



Synthesis of 1,1-Diacetates Catalyzed by Cellulose Sulfonic Acid from Aldehydes and Acetic Anhydride

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1,1-Diacetates have been synthesized in good to excellent yields *via* a reaction of corresponding aldehydes and acetic anhydride in the presence of cellulose sulfonic acid as a heterogeneous catalyst at room temperature. The protection of aldehydes generated an anhydromer as single product under similar reaction conditions. The catalysis is equally applicable for the deprotection of acylal in acetonitrile.

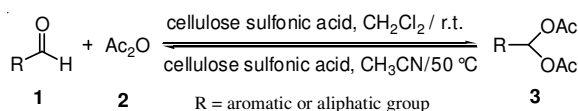
Keywords: 1,1-Diacetates, Cellulose sulfonic acid, Reusable catalyst, Protection, Deprotection.

INTRODUCTION

Selective protection and deprotection of carbonyl groups have been a subject of great interest to research workers in modern organic chemistry¹⁻⁵. The use of protecting groups is of great importance in organic synthesis, being often a valuable intermediate in various organic syntheses^{6,7}. About the protection of the carbonyl group, the preparation of 1,1-diacetates from aldehydes and acetic anhydride is the most common route. 1,1-Diacetates are stable in neutral and basic media and easy to convert to corresponding aldehydes⁸⁻¹⁰.

So far, several improved methods have been reported using a variety of catalysts such as $\text{Al}(\text{HSO}_4)_3$ ¹¹, zinc metal¹², $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ ¹³, $\text{P}_2\text{O}_5/\text{Al}_2\text{O}_3$ ¹⁴, SbCl_3 ¹⁵, KHSO_4 ¹⁶, $\text{HClO}_4\text{-SiO}_2$ ¹⁷, FeCl_3 ¹⁸, LiBr ¹⁹, $\text{In}(\text{OTf})_3$ ¹⁹, $\text{TiCl}_3(\text{OTf})$ ²⁰, InBr_3 ²¹, $\text{HBF}_4\text{-SiO}_2$ ²², $\text{SO}_4^{2-}/\text{SnO}_2$ ²³ and LiBF_4 ²⁴ under different kinds of conditions. However, most of these methods require expensive or wasteful reagents, long reaction times, tedious work-up procedure and give unsatisfied yields. So, a simple, efficient, environmental and economical catalyst is in great demand.

As a solid acid catalyst, cellulose sulfonic acid is efficient and easy to handle. In addition, cellulose has several unique properties, which make it attractive alternative for the support for catalytic applications. Cellulose is the most abundant natural material on earth and it has been widely studied recently. Hereby, we wish to report an efficient and reusable catalyst called cellulose sulfonic acid to these reactions (**Scheme-I**).



Scheme-I: Protection-deprotection reactions of aldehydes

EXPERIMENTAL

All reagents and solvents were purchased from commercial sources, unless otherwise noted and were used without purification. Melting points were determined on a SGW X-4 melting-point apparatus with microscope and were uncorrected. Infrared spectra were recorded on an IR Prestige-21 FTIR spectrophotometer (KBr). ¹H NMR spectra were recorded on a Bruker Avance-II spectrometer at 400 MHz with TMS and referenced to CDCl_3 ; δ values are reported in ppm and *J* values in Hz.

Catalyst preparation: To a magnetically stirred mixture of cellulose (3 g, DEAE for column chromatography) in CHCl_3 (20 mL), chlorosulfonic acid (0.60 g) was added dropwise at 0 °C during 1 h. After addition was complete, the mixture was stirred for 1 h until HCl was removed from reaction vessel. Then, the mixture was filtered and washed with ice water (30 mL) and dried at room temperature to obtain cellulose sulfonic acid as white powder.

General procedure for the preparation of 1,1-diacetates: To a mixture of aldehyde (2 mmol) and acetic anhydride (1 mL) was added cellulose sulfonic acid (0.05 g), the reaction mixture was mixed well and stirred at room temperature. After completion of the reaction, as indicated by TLC, dichloromethane (20 mL) was added and the catalyst was separated by filtration. The organic substance was washed with 10 % NaHCO_3 solution. The organic layer was dried over anhydrous Na_2SO_4 and evaporated. The isolated crude product was purified by preparative TLC to provide the corresponding 1,1-diacetates.

General procedure for the deprotection of 1,1-diacetates: The cellulose sulfonic acid (0.05 g) was added to a stirred solution of 1,1-diacetate (2 mmol) in acetonitrile (10 mL) at

50 °C in a round-bottom flask with a reflux condenser. After completion of the reaction (monitored by TLC), the reaction mixture was filtered to separate the catalyst which is reusable. The filtrate was extracted with dichloromethane and dried over anhydrous Na_2SO_4 . The dichloromethane solution was evaporated under reduced pressure to provide the crude product. Then the isolated crude product was purified by TLC to provide the corresponding aldehydes in pure form.

1,1-Diacetoxy-1-phenyl-methane (entry 1): ^1H NMR (CDCl_3 , 400 MHz): δ = 2.02 (s, 6H), 7.35-7.43 (m, 3H), 7.52-7.55 (s, 2H), 7.72 (s, 1H); IR (KBr, ν_{max} , cm^{-1}): 3060, 1752, 1602, 1470, 1378, 1245, 1210, 1065, 1015, 758, 702.

1,1-Diacetoxy-1-(4-chlorophenyl)methane (entry 2): ^1H NMR (CDCl_3 , 400 MHz): δ = 2.18 (s, 6H), 7.38 (d, J = 6.4 Hz, 2H), 7.46 (d, J = 6.4 Hz, 2H), 7.63 (s, 1H); IR (KBr, ν_{max} , cm^{-1}): 3014, 2913, 1764, 1749, 1609, 1477, 1370, 1237, 1201, 1037, 795, 675.

1,1-Diacetoxy-1-(2-methoxyphenyl)methane (entry 3): ^1H NMR (CDCl_3 , 400 MHz): δ = 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 Hz, 1H), 7.48 (dd, J = 7.6, 1.8 Hz, 1H), 8.02 (s, 1H); IR (KBr, ν_{max} , cm^{-1}): 1760, 1244, 1203, 1000, 760.

1,1-Diacetoxy-1-(4-methoxyphenyl)methane (entry 4): ^1H NMR (CDCl_3 , 400 MHz): δ = 2.11 (s, 6H), 3.81 (s, 3H), 6.75 (d, J = 9.0 Hz, 2H), 7.38 (d, J = 9.0 Hz, 2H), 7.42 (s, 1H);

IR (KBr, ν_{max} , cm^{-1}) = 3045, 3015, 1760, 1615, 1521, 1375, 1240, 1205, 995, 930.

1,1-Diacetoxy-1-(2-nitrophenyl)methane (entry 5): ^1H NMR (CDCl_3 , 400 MHz): δ = 2.15 (s, 6H), 7.54-7.66 (m, 1H), 7.70-7.73 (m, 2H), 8.05-8.08 (m, 1H), 8.21 (s, 1H); IR (KBr, ν_{max} , cm^{-1}): 3019, 1763, 1534, 1374, 1216, 757, 669.

1,1-Diacetate-1-(3-nitrophenyl)methane (entry 6): ^1H NMR (CDCl_3 , 400 MHz): δ = 8.39 (s, 1H), 8.28-8.24 (dd, J = 8.2, 1.2 Hz, 1H), 7.83 (d, J = 7.7 Hz, 1H), 7.72 (s, 1H), 7.61-7.57 (t, J = 8.0 Hz, 1H), 2.14 (s, 6H); IR (KBr, ν_{max} , cm^{-1}): 2963, 1760, 1533, 1358, 1255, 1203, 1091, 1016, 809, 685.

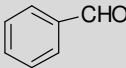
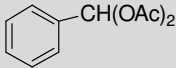
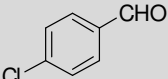
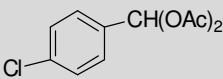
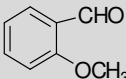
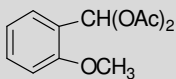
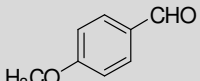
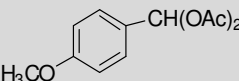
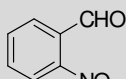
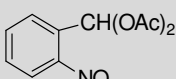
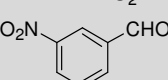
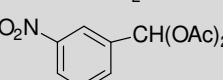
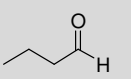
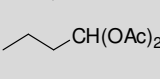
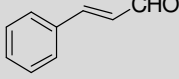
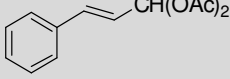
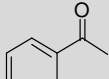
1,1-Diacetoxybutane (entry 7): ^1H NMR (CDCl_3 , 400 MHz): δ = 0.94 (t, J = 3.5 Hz, 3H), 1.42-1.45 (m, 2H), 1.77-1.79 (m, 2H), 2.06 (s, 6H), 6.80 (t, J = 5.5 Hz, 1H); IR (KBr, ν_{max} , cm^{-1}): 2956, 2880, 1755, 1250, 1225, 1080.

1,1-Diacetoxy-1-(cinnamyl)methane (entry 8): ^1H NMR (CDCl_3 , 400 MHz): δ = 2.11 (s, 6H), 6.15 (dd, J = 15.0 Hz, 6 Hz, 1H), 6.82 (d, J = 15.0 Hz, 1H), 7.28-7.34 (m, 5H), 7.38 (d, J = 6.0 Hz, 1H); IR (KBr, ν_{max} , cm^{-1}): 3020, 2971, 2876, 1759, 1601, 1472, 1216, 1011, 759, 669.

RESULTS AND DISCUSSION

As shown in Table-1, both aromatic and aliphatic aldehydes reacted smoothly with acetic anhydride to afford the corresponding *geminal* diacetates in good to excellent

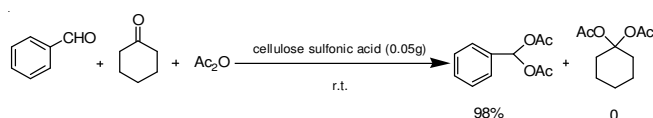
TABLE-1
PROTECTION REACTION OF ALDEHYDE CARBONYL CATALYZED BY CELLULOSE SULFONIC ACID

Entry	Substrate	Product	Time (min)	Yield ^a (%)	m.p. (°C)	
					Reported	Found
1			3	98	44-45 ¹⁰	41-42
2			3	92 ^b , 95, 95 ^c	82-83 ²⁵	81-83
3			3	88	68-70 ²⁶	69-70
4			3	95	65-66 ²⁶	65-67
5			3	92	88 ¹⁶	86
6			3	96	65-66 ²⁶	65
7			3	95	Oil ²⁷	Oil
8			3	93	86 ²⁷	85-87
9		-	180	0	-	-
10		-	180	0	-	-

^aYields refer to the isolated pure products. ^b0.045 g cellulose sulfonic acid, ^c0.055 g cellulose sulfonic acid was used

yields. Optimization of the reaction condition was studied with different quality of the catalyst. When 2 mmol of water participate in the reaction, 0.05 g of catalyst was the most appropriate condition (Table-1, Entry-2).

However, when cyclohexanone and acetophenone were used in this reaction, no corresponding product was obtained (Table-1, Entry 9, 10). In the case of substrates bearing aldehyde and ketone functionalities, only aldehyde was converted into 1,1-diacetate (**Scheme-II**).



Scheme-II: Protection reactions of aldehydes and ketones

Deprotection of acylals to their parent aldehydes is another important manipulation. The data shown in Table-2 indicates that the generality of this procedure is then proved by the deprotection of various acylals. It shows the results of the deprotection of acylals to the corresponding aldehydes using catalytic amounts of cellulose sulfonic acid in acetonitrile at different temperatures from Table-2, Entry 2, 3. It is observed that at room temperature the productive rate is lower.

Entry	Substrate	Time (h)	Product	Yield ^a (%)
1		0.5		85
2		0.5		30 ^b , 89
3		0.5		35 ^b , 92
4		0.5		93
5		0.5		90
6		0.5		87
7		0.5		88
8		0.5		96

^aYields refer to the isolated pure products; ^bHeating at room temperature

Conclusion

In summary, at room temperature, synthesis of 1,1-diacetates catalyzed by cellulose sulfonic acid can be achieved from aldehydes and acetic anhydride efficiently. The advantages of this protocol are mild reaction conditions, short reaction times and good yields. In addition, the catalysts equally applicable for the deprotection of acylal available.

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