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$HClO_4$-SiO_2 catalyzed chemoselective synthesis of acylals from aldehydes under solvent-free conditions☆

Rishi Kumar, Pallavi Tiwari, Prakas Ranjan Maulik, Anup Kumar Misra*

Medicinal and Process Chemistry Division and Molecular and Structural Biology Division, Central Drug Research Institute, Chattar Manzil Palace, Lucknow 226001, UP, India

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Abstract

A mild and efficient method has been devised for the preparation of acylals from aldehydes in the presence of catalytic amounts of $HClO_4$-SiO_2 under solvent-free conditions in very good to excellent yield.

Keywords: Acylals; Aldehydes; Catalysis; Solvent-free reactions; $HClO_4$-SiO_2

1. Introduction

Selective protection and deprotection plays a pivotal role in many multistep organic syntheses. Acylals (1,1-diacetates) have been recognized as an important protecting group alternative to acetals because of their stability under various reaction conditions and their easy conversion into the parent aldehydes [1]. Being a masked aldehydic functionality, acylals have been used as a valuable intermediate in various organic syntheses [2–4]. Acylals have been used as precursors of 1-acetoxydienes, 2,2-dichlorovinylacetates for Diels-Alder reactions [5]. Acylals have also been used as a cross-linking agent for cellulose in cotton [6]. There is a plethora of methods available in the literature for the preparation of acylals. Generally, acylals are prepared by treating aldehydes with acetic anhydride in the presence of protonic acids [7], Lewis acids [1,8–15], heteropoly acids or clays. Except a few, many of the above mentioned methodology suffers from the drawbacks such as, prolonged reaction time, use of excess acetic anhydride, high temperatures, use of moisture-sensitive and expensive catalysts, use of solvents, stringent conditions, difficulty in scaling up, etc. Therefore, development of catalysts working under mild reaction conditions is desirable. Recently, our group and others have reported the catalytic potentiality of $HClO_4$-SiO_2 in the Ferrier reaction to prepare 2,3-unsaturated *O*-, *S*- and *C*-glycosides [16,17] and per-*O*-acetylation of carbohydrates [18] and acetylation of phenols, thiols and amines [19]. In this paper, we are disclosing an efficient method for the preparation of acylals from a series of aldehydes catalyzed by silica supported $HClO_4$ under solvent-free reaction condition.

2. Results and discussion

Although $HClO_4$ had been used earlier to catalyze acylal formation from aldehydes, it requires excess of Ac_2O and a longer reaction time to afford acylals, maybe due to the presence of water in the reaction medium. In order to avoid the presence of water in the reaction medium that certainly has a deleterious effect in the formation of the product, $HClO_4$ has been impregnated over silica gel. Therefore, $HClO_4$-SiO_2 has acted as an insoluble catalyst, which could be removed from the reaction mixture by simple filtration. The catalyst system is a non-corrosive free flowing powder, which can be stored at room temperature for several months without losing of its catalytic potentiality. Therefore, $HClO_4$-SiO_2 may be considered as a very cheap source of solid supported acidic catalyst compared to other commercially available expensive solid supported acids.

To ascertain the catalytic potential of $HClO_4$-SiO_2 for this transformation, a series of experiments have been carried out varying the quantity of Ac_2O and $HClO_4$-SiO_2 and it was observed that use of 1.5 eq. of Ac_2O in the presence of 0.025 eq.

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* Corresponding author. Tel.: +91 522 262 5478; fax: +91 522 262 3938.
E-mail address: akmisra69@rediffmail.com (A.K. Misra).

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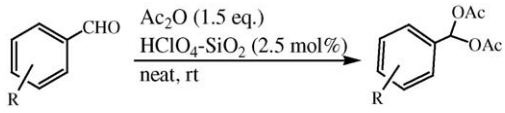
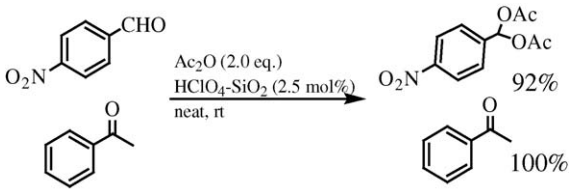


Scheme 1.



Scheme 2.

of $HClO_4$-SiO_2 can produce excellent yield of acylals at ambient temperature (Scheme 1; Table 1). The rate of formation of the product was exceptionally fast and in most of the cases the products were isolated as solids. The reaction works well with aliphatic as well as aromatic aldehydes containing electron-donating and electron-withdrawing substituents present in the aromatic rings. The catalyst can be recycled up to four cycles without any noticeable loss of catalytic activity (Table 1, entries 3–5). From Table 1, it is clear that the reactivity of aromatic aldehydes towards the formation of acylals depends on the substituents present in the aromatic nucleus. Benzaldehyde or aromatic aldehydes containing electron withdrawing substituent attached to the aromatic ring react very fast to furnish acylals may be due to the better electrophilicity at the carbonyl center compared to the aromatic aldehydes with electron donating substituent present in the aromatic nucleus, which may reduces the electophilicity at the carbonyl center by virtue of the conjugation. In addition, formation of acylals from aliphatic aldehydes were also very fast. It is noteworthy that ketones did not produce the corresponding diacetates under the same reaction conditions. This result indicated that the present protocol could be applicable to the chemoselective protection of aldehydes in the presence of ketones. An equimolecular mixture of 4-nitrobenzaldehyde and acetophenone was allowed to react with 2.0 eq. of Ac_2O in the presence of $HClO_4$-SiO_2 (0.025 eq.) at ambient temperature. TLC showed that 4-nitrobenzaldehyde reacted almost instantly to form corresponding acylals whereas, acetophenone remained unreacted even after 24 h (Scheme 2). In order to compare the catalytic potentiality of $HClO_4$-SiO_2 with some recently reported catalysts, a series of reactions were carried out using 4-nitrobenzaldehyde as substrate and the results are presented in Table 2, which clearly shows that $HClO_4$-SiO_2 should be con-

Table 1
$HClO_4$-SiO_2 catalyzed efficient formation of acylals from aldehydes using Ac_2O (1.5 eq.) at ambient temperature

Entry	Aldehydes	Time (min)	Isolated yield (%)	mp (°C)		Reference
				Found	Lit.	
1	Benzaldehyde	2	95	46	44–45	14
2	4-Methylbenzaldehyde	2	95	84	82–83	14
3	4-Methylbenzaldehyde	5[a]	95			
4	4-Methylbenzaldehyde	10[b]	92			
5	4-Methylbenzaldehyde	10[c]	90			
6	2-Methoxybenzaldehyde	5	92	76	75–76	14
7	4-Methoxybenzaldehyde	10	90	65	64–65	14
8	4-Chlorobenzaldehyde	2	95	82	80–81	14
9	3-Chlorobenzaldehyde	2	95	67	65–66	14
10	2-Nitrobenzaldehyde	2	95	85	86–87	14
11	3-Nitrobenzaldehyde	2	95	66	66–67	14
12	4-Nitrobenzaldehyde	2	96	125	127–128	14
13	4-Fluorobenzaldehyde	5	90	51	50–51	14
14	Furfural	10	92	51	50–51	14
15	4-Hydroxybenzaldehyde	10	90	91	89–91	14
16	2-Bromobenzaldehyde	5	92	76–77	–	–
17	4-Benzyloxybenzaldehyde	10	92	108-10	–	–
18	3-Bromobenzaldehyde	2	90	83	–	–
19	3-Fluorobenzaldehyde	2	92	39–40	–	–
20	1-Napthaldehyde	15	85	90	90–92	13
21	3-Methylbenzaldehyde	2	95	Oil	–	–
22	2-Hydroxy-5-bromo-benzaldehyde	10	90	92–93	–	–
23	4-Trifluoromethylbenzaldehyde	10	92	Oil	31–33	13
24	3,4-(Methylenedioxy)-benzaldehyde	2	96	77	78–79	14
25	3-Methoxy-4-hydroxybenzaldehyde	5	92	91	90–91	14
26	Hexanal	2	90	Oil	–	14
27	Decanal	2	85	Oil	–	14
28	Acetophenone	24 h	0	–	–	–
29	2,5-Dimethylacetophenone	24 h	0	–	–	–

[a] Catalyst used after single recovery.
[b] Catalyst used after double recovery.
[c] Catalyst used after triple recovery.

Table 2
Comparison of the effect of catalysts in the acylal formation of 4-nitrobenzaldehyde at ambient temperature

Entry	Catalysts	Catalyst load (mol%)	Time	Yield (%)
1	$InCl_3$	10	5 h	90
2	$(NH_4)_2Ce(NO_3)_6$	10	24 h	85
3	$Cu(OTf)_2$	10	4 h	85
4	$Sc(OTf)_3$	5	20 min	95
5	$ZrCl_4$	5	30 min	85
6	$LiBF_4$	50	12 h	75
7	$BiCl_3$	50	12 h	70
8	I_2	100	12 h	80
9	$HClO_4$-SiO_2	2.5	2 min	96

sidered as one of the best choice for selecting the economically convenient, user-friendly catalyst and for the scaling up purpose.

3. Conclusion

In conclusion, $HClO_4$-SiO_2 has been found to be a novel, highly efficient, low-cost catalyst for 1,1-diacetate formations from aliphatic and aromatic aldehydes. Operational simplicity, without need of any solvent, exceptionally fast, low cost of the catalyst used, high yields, excellent chemo selectivity, applicability to large-scale reactions are the key features of this methodology.

4. Experimental

Preparation of $HClO_4$-SiO_2 catalyst [19]: $HClO_4$ (1.8 g, 12.5 mmol, as a 70% aq solution) was added to a suspension of SiO_2 (230–400 mesh, 23.7 g) in Et_2O (70.0 mL). The mixture was concentrated and the residue was heated at 100 °C for 72 h under vacuum to furnish $HClO_4$-SiO_2 (0.5 mmol/g) as a free flowing powder (50 mg = 0.025 mmol of $HClO_4$). *Caution*!: Although no explosions were reported under these conditions, extreme care has to be exercised for large-scale reactions. The generation of the catalyst should be performed with special care and in a safe environment.

Typical procedure for the formation of acylals: To a suspension of 4-nitrobenzaldehyde (610 mg, 4.0 mmol) in Ac_2O (566 μL, 6.0 mmol) was added $HClO_4$-SiO_2 (200 mg, 0.1 mmol $HClO_4$) at room temperature and the neat reaction mixture was allowed to stir magnetically for appropriate time (as mentioned in Table 1). After completion of the reaction (TLC), the reaction mixture was filtered through a celite bed, washed with EtOAc and concentrated under reduced pressure to furnish almost pure product as pale yellow solid, which was in full agreement with mp and spectral data. Following the similar reaction methodology, a series of acylals were prepared in excellent yield. Analytical samples were prepared by recrystallization from EtOAc-hexane. All products were characterized by their NMR, mass spectra and elemental analysis.

Spectral data for selected compounds that are not reported earlier:

Diacetoxy-1-(2-bromophenyl)methane (entry 16): mp 76–77 °C; IR (KBr): 1758, 1638, 1236 cm^{-1}; ^1H NMR (200 MHz): δ 7.91 (s, 1 H), 7.59–7.53 (m, 2 H), 7.38–7.25 (m, 2 H), 2.13 (s, 6 H); FABMS: 287 [$M+1$]; anal. calcd. for $C_{11}H_{11}BrO_4$ (286): C, 46.02; H, 3.86; found: C, 45.88; H, 4.0.
Diacetoxy-1-(4-benzyloxyphenyl)methane (entry 17): mp 108–110 °C; IR (KBr): 1753, 1594, 1362, 1235, 1012 cm^{-1}; ^1H NMR (200 MHz): δ 7.62 (s, 1 H), 7.47–7.34 (m, 9 H), 7.01 (d, J = 10 Hz, 1 H), 5.07 (s, 2 H), 2.10 (s, 6 H); FABMS: 314 [M]; anal. calcd. for $C_{18}H_{18}O_5$ (314): C, 68.78; H, 5.77; found: C, 68.62; H, 5.90.
Diacetoxy-1-(3-bromophenyl)methane (entry 18): mp 83 °C; IR (KBr): 1760, 1646, 1240 cm^{-1}; ^1H NMR (200 MHz): δ 7.62 (s, 1 H), 7.61–7.26 (m, 4 H), 2.13 (6 H); FABMS: 287 [$M+1$]; anal. calcd. for $C_{11}H_{11}BrO_4$ (286): C, 46.02; H, 3.86; found: C, 45.90; H, 4.0.
Diacetoxy-1-(3-fluorophenyl)methane (entry 19): mp 39–40 °C; IR (KBr): 1755, 1650, 1237 cm^{-1}; ^1H NMR (200 MHz): δ 7.66 (s, 1 H), 7.40–7.12 (m, 4 H), 2.13 (s, 6 H); FABMS: 227 [$M+1$]; anal. calcd. for $C_{11}H_{11}FO_4$ (226): C, 58.41; H, 4.90; found: C, 58.30; H, 5.0.
Diacetoxy-1-(3-methylphenyl)methane (entry 21): Yellow oil; IR (neat): 1762, 1657, 1243 cm^{-1}; ^1H NMR (200 MHz): δ 7.64 (s, 1 H), 7.32–7.20 (m, 4 H), 2.38 (s, 3 H), 2.13 (s, 6 H); FABMS: 223 [$M+1$]; anal. calcd. for $C_{12}H_{14}O_4$ (222): C, 64.85; H, 6.35; found: C, 64.68; H, 6.52.
Diacetoxy-1-(2-hydroxy-5-bromophenyl)methane (entry 22): mp 92–93 °C; IR (KBr): 2362, 1765, 1599, 1374, 1194 cm^{-1}; ^1H NMR (200 MHz): δ 7.84 (s, 1 H), 7.76 (d, J = 2.0 Hz, 1 H), 7.56–7.51 (dd, J = 10.5 and 1.8 Hz, 1 H), 7.01 (d, J = 8.6 Hz, 1 H), 2.33 (s, 3 H), 2.11 (s, 6 H); FABMS: 303 [$M+1$]; anal. calcd. for $C_{11}H_{11}BrO_5$ (302): C, 43.59; H, 3.66; found: C, 43.45; H, 6.80.

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