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Ying Zhao^a, Li-Bin Liu^a, Zhuo Chen^a, Tong-Shuang Li^a & Tong-Shou Jin^a ^a Department of Chemistry, College of Chemistry and Environmental Science, Hebei University, Baoding, China Published online: 24 Feb 2007.

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Rapid and Efficient Method for Acetylation of Alcohols and Phenols with Acetic Anhydride Catalyzed by Silica Sulfate

Tong-Shou Jin, Ying Zhao, Li-Bin Liu, Zhuo Chen, and Tong-Shuang Li Department of Chemistry, College of Chemistry and Environmental

Science, Hebei University, Baoding, China

Abstract: A rapid and efficient method is described for acetylation of a series of alcohols and phenols with acetic anhydride catalyzed by silica sulfate solid acid at room temperature or at refluxing temperature in excellent yield.

Keywords: Acetylation, alcohol, phenol, silica sulfate

INTRODUCTION

The hydroxyl group is nucleophilic and easily oxidized by a wide range of reagents. Because it can participate in a great number of transformations under mild conditions, the most important thing in organic synthesis is to ensure that a specific hydroxyl function in a multifunctional molecule is protected from unwanted reactions. Esters are the most used protective groups in organic synthesis.^[1] The routine acylation of alcohols and phenols is carried out by acetic anhydride or acetyl chloride in the presence of tertiary amines such as triethylamine and pyridine.^[2] Protonic acids, Lewis acids, and several solid catalysts have recently been found to get better results for the acetylation of alcohols and phenols.^[3–10] Each of the methods has its merits and shortcomings. These methods have not been

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Address correspondence to Tong-Shou Jin, Department of Chemistry, College of Chemistry and Environmental Science, Hebei University, No. 88 Hezuo Road, Baoding 071002, China. E-mail: orgsyn@mail.hbu.edu.cn entirely satisfactory; for example, triethylamine and pyridine have unpleasant odor and are not easy to remove. In this article we reveal a novel method for the acylation of alcohols and phenols with acetic anhydride catalyzed by silica sulfate.

Silica sulfate, a new type of solid acid, has been studied recently.^[11,12] We believe that the silica sulfate is superior to the other reported acidic solid supports or acidic resins, such as polysyrene sulfonic acid and Nafion-H, for running reactions under heterogeneous conditions. Therefore, we are interested in using this inorganic acidic resin as a new sulfuric acid function. Herein we demonstrate a rapid and efficient method for acetylation of a series of alcohols and phenols with acetic anhydride catalyzed by silica sulfate solid acid at room temperature or at refluxing temperature (Scheme 1).

RESULTS AND DISCUSSION

The results of a series of alcohols and phenols with acetic anhydride catalyzed by silica sulfate solid acid at room temperature or at refluxing temperature are summarized in Table 1.

As shown in Table 1, a series of alcohols and phenols were treated with acetic anhydride in the presence of silica sulfate in CH_2Cl_2 , $CHCl_3$ at room temperature or at refluxing temperature. As for alcohols, primary (1, 2, 3, 4, 5, and 9) and secondary (6,7, 8, 9, and 10) alcohols can be easily acetylated at room temperature. However, the hindered tertiary alcohol shows the lowest activity. For example, triphenylmethanol (11) is acetylated with acetic anhydride in the presence of silica sulfate at refluxing temperature with a longer reaction time (3 h), but it remains unchanged. Therefore, primary and secondary alcohols can be acetylated more easily than tertiary alcohol.

The phenols with either electron-donating or electron-withdrawing groups (12, 13, 14, 16, 17, 18, 19, 23, and 24) can afford high yields of products at room temperature in a short time. When 2-nitrophenol (15) was treated with acetic gave anhydride in the presence of silica sulfate, conversion to 2-nitrophenyl acetate gave only 58% yield at room temperature in 3 h, but only 5 min at refluxing CHCl₃ under catalysis of silica sulfate gave 92% yield. The explanation for this result may be the formation of a intramolecular hydrogen bond in 2-nitrophenol, which would reduce the activity of the molecule at room temperature, whereas heating destructs this structure. Furthermore, we also find that polyhydroxy compounds could be transformed

R-OH +
$$Ac_2O$$
 silica sulfate
r.t or reflux R-OAc + AcOH
1 2 3

Scheme 1.

	Substrate	Solvent/ Temp (°C)/T (min)	Yield $(\%)^a$	Product	Bp (Torr) or Mp (°C)	
Entry					Found	Reported ^[13]
1	1-Heptanol 1	CHCl ₃ /rt/2	91	1-Heptanyl acetate	96-98/20	191-192/760
2	1-Octanol 2	$CHCl_3/rt/1$	90	1-Octyl acetate	102 - 104/20	211.5/760
3	1-Octadecanol 3	$CHCl_3/rt/1$	79	1-Octadecanyl acetate	32-33	33
4	Benzyl alcohol 4	$CHCl_3/rt/2$	90	Benzyl acetate	115-117/20	134/102
5	2-Phenylethanol 5	$CHCl_3/rt/3$	93	2-Phenylethyl acetate	122 - 124/20	232/760
6	Benzoin 6	$CHCl_3/rt/3$	87	Benzoin acetate	82-83	83
7	Cyclohexanol 7	$CHCl_3/rt/4$	92	Cyclohexyl acetate	80 - 82/25	175/760
8	Cholesterol 8	$CHCl_3/rt/1$	80	Cholesteryl acetate	113-114	114-115
9	Betulinol 9	$CHCl_3/rt/2$	82	Betulin-3,22-diyl diacetate	218-220	218-220
10	Diphenyl methanol 10	CHCl ₃ /rt/1	90	Diphenyl methanyl acetate	41-42	41-42
11	Triphenyl methanol 11	CHCl ₃ /62/180	NR^b			
12	Phenol 12	$CH_2Cl_2/rt/1.5$	87	Phenyl acetate	95-96/20	196/760
13	3-Methylphenol 13	$CHCl_3/rt/3$	94	3-Methylphenyl acetate	102 - 104/20	212/760
14	4-Methylphenol 14	$CH_2Cl_2/rt/2$	94	4-Methylphenyl acetate	102 - 104/20	212-213/760
15	2-Nitrophenol 15	CHCl ₃ /62/5	92	2-Nitrophenyl acetate	39-40	40-41
16	3-Nitrophenol 16	$CH_2Cl_2/rt/3$	98	3-Nitrophenyl acetate	55-56	55-56
17	4-Nitrophenol 17	$CH_2Cl_2/rt/1$	93	4-Nitrophenyl acetate	80-82	81-82
18	4-Chlorophenol 18	$CH_2Cl_2/rt/1$	94	4-Chlorophenyl acetate	106-108/20	226-228/760

Table 1.	Acetylation	of alcohols and	phenols catal	yzed by	/ silica	sulfate
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(continued)

Acetylation of Alcohols and Phenols

Table 1.	Continued.
1 11010 11	Commucu.

		Solvent/ Temp (°C)/T (min)	Yield $(\%)^a$	Product	Bp (Torr) or Mp (°C)	
Entry	Substrate				Found	Reported ^[13]
19	2,4-Dichlorophenol 19	$CH_2Cl_2/rt/5$	86	2,4-Dichlorophenyl acetate	124-126/20	244-245/760
20	Catechol 20	CHCl ₃ /rt/1	88	Benzene-1,2-diyl diacetate	62-63	63.5
21	Resorcinol 21	CHCl ₃ /rt/0.5	91	Benzene-1,3-diyl diacetate	158-160/20	278/760
22	Hydroquinone 22	CHCl ₃ /rt/1	83	Benzene-1,4-diyl diacetate	121-122	123-124
23	1-Naphthol 23	CHCl ₃ /rt/1	90	1-Naphthyl acetate	48-49	48-49
24 25	2-Naphthol 24 2,4,6-Tritertbutylphenol 25	CH ₂ Cl ₂ /rt/1 CHCl ₃ /62/60	$\frac{88}{\mathrm{NR}^b}$	2-Naphthyl acetate	69-70	70

^{*a*}Yields refer to isolated products. ^{*b*}No reaction.

Acetylation of Alcohols and Phenols

into the corresponding polyacetates (9, 20, 21, and 22). In addition, 2,4,6-tritertbutylphenol 25 treated with acetic anhydride remained unchanged in the presence of silica sulfate in refluxing $CHCl_3$ for 1 h. This result may be due to the steric effect.

The catalyst was easily regenerated by washing with diethyl ether, followed by drying at room temperature for 4 h. The catalyst could be reused five times for the synthesis of **16** without significant loss of activity.

In conclusion, silica sulfate is good for acetylation of alcohols, phenols, and polyhydroxy compounds. This method offers several advantages including mild reaction conditions, cleaner reactions, and high yield of products, as well as simple experimental and isolation procedures, which make it a useful and attractive process for the acetylation.

EXPERIMENTAL

Melting and boiling points are uncorrected. Liquid alcohols and phenols were purified by distillation before use. The products were characterized by their melting or boiling points and/or IR and ¹H NMR. IR spectra were recorded on a Bio-Rad FIS-40 spectrometer (KBr). ¹H NMR spectra were measured on an Avance-400 spectrometer using TMS as internal standard and CDCl₃ as solvent.

Preparation of the Catalyst^[12]

Silica gel (100 g) was soaked with CH_2Cl_2 (50 mL), and then chlorosulfonic (58.3 g, 0.5 moL) acid was added slowly with stirring at room temperature. After the addition was completed, the mixture was shaken for 60 min. The solvent was evaporated under reduced pressure. A white solid powder was obtained and stored in a desiccator until use.

General Procedure

Mixture of the alcohol or phenol (1, 1 mmol), acetic anhydride (2, 2 mmol), silica sulfate (80 mg), and solvent (CH₂Cl₂ or CHCl₃, 5 mL) is stirred at room temperature or refluxing temperature for the length of time indicated in Table 1. The progress of the reactions is monitored by TLC. After completion of the reaction, the solvent was evaporated and diethyl ether (10 mL) was added to the mixture. The catalyst was removed by filtration and washed with diethyl ether (2 \times 5 mL). The filtrate was washed with 5% HCl (10 mL), 5% NaHCO₃ (10 mL), and brine (2 \times 10 mL) successively. After drying with anhydrous sodium sulfate, the solvent was evaporated under reduced pressure and the crude product purified by reduced pressure distillation or recrystallization from 95% ethanol to get the pure product.

Selected Spectral Data of Some Products

1-Octyl acetate: $\delta_{\rm H}$ 0.88 (3H, t, $-CH_3$), 1.20–1.43 [10H, m, $CH_3(CH_2)_5$ -], 1.78 (2H, m, CH_2CH_2 OOC CH_3), 2.04 (3H, s, $-OCOCH_3$), 4.05 (2H, t, $-CH_2OCOCH_3$).

Benzyl acetate: δ_H 2.07 (3H, s, -OCOCH₃), 5.09 (2H, s, ArCH₂-), 7.26–7.36 (5H, m, -C₆H₅).

2-Phenylethyl acetate: $\delta_{\rm H}$ 2.04 (3H, s, 1-OCOCH₃), 2.82 (2H, t, J = 7 Hz, 2-CH₂), 4.83 (2H, t, J = 7 Hz, 1-CH₂), 7.15–7.38 (5H, m, 2-C₆H₅).

1–Octadecanyl acetate: $\delta_{\rm H}$ 0.89 (3H, t, –CH₃), 1.27 [30H, m, CH₃(CH₂)₁₅-], 1.80 (2H, m, –CH₂CH₂OOC CH₃), 4.34 (2H, t, –CH₂OCOCH₃), 2.02 (3H, s, –OCOCH₃).

Benzoin acetate: δ_H 7.30–8.01 (10H, m, Ar-H), 5.82 (1H, s, –CH), 2.03 (3H, s, –OCOCH₃).

Cyclohexyl acetate: $\delta_{\rm H}$ 1.25–1.60(10H, m, $-C_6H_{11}$), 3.02 (1H, m, $-CHOOCCH_3$), 2.00 (3H, s, $-OCOCH_3$).

Cholesteryl acetate: $\delta_{\rm H}$ 5.39 (1H, d, J = 4.4 Hz, 6-H), 4.64 (1H, m, 3α -H), 1.04 (3H, s, 19-CH₃), 0.94 (3H, d, J = 6.4 Hz, 21–CH₃), 0.88 (6H, d, J = 6.4 Hz, 26, 27–CH₃), 0.70 (3H, s, 18–CH₃), 2.05 (3H, s, 3-OCOCH₃).

Betulinyl-3,22-diyl diacetate: $\delta_{\rm H}$ 4.71 (1H, s, 29-H), 4.61 (1H, s, 29-H'), 4.27 (1H, d, J = 11.2 Hz, 28-H), 3.87 (1H, d, J = 11.2 Hz, 28-H'), 2.32 (1H, m, 3-H), 1.66–1.08 (complex, CH₂, CH), 1.70 (3H, s, 30–CH₃), 1.41, 1.05, 0.99, 0.87, 0.85 (15H, all s, 5 × CH₃), 2.09 (3H, s, 3-OCOCH₃), 2.06 (3H, s, 22–OCOCH₃).

4-Methylphenyl acetate: δ_H 2.01 (3H, s, –OCOCH₃), 2.25 (3H, s, -Ar-CH₃), 6.92 (2H, d, 2',6'-Ar-H), 7.04 (2H, d, 3',5'-Ar-H).

4–Chlorophenyl acetate: $\delta_{\rm H}$ 1.98 (3H, s, –OCOCH₃), 6.98 (2H, d, 2',6'-Ar-H), 7.25 (2H, d, 3',5'-Ar-H).

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