicity of acylation procedure, a clean work-up, a short reaction time, and high yields. The catalyst system is a free flowing powder that can be stored at room temperature for several months without losing its catalytic potentiality and it may be considered a very cheap source of solid supported acidic catalyst compared to other commercially available expensive solid supported acids. However, preparation of H_2SO_4-silica is straightforward and handling of the reagent is also easy. In addition, this reagent acts as an insoluble catalyst that could be removed from the reaction mixture by simple filtration.



Scheme 2.

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