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A Mild and Efficient Method for the Chemoselective Synthesis of Acylals from Aromatic Aldehydes and their Deprotections Catalyzed by Sulfated Zirconia

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Aldeídos podem ser convertidos a acilas por tratamento com anidrido acético na presença de zircônia sulfatada a 0 °C, com excelentes rendimentos. Cetonas e aldeídos alifáticos não são afetados nessas condições de reação. A desproteção das acilas resultantes é obtida usando-se o mesmo catalisador a 60 °C. O catalisador pode ser reutilizado por duas vezes sem perder sua atividade.

Aldehydes can be converted to acylals by treatment with acetic anhydride in the presence of sulfated zirconia in excellent yield at 0 °C. Ketones and aliphatic aldehydes are found to be unaffected under the reaction conditions. The deprotection of the resulting acylals is achieved using the same catalyst at 60 °C. The catalyst can be reused in two cycles without losing its activity.

Keywords: acylals, sulfated zirconia, protection, deprotection

Introduction

The use of protecting groups is very important in organic synthesis, being often the key for the success of many synthetic enterprises. *Geminal* or 1,1-diacetates are synthetically useful as aldehyde protecting groups,[1] as alternatives to acetals. These diacetates are stable towards aqueous acids and mild bases.[2] In addition, they can be used as building blocks for the synthesis of dienes for Diels-Alder cycloaddition reactions.[3] Chiral allylic esters have been obtained using palladium catalysts by an asymmetric allylic alkylation of gem-diesters[4] and also preparation of homoallyl acetates by allylation of 1,1-diacetates have been described.[5] Acetic anhydride is the most commonly reagent used for acylal formation, products are named 1,1 –diacetates. Some other substances and catalysts have been used for this reaction, $Bi(CF_3SO_3)_3.4H_2O$,[6] $Bi(NO_3)_3.5H_2O$,[7] $ZrCl_4$,[8] $(ALPW_{12}O_{40})$,[9] $Zn(BF_4)_2$,[10] LiOTf,[11] $(NH_4)_2Ce(NO_3)_6$,[12] $InCl_3$,[13] H_2NSO_3H,[14] $LiBF_4$,[15] $Cu(OTf)_2$,[16] H_2SO_4,[17] PCl_3,[18] NBS,[19] I_2,[20] $Sc(OTf)_3$,[21] TMSCl-NaI,[22] anhydrous $FeSO_4$,[23] $FeCl_3$,[24] $AlCl_3$.[25] Several inorganic heterogeneous catalysts: Nafion-H,[26] Zeolites,[27] Montmorillonite,[28] Envirocatsw,[29] Amberlyst,[30] zirconium sulfohenyl phosphonate,[31] have also been developed as catalysts for synthesis of acylals. The use of solid catalysts have received considerable attention in different areas of organic synthesis, due to their environmental compatibility, reusability, greater selectivity, experimental simplicity, low cost and ease of isolation of the products. In this context sulfated zirconium, was applied for performing the synthesis of heterocycles,[32,33] acylation of aromatics ketones,[34] and stereocontrolled glycosidations.[35]

Results and Discussion

Sulfated zirconia characterization, Figure 1 shows XRD plot corresponding to the crystalline zirconia. The sample analyzed presented tetragonal as unique phase (ICSD collection code: 066787) given by reflections in 2θ = 30.18° (relative intensity in 100) as well as peaks 34.616°, 35.283°, 43.002°, 50.214°, 50.770°, 59.291°, 60.187°, 62.724°, 72.894°, 74.617° and 81.768°.

Adsorption-desorption of nitrogen gave an isotherm plot type IV of BET classification (Brunauer Emmett and Teller theory), no microporous area was observed by t-plot equation. BET specific surface-area, pore volume and pore size values are in Table 1. The TPD curve consisted on two desorption peaks at 216 °C and 582 °C, and the number of

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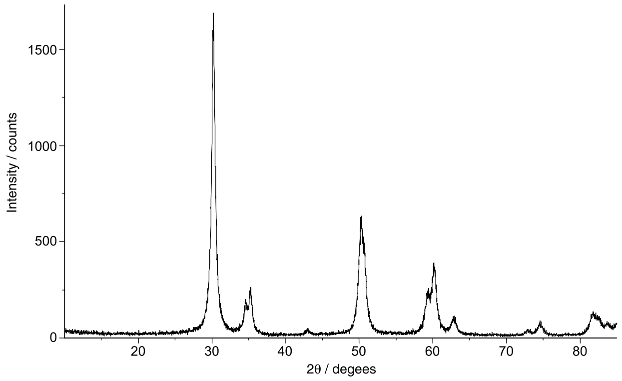


Figure 1. Difraction pattern of sulfated zirconia.

Table 1. Sulfated zirconia surface features.

Surface area	92.62 $m^2 g^{-1}$
Pore volume	0.10 cc g^{-1}
Pore size	46.05 Å

acid sites was measured by integration of peak area. The acidity result is 322 mmole NH_3 g^{-1}, desorption curve is showed in Figure 2.

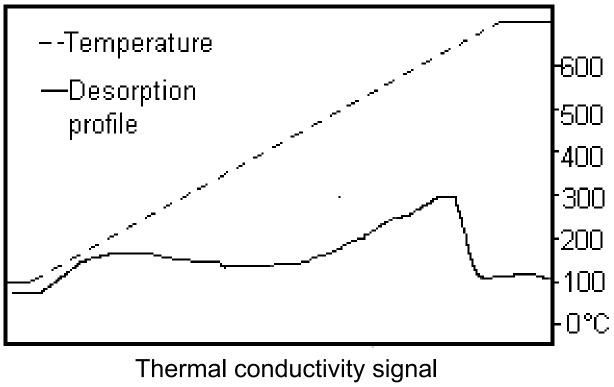
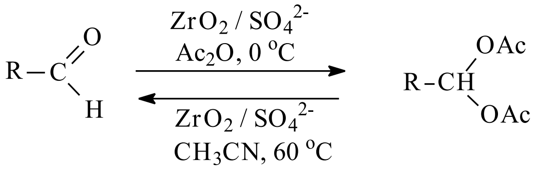


Figure 2. Ammonia desorption curve of sulfated zirconia.

To test the reciclability, the sulfated zirconia catalyst was filtered after reaction and activated at 500 °C for 1 h in air flow. There is no significant change in the activity and selectivity after two cycles.

A variety of aldehydes and ketones react with acetic anhydride at 110 °C in the presence of commercial sulfated zirconia[36] (10% m/m of carbonyl compound) with surface area of 10 $m^2 g^{-1}$ to afford the corresponding 1,1-diacetates. Sulfated metal oxides have gained attention due to their unusual ability to initiate acid catalyzed reactions at low temperatures.[37,38] We now wish to describe an more mild and efficient method for the chemoselective preparation and deprotection of acylals from aromatic and heteroaromatic aldehydes using prepared sulfated zirconia as catalyst (Scheme 1).



Scheme 1.

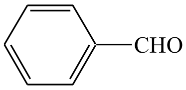
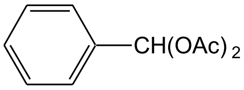
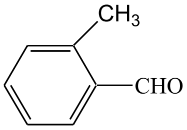
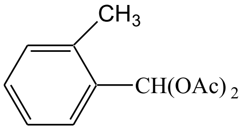
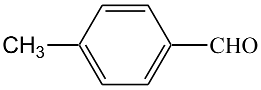
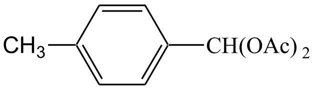
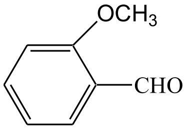
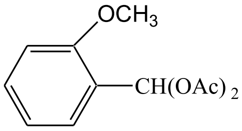
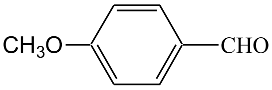
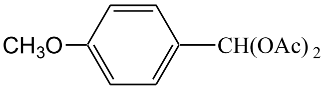
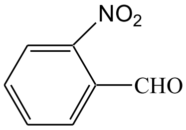
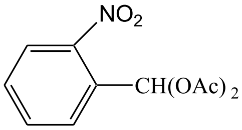
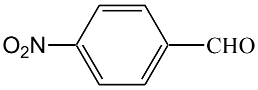
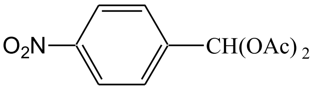
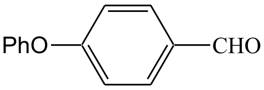
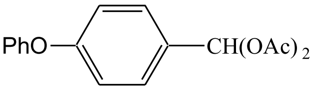
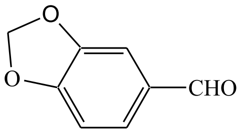
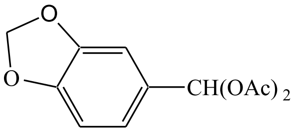
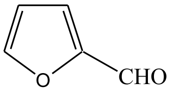
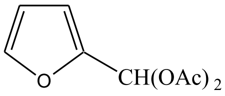
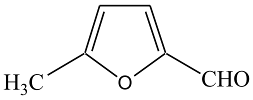
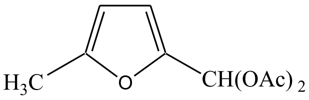
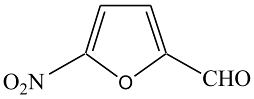
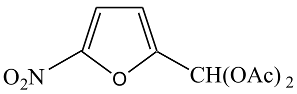
As shown in Table 2 different aromatic and heteroaromatic aldehydes are converted to the corresponding 1,1-diacetales in CH_3CN or solvent free conditions, using acetic anhydride as acylating agent in the presence of a catalytic amount of sulfated zirconia with a surface area of 92 $m^2 g^{-1}$ at 0 °C in high yield and short reaction time.

Acetaldehyde, chloroacetaldehyde and heptanal did not react under the same conditions. The presence of electron-donating and electron-withdrawing groups on the aromatic ring of aldehydes did not influenced in the significant yield. In a control experiment an equimolecular mixture of acetophenone and of benzaldehyde were kept under usual acylating conditions affording after 6 h the corresponding acylal of benzaldehyde. This experiment suggested that chemoselective protection of an aldehyde could be achieved. A few methods are reported in the literature for the conversion of acylals to the corresponding aldehydes.[39-41] However the strong acidic or basic conditions, the unsatisfactory yields, and high reaction temperatures discourage their use. Thus we next investigated the use of our catalyst in the deprotection of 1,1-diacetates to the corresponding aldehydes by treatment of 1,1-diacetates with sulfated zirconia in distilled acetonitrile at 60 °C. Under these conditions the acylals of *o*-anisaldehyde, 4-phenoxybenzaldehyde, *o*-tolualdehyde and *p*-tolualdehyde have been transformed into the corresponding aldehydes in quantitative yields.

Experimental

The reaction products of the protection were determined and analyzed by means of a Hewlett Packard GC/MS system 6890/5973 gas chromatograph with an HP-5 column, 70-270 °C (5 °C min^{-1}), Inj. 250 ºC, Det. 280 °C. Powder X-ray diffraction (XRD) patterns were obtained with a Philips X´Pert instrument using Cu Kα radiation (45kV, 40mA), Nitrogen adsorption/desorption isotherms were plotted at -196 °C on a Micromeritics ASAP 2020 equipment. UV-Vis difusse reflectance spectra were performed with a Varian CARY 16 spectrometer using a quartz cell. Temperature programmed desorption (TPD) measurements were acquired on a Micromeritics TPD/TPR 2900 instrument (sample was activated at 370 °C for 10 min in flowing He (10 mL min^{-1}) an then, saturation of

Table 2. Aldehydes convertion results

Entry	Substrate	time (h)	Product	Yield (%)[a]
1		6		97
2		5		99
3		5		94
4		5		97
5		5		95
6		7		86
7		6		90
8		6.5		92
9		9		753
10		5		85
11		8		98
12		8		95

[a] Isolated yields. Products were characterized by ^{1}H NMR, IR and Mass Spectroscopy.

ammonia at 100 °C (20% NH_3 in He) and desorption at 10 °C min^{-1} to 600 °C. The structure of all final compounds was supported by comparison with the standard mass spectrometry of organic compounds and their fragmentation pattern.[6,7,23,24,42] ^{1}H NMR spectra were measured on a Varian UNITY-300 spectrometer. Chemical shifts are reported in parts per million (δ) with tetramethylsilane as internal standard, coupling constants in Hz. Infrared (IR) spectra were recorded on a MAGNA-IR NICOLET spectrometer 750.

Procedure for the preparation of sulfated zirconia catalysts

1 mL of sulfuric acid (98% wt) was mixed with 3.5 mL of deionized water, 20 mL of zirconium isopropoxide (70% wt in 1-propanol) were diluted with 30.5 mL of n-propanol. The acid solution was added by dropwise to the alcoxide solution under vigorous stirring, until a viscous solution was obtained. The gel was heated at 80 °C to evaporate excess alcohol. After, the dry gel was calcinated at 600 °C for 7 h in air, leading to a white solid. The X-ray powder diffraction analysis of the sample revealed the presence of tetragonal zirconia sulfate species.[42]

General procedure for the preparation of glycal derivatives

A suspension of 25 mg of sulfated zirconia in acetonitrile HPLC grade (0.5 mL) was treated with 0.83 mmol of aldehyde and 2.50 mmol of acetic anhydride. The suspension mixture was stirred for the appropriate time (see Table 1) at 0 °C. The catalyst was then filtered and washed with EtOAc. The filtrate was evaporated under reduced pressure and extracted with EtOAc. The combined organic layers were dried (Na_2SO_4) and evaporated affording the corresponding gem-diacetates in excellent yield.

General procedure for acylal deprotection

A suspension of 25 mg of sulfated zirconia in HPLC acetonitrile (0.5 mL) was treated with 1 mmol of acylal at 60 °C for 6 hrs under nitrogen atmosphere. The catalyst was then filtered and washed with EtOAc. The filtrate was evaporated under reduced pressure, extracted with EtOAc and dried (Na_2SO_4).

1,1-Diacetoxy-1-(2-metoxy phenyl) methane. White solid (0.1 g, 95%) yield, mp 70-71 °C, Found: C, 60.63; H, 6.10; O, 33.27. Calc. For $C_{12}H_{14}O_5$: C, 60.50; H, 5.92; O, 33.58 %. IR (KBr) ν_{max}/cm^{-1}: 1760, 1244, 1203, 1000, 760; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.11 (s, 6H, CH3), 3.85 (s, 3H, CH3), 6.91 (dd, *J* 8.1, 1.5 Hz, 1H, Ar), 6.99 (td, *J* 7.6, 1.8 Hz,1H, Ar), 7.37 (td, *J* 8.1, 1H, 1.5 Ar), 7.48 (dd, *J* 7.6, 1.8 Hz, 1H, Ar), 8.02 (s, 1H, CH); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 20.9, 55.7, 85.7, 111.0, 120.5, 123.9, 126.9, 130.9, 157.0, 158.6; CIMS: *m/z* 239 (M+1)$^+$, 267 (M+29)$^+$, 279 (M+41)$^+$, 179, 137 (100%), 109, 61.

1,1-Diacetoxy-1-(4-phenoxy phenyl) methane. White solid isolated (0.13 g, 98%), mp 65-66 °C, Found: C, 68.22; H, 5.50; O, 26.28. Calc. For $C_{17}H_{16}O_5$: C, 67.99; H, 5.37; O, 26.64%. IR (KBr) ν_{max}/cm^{-1}: 1589, 1490, 1369, 1240, 1197; ^{1}H NMR (300 MHz, $CDCl_3$, δ 2.12 (s, 6H, CH_3), 6.99 (d, 2H, *J* 8.6 Hz, Ar), 7.02 – 7.14 (m, 3H, Ar), 7.35 - 7.49 (m,2H, Ar), 7.46 (d, 2H, *J* 8.6 Hz, Ar), 7.64 (s, 1H, CH) ^{13}C NMR ($CDCl_3$, 50 MHz) δ 20.8, 89.5, 118.3, 119.4, 123.8, 128.3, 129.8, 130.0, 156.4, 158.7, 168.7; CIMS: *m/z* 301 (M+1)$^+$, 329 (M+29)$^+$, 341 (M+41)$^+$, 241, 227, 199, (100%), 171, 89, 61.

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