Solvent-free Preparation of 1,1-Diacetates from Aldehydes Mediated by Zirconium Hydrogen Sulfate at Room Temperature

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A mild and efficient method has been developed for the preparation of acylals in good yields through a reaction of aldehydes with acetic anhydride using $Zr(HSO_4)_4$ as catalyst at room temperature and under solvent-free conditions.

Keywords: Acylals; 1,1-Diacetates; Zirconium hydrogen sulfate; Solvent-free; Aldehydes; Solid acid.

INTRODUCTION

Acylals are synthetically useful protecting groups for carbonyl compounds due to their stability and also are important building blocks for the synthesis of 1-acetoxy dienes in Diels-Alder reaction.[1] Acylals are useful intermediates in various transformations such as nucleophilic substitution reactions.[2-6]

Several reagents or catalysts such as $Bi(OTf)_3.xH_2O$,[7] $ZrCl_4$,[8] P_2O_5/SiO_2,[9] NBS,[10] $Bi(NO_3)_3.5H_2O$,[11] $In(OTf)_3$,[12] $InBr_3$,[13] zirconium sulfophenyl phosphonate,[14] H_2NSO_3H,[15] $LiBF_4$[16], $Zn(OTf)_2$, $6H_2O$,[17] Sulfated Zirconia[18] and Aluminum dodecatungstophosphate[19] have been employed for the preparation of acylals from aldehydes and acetic anhydride.

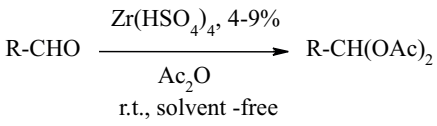
Solid acids have many advantages such as simplicity in handling, decreasing reactor and plant corrosion problems and environmentally safe disposal. On the other hand, any reduction in the amount of sulfuric acid needed and/or any simplification in handling procedures is required for risk reduction and economic advantage. Thus, inorganic acidic salts such as, $Al(HSO_4)_3$[20-21] or $Zr(HSO_4)_4$ [22] can be recommended for the above mentioned purposes. Although there are a few reports on the application of these salts in synthetic methodology, recently more attention has been paid to the investigation of their potentials in organic synthesis.

To the best of our knowledge, there is not any report on $Zr(HSO_4)_4$ application in acylal formation. This salt is a stable and non-hygroscopic solid material that is insoluble in most organic solvents.

RESULTS AND DISCUSSION

In continuation of our studies on the application of metallic hydrogensulfate salts in organic synthesis, we wish to report a catalytic method for the synthesis of acylals using $Zr(HSO_4)_4$ at room temperature and under solvent-free conditions. Various aldehydes were converted to acylals using 4-9 mol % of catalyst under grinding and room temperature conditions (Scheme I and Table 1).

Scheme I



The catalytic nature of the above acidic salts can be attributed to the presence of hydrogensulfate anion, which acts as a source of protons, and Zr^{4+}, which act as a Lewis acid. The results reveal that the $Zr(HSO_4)_4$ catalysis generally results in good yields with aromatic aldehydes includ-

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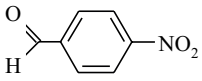
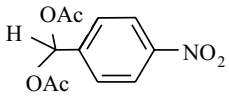
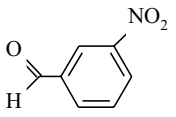
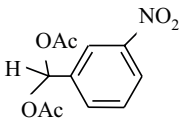
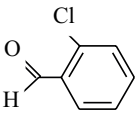
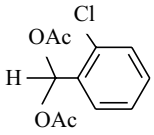
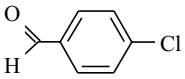
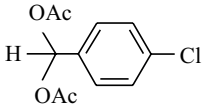
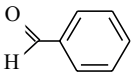
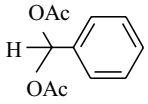
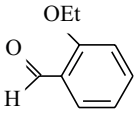
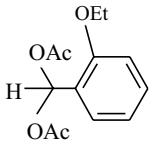
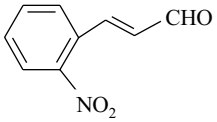
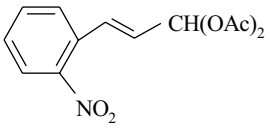
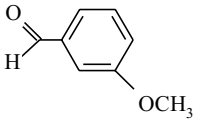
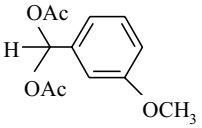
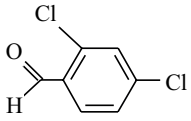
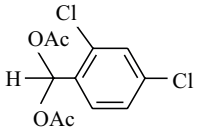
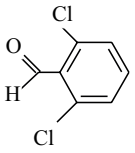
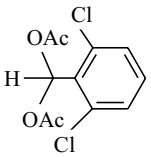
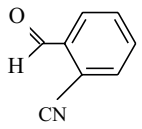
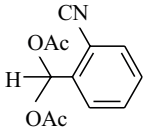
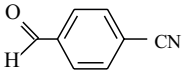
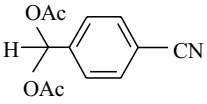
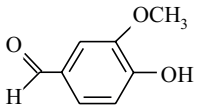
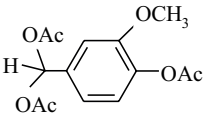
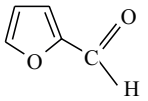
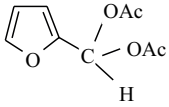
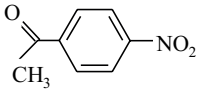
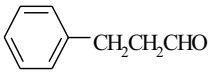
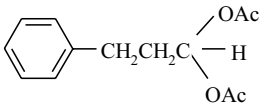
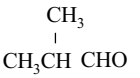
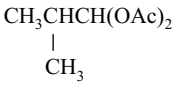
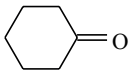
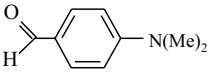
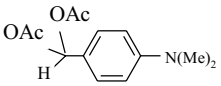
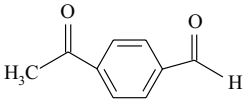
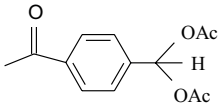
Table 1. Chemoselective conversion of carbonyl compounds to corresponding acylals using $Zr(HSO_4)_4$ as catalyst by grinding at room temperature and under solvent-free conditions

Entry	Substrate	Product	Subs./cat./acet.anhy (mmole)	Mp (bp) °C	Time (min)	Yield[a] (%)
1			3/ 0.12 / 3	124	5	90
2			3/ 0.12 / 3	66	5	86
3			3/ 0.12 / 3	53	7	84
4			3/ 0.276 /3	79	7	89
5			3/ 0.24 / 3	43	10	76
6			3/ 0.24/ 3	84	30[b]	40
7			3/ 0.276 / 3	78	10(20)[c]	30(45)[c]
8			3/ 0.24 / 3	(193)	7	62
9			3/ 0.12 / 3	93	5	89
10			3/ 0.12 / 3	87	5	78

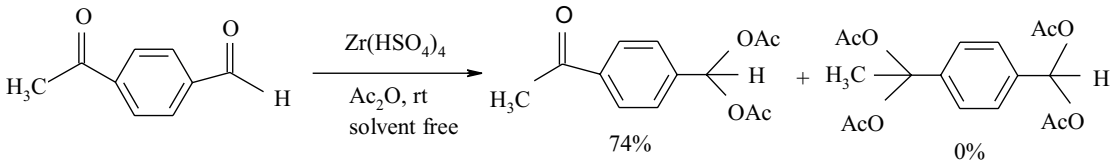
11			3/ 0.24 / 3	79	7	76
12			3/ 0.24 / 3	95	7	78
13			3/ 0.24 / 3	93	30	71[d], (24)[e]
14			3/ 0.138/ 3	47	30	42
15		-	3/ 0.24 / 3	–	15	0
16			3/ 0.12 / 3	(187)	10	28
17			3/ 0.12 / 3	(184)	8	50
18		-	3/ 0.24 / 3	–	15	0
19			3/ 0.12 / 3	–	15(30)[c]	0(10)[c]
20			3/ 0.12 / 3	57	5	74

[a] Yields refer to isolated pure products.
[b] n-Hexane was used as solvent and reaction was carried out at r.t.
[c] The reaction was carried out under reflux conditions in n-hexane as solvent.
[d] Vanillin gave the corresponding triacetates.
[e] Only the Phenolic group of vanillin was converted to OAc.

ing electron-withdrawing substituents (Table, entries 1-4 and 9-12). Mention must be made here that other methods such as the $AlPW_{12}O_{40}$[19] catalyzed reaction have provided poor yields in the presence of electron-withdrawing substituents.

Cyclohexanone, 4-nitroacetophenone and 4-acetyl benzaldehyde were also checked for reaction. The keto group of these compounds have not reacted under either

Scheme II



room temperature or reflux conditions (Scheme II). It is suggested that the chemoselective protection of aldehydes in the presence of ketones can be achieved by this method.

Likewise, 4-N,N-dimethyl amino benzaldehyde failed to give the expected acylal under grinding conditions at room temperature. The explanation for this result may be due to the strong electron donating dimethyl amino group which will reduce the reactivity. Mention must be made here that the phenolic group was also protected as acetate in an hydroxyl containing aromatic aldehyde (Table 1, entry 13) under this condition. Because of aldol condensation as a competition reaction, the yield of corresponding acylals of aliphatic aldehydes were low (Table 1, entries 16, 17). Furfural under the described experimental conditions formed an unidentified polymer and acylal.

In conclusion, we have developed a facile and solvent-free method for the synthesis of 1,1-diacetates from aldehydes using $Zr(HSO_4)_4$ as a catalyst. Advantages of this method include: a) the use of an inexpensive and relatively non-toxic catalyst, b) high catalytic efficiency and, c) the observed chemoselectivity.

EXPERIMENTAL

General

Chemicals were purchased from Fluka, Merck and Aldrich chemical companies. Yields refer to isolated products. $Zr(HSO_4)_4$ was synthesised according to previously reported procedures.[22] The acylal products were characterized by their spectral (IR, ^{1}H NMR) and physical data.

Typical Procedure for the preparation of 1,1-diacetoxy-1-(3-nitrophenyl) methane from 3-nitrobenzaldehyde at room temperature and solvent-free conditions

In a mortar, a mixture of 3-nitrobenzaldehyde (0.453 g, 3 mmol), acetic anhydride (0.3 mL, 3 mmol), and $Zr(HSO_4)_4$ (0.057 g, 0.12 mmol) was pulverized for 5 min at room temperature. The reaction progress was followed by TLC (eluent, dichloromethane : petroleum ether = 3:2). After 5 minutes of pulverization, the conversion percentage was > 99%. After completion of the reaction, diethyl ether was added to the mixture and filtered. The organic layer was washed with saturated $NaHCO_3$ (2 × 25 mL) and water (30 mL). The organic phase was dried over anhydrous Na_2SO_4, filtered and the solvent was evaporated to give the pure desired compound as a white crystalline compound Yield: 0.63 g (86%), m.p: 66 °C. [Lit[12] m.p: 64-66 °C].

Selected spectroscopic data of products (Table 1)

(a) the product has been reported before but spectral data were not given.

1,1-Diacetoxy-1-(2-chlorophenyl)methane[18] (entry 3): IR (KBr): ν = 2880-3100 (w), 1750 (s), 1600 (w), 1500 (m), 1220 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 90 MHz): δ = 2.2 (6H, s), 7.3 (4H, m), 7.8 (1H, s) ppm; MS (EI, 70 eV): *m/z* = 183 ($M^{+\bullet}$ - CH_3CO), 139 (100%), 111,109, 105, 104, 103.

1,1-Diacetoxy-1-(4-chlorophenyl)methane[11] (entry 4): IR (KBr): ν = 2880-3100 (w), 1750 (s), 1600 (m), 1500 (m), 1250 (s), 1200 (s) cm^{-1}. ^{1}H NMR, ($CDCl_3$, 90 MHz): δ = 2.2 (6H, s), 7.4 (4H, sbr), 7.6 (1H, s) ppm.

1,1-Diacetoxy-1-(4-cyanophenyl)methane[19] (entry 12): IR (KBr): ν = 2880-3100 (w), 2250 (m), 1750 (s), 1600 (w), 1500 (m), 1375 (m), 1250 (s), 1200 (s) cm^{-1}; ^{1}H-NMR ($CDCl_3$, 90 MHz): δ = 2.14 (6H, s), 7.68 (5H, br s) ppm; 233 (M^+), 190, 174, 130 (100%), 103, 102.

1,1-Diacetoxy-2-methylpropane[16] (entry 17): b.p.: 183-185 ºC, IR (KBr): ν = 2870-3000 (w), 1750 (s), 1440 (m), 1380 (s), 1200 (s) cm^{-1}; ^{1}H-NMR ($CDCl_3$, 90 MHz): δ = 0.65 (6H, d), 0.7 (1H, m), 1.72 (6H, s), 6.2 (1H, d) ppm.

1,1-Diacetoxy-1-(4-acetylphenyl)methan (entry 20): IR (KBr): ν = 3100-2976 (w), 1767 (s), 1678 (s), 1609 (m), 1373 (m), 1200 (s), 1011 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.1 (6H, s), 2.6 (3H, s), 7.5 (2H, d, *J* = 8.5 Hz), 7.7 (1H, s), 8.3 (2H, d, *J* = 8.5 Hz) ppm; ^{13}C NMR ($CDCl_3$,

62.9 MHz): δ = 197.44, 168.67, 140.01, 138.03, 128.58, 126.69, 88.97, 26.71, 20.79.

(b) Synthesis and spectroscopic data for these products are reported here for the first time.

1,1-Diacetoxy-1-(2-ethoxyphenyl)methane (entry 6): IR (KBr): ν = 2870-3100 (w), 1740 (s), 1600 (w), 1500 (m), 1450 (m), 1370 (m), 1250 (s), 1200 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz): δ = 1.32 (3H, t, *J* = 6 Hz), 2.04 (6H, s), 4.03 (2H, q, *J* = 6 Hz), 6.8-7.3 (4H, m), 7.96 (1H, s) ppm; MS (EI, 70 eV): *m/z* = 252 ($M^{+\bullet}$), 193, 151, 150, 149, 135, 123, 121, 76, 43 (100%).

(2*E*)-3-(2′-Nitrophenyl)prop-2-ene-1,1-diacetate (entry 7): IR (KBr), ν = 2850-3100 (w), 1750 (s), 1770 (s), 1620 (m), 1570 (m), 1520 (s), 1450 (w), 1375 (s), 1200-1270 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ = 2.2 (6H, s), 6.2 (1H, dd, *J* = 16 and 4 Hz), 7.35 (1H, d, *J* = 4 Hz), 7.4 (1H, d, *J* = 16 Hz), 7.5 (1H, m), 7.6 (2H, m), 8 (1H, d, *J* = 8 Hz) ppm; MS (EI, 70 eV): *m/z* = 220 ($M-COCH_3$), 178 (100%), 160, 148, 132.

1,1-Diacetoxy-1-(2-cyanophenyl)methane (entry 11): IR (KBr), ν = 2850-3100 (m), 2250 (s), 1750 (s), 1600 (m), 1500 (s), 1450 (m), 1370 (s), 1250 (s), 1200 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz): δ = 2.05 (6H, s), 7.5-7.8 (5H, m) ppm; MS (EI, 70 eV): *m/z* = 233 ($M^{+\bullet}$), 174, 148, 132 (100%), 130, 103, 102.

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