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Preparation and deprotection of 1,1-diacetates (acylals) using zirconium sulfophenyl phosphonate as catalyst

Massimo Curini,[a,]* Francesco Epifano,[a] Maria Carla Marcotullio,[a] Ornelio Rosati[a] and Morena Nocchetti[b]

[a]*Dipartimento di Chimica e Tecnologia del Farmaco, Sezione di Chimica Organica, Facoltà di Farmacia, Università degli Studi, Via del Liceo, I-06123 Perugia, Italy*
[b]*Dipartimento di Chimica, Università degli Studi, Via del Liceo, I-06123 Perugia, Italy*

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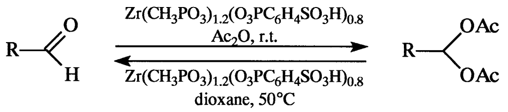
Abstract—Layered zirconium sulfophenyl phosphonate was found to be an efficient heterogeneous catalyst for the preparation and deprotection of 1,1-diacetates. © 2002 Elsevier Science Ltd. All rights reserved.

Acylals[1] are synthetically useful protecting groups for carbonyl compounds due to their stability and also important building blocks for the synthesis of dienes in Diels–Alder reaction.[2]

Usually the preparations of acylals were carried out using several catalysts such as protic[3] or Lewis acid,[4] iodine,[5] NBS.[6] The reported methods entail the problems of yield, long reaction time, corrosivity and difficult work-up. More recently the use of bismuth triflate[7] and lithium tetrafluoroborate[8] as catalysts has been reported. Several reports are available using heterogeneous catalyst such as zeolites,[9] sulfated zirconia,[10] montmorillonite clay,[11] expansive graphite[12] and zeolite HSZ-360.[13] However, none of the above mentioned catalysts is claimed to give protection as well as deprotection except expansive graphite[12] and HSZ-360.[13]

We have recently reported that layered zirconium sulfophenyl phosphonate bearing strongly acidic C_6H_4–SO_3H groups anchored to inorganic layers is an excellent heterogeneous catalyst for acid-catalyzed reactions.[14] The acid strength (Ho) of the catalyst should lie between pK_a values of −5.6 and −8.2 and it is similar to that of hydrogen montmorillonite but higher than that of Amberlyst 15. The strongly acidic catalyst compares favorably with the more common styrene–divinylbenzene sulfonic resin, does not show marked swelling phenomena in the presence of apolar or slightly polar solvents and possesses a good thermal resistance.

Herein we report a simple and efficient method for the preparation and deprotection of 1,1-diacetates from aldehydes using zirconium sulfophenyl phosphonate as catalyst (Scheme 1).



Scheme 1.

As shown in Table 1 different aromatic aldehydes are converted to the corresponding 1,1-diacetates in solvent free conditions using acetic anhydride as acylating agent in the presence of zirconium sulfophenyl phosphonate at room temperature in high yield and short reaction time (entries 1–8). Aliphatic as well as α,β-unsaturated aldehydes react in the same conditions leading acylals in good yield (entries 9–12).

It is worth noting that ketones were acetilated under these conditions in very poor yield (entry 13), or did not react at all (entry 14), hence the above method represents a selective preparation of acylals of aldehydes in the presence of ketones.

In a separate experiment an equimolar mixture of cyclohexanecarbaldehyde and cyclohexanone were kept

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Keywords: 1,1-diacetates (acylals); aldehydes; protection; deprotection; zirconium sulfophenyl phosphonate.

* Corresponding author. Tel.: +39-075-5855106; fax: +39-075-5855116; e-mail: curmax@unipg.it

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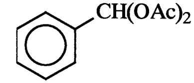
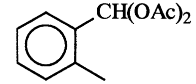
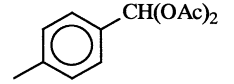
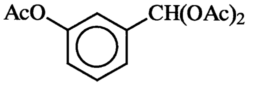
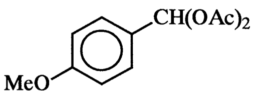
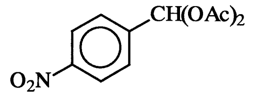
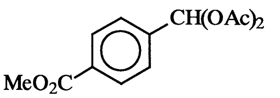
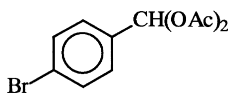
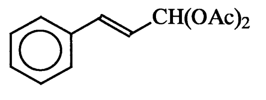
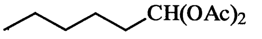
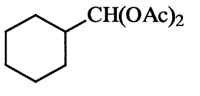
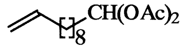
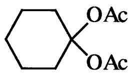
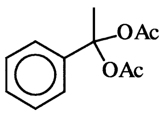
Table 1. Zirconium sulfophenyl phosphonate-catalyzed acylal formation and deprotection

		Preparation[18]		Deprotection[19]	
#	**1,1 Diacetates**	**Yield (%)[a]**	**Time (h)**	**Yield (%)[a]**	**Time (h)**
1		84	0.2	87[d]	4
2		83	0.2	86[d]	2
3		75	0.2	92[d]	1
4		71[b]	0.5	81[c,d]	5
5		84	1	90[d]	1
6		91	0.4	91[d]	24
7		74	0.4	89[d]	2
8		55	2.5	90[d]	5
9		72	3	95[d]	1
10		80	0.2	--[e]	24
11		71	5	32[d]	24
12		78	3	--[e]	24
13		21	4	--[e]	24
14		--	24	--[e]	24

[a] Isolated yields.

[b] Yields refers to pure triacetate.

[c] Yields refers to pure 4-formylphenyl acetate.[16]

[d] ^{1}H NMR and GC-MS of products are identical to commercial samples (Aldrich).

[e] No reaction.

under usual acylating conditions affording after 12 h the corresponding acylals with 73% of total yield and a 16:1 ratio; no other products were observed.

We next investigated the use of catalyst in deprotection of 1,1-diacetates to the corresponding aldehydes by treatment of 1,1-diacetates with zirconium sulfophenyl phosphonate in commercial dioxane at 50°C; by this procedure only aromatic and α,β-unsaturated acylals have been transformed into the corresponding aldehydes in high yields (entries 1–8).

When the reaction was carried out using aliphatic acylals, we obtained poor yields (32% for entry 11) or we recovered unreacted starting material (entries 10, 12 and 13).

The important features of this method are: mild reaction condition, simple work up and recyclable nature of the catalyst,[15] the preparation of which does not require particular skill.[14a]

In conclusion we report an efficient and selective method for the preparation of 1,1-diacetates from aldehydes in solvent free conditions, and a selective regeneration of aromatic aldehydes from the corresponding acylals using zirconium sulfophenyl phosphonate as catalyst.

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15. The catalyst, washed with dichloromethane and dried at 160°C, can be reused for several experiments. The reaction in entry 3 has been repeated three times with the following yields: 90, 87, 88%.
16. Analytical data for **4-formylphenyl acetate**. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 2.38 (s, 3H), 7.35 (ddd $J=8.0$, 2.6 and 1.2 Hz, 1H), 7.54 (t, $J=8.0$ Hz, 1H), 7.60 (m, 1H), 7.74 (br ddd, $J=7.5$, 1.2 and 1.2 Hz, 1H), 9.82 (s, 1H); GC–MS (m/z) 93, 122, 164 (M^+). Anal. calcd for $C_9H_8O_3$: C, 65.85; H, 4.91. Found: C, 65.82; H, 4.93.
17. Analytical data for selected compounds:
    (2*E*)-3-Phenylprop-2-ene-1,1-diacetate: ^{1}H NMR ($CDCl_3$, 200 MHz): δ 2.15 (s, 6H), 6.20 (dd $J=15.1$ and 6.8 Hz, 1H), 6.75 (d, $J=15.1$ Hz, 1H), 7.25–7.65 (m, 6H); GC–MS (m/z) 77, 104, 131, 174, 234 (M^+). Anal. calcd for $C_{13}H_{14}O_4$: C, 66.66; H, 6.02. Found: C, 66.63; H, 6.05.
    (4-Methoxyphenyl)methanediacetate: ^{1}H NMR ($CDCl_3$, 200 MHz): δ 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); GC–MS (m/z) 77, 92, 109, 137, 179, 238 (M^+). Anal. calcd for $C_{12}H_{14}O_5$: C, 60.50; H, 5.92. Found: C, 60.48; H, 5.95.
18. **Typical procedure for the preparation of 1,1-diacetates**: To a stirred suspension of aldehydes (1 mmol) and zirconium sulfophenyl phosphonate (20 mg) acetic anhydride (3 mmol) was added at room temperature with progress of reaction monitored by GC–MS. Stirring was continued for the appropriate time (see Table 1). The catalyst was then filtered and washed with dichloromethane, the organic layer was washed twice with a 5% solution of sodium bicarbonate, dried over anhydrous sodium sulfate and evaporated under reduced pressure. The residue was purified by flash chromatography (eluent hexane/ethyl acetate 19:1) or crystallization to give the corresponding 1,1-diacetates. All compounds were characterized by ^{1}H NMR and GC–MS.[17]
19. **Typical procedure for the deprotection of 1,1-diacetates**: To a stirred solution of 1,1-diacetate (1 mmol) in commercial dioxane (1 ml) was added zirconium sulfophenyl phosphonate (20 mg) at 50°C. Stirring was continued for the appropriate time (see Table 1) with progress of reaction monitored by GC–MS. The catalyst was then filtered and washed with dichloromethane. The organic layer was washed twice with 5% solution of sodium bicarbonate, dried over sodium sulfate and evaporated under reduced pressure. The residue was purified by flash chromatography (eluent hexane/EtOAc 15:1) to give the corresponding aldehydes.