

Chemoselective and convenient preparation of 1,1-diacetates from aldehydes, mediated by solid lithium perchlorate under solvent-free conditions

Azim Ziyaei, Najmedin Azizi, Mohammad R. Saidi*

Department of Chemistry, Sharif University of Technology, P.O. Box 11365-9516, Tehran, Iran

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Abstract

A simple, efficient, and general method has been developed for the conversion of aldehydes to 1,1-diacetates with the use of acetic anhydride and solid LiClO_4 under first solvent-free and mild conditions in good yields. This method applies to not only simple but also to conjugated aldehydes.

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1. Introduction

Protection and deportation of functional groups are indispensable ingredients of the synthesis of poly functional compounds. The protection of carbonyl groups as a 1,1-diacetates (*geminal* diacetates or acylals) is an important synthetic methods. Because of their stability in basic media [1], the acylals are gaining important role in synthetic organic chemistry for the protecting of aldehyde group as an alternative to acetals [2]. The acylals of α,β -unsaturated aldehydes are important starting materials for the synthesis of acetoxydienes and vinyl acetate for Diels-Alder cycloaddition reactions [3]. Acylals have been applied as cross linking reagents for cellulose in cotton and serve as an activator in the composition of the bleaching mixture used for the treatment of wine-stained fabrics [4a]. In addition, 1,1-diacetates are also used as substrates in nucleophilic substitution reactions [4b].

The conventional method available for the preparation of these compounds involves the reaction of aldehydes with acetic anhydride using a strong acid, such as sulfuric acid,

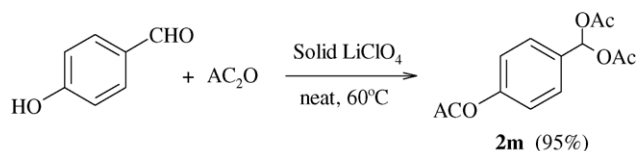
phosphoric acid, or methanesulfonic acid [5], or Lewis acids, such as $\text{Fe}_2(\text{SO}_4)_3 \cdot x\text{H}_2\text{O}$ [6a], $\text{Zr}(\text{SO}_4)_2 \cdot 4\text{H}_2\text{O}/\text{SiO}_2$ [6b], Fe^{3+} -montmorillonite [6c], Montmorillonite K-10 [6d], InBr_3 [6a,6e], PCl_3 [7a], InCl_3 [7b], $\text{Sc}(\text{OTf})_3$ [7c], $\text{Cu}(\text{OTf})_2$ [7d], FeCl_3 , ZnCl_2 [7e], I_2 [8], $\text{Bi}(\text{NO}_2)_3$ [9], ZrCl_4 [10], amberlyst-15 [11], $\text{Cu}(\text{BF}_4)_2$ [12], zinc metal [13], zirconium sulfophenyl phosphorate [14], solid superacid, such as Nafion-H [15], and aluminum dodecatungstophosphate [16] as catalyst for this conversion. However, many of these methods involve strong acidic or oxidizing conditions, expensive and hazardous reagents, and long reaction time for the protection of aldehydes. Therefore, development of inexpensive reagents with greater efficiency, more convenient procedures with better yield are of great interests.

2. Results and discussion

Solvent-free reactions are gaining considerable attention in organic synthesis, especially for the large-scale production of widely used compounds.

In recent years, the use of concentrated solution of lithium perchlorate in diethyl ether (LPDE) as a medium has attracted attention due to the enhanced rate and selectivity

* Corresponding author. Tel.: +98 21 600 5718; fax: +98 21 601 2983.
E-mail address: saidi@sharif.edu (M.R. Saidi).



Scheme 1.

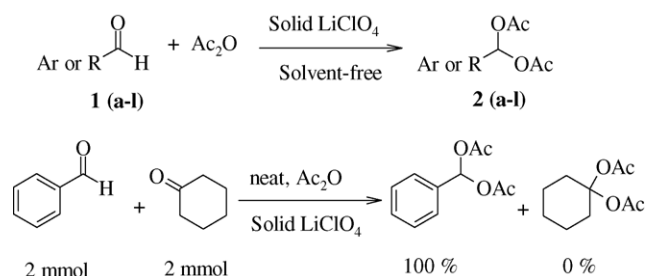
to various organic transformations. The LPDE medium provides a convenient procedure to carry out reaction under neutral condition [17]. In continuation of our interest on the application of lithium perchlorate for various organic transformation as a cheap, reusable, heterogeneous and easily available catalyst [18], we herein describe a simple and efficient method for the protection of carbonyl compounds, using solid LiClO_4 under solvent-free and neutral conditions (Scheme 1).

Various aldehydes reacted smoothly with the Ac_2O to afford the corresponding 1,1-diacetates in high yields. The reaction proceeds smoothly at 60°C within 15–40 min. Both aromatic and aliphatic aldehydes afforded excellent yields of products (80–92%) in a short period of time. This method is effective even with aldehydes bearing electron-withdrawing substituents, such as nitro groups in the aromatic ring. Furthermore, acid sensitive aldehydes, such as furfural and α , β -unsaturated aldehydes, such as cinnamaldehyde and crotonaldehyde, worked well without any decomposition or polymerization under the reaction conditions. The results are in sharp contrast for the use of some Lewis acids such PCl_3 [7a]. The nature of constituents on the aromatic ring seems to have no effect on the reaction condition. Both activated and deactivated aromatic aldehydes were converted to their corresponding acylals under these conditions. In the case of aliphatic aldehydes, one also observed high yields of product in short reaction time. When 4-hydroxybenzaldehyde was subjected to the similar reaction conditions, the hydroxyl group was also acetylated to afford the corresponding triacetates in excellent yields.

On the other hand, 4-(dimethylamino)benzaldehyde remained unaffected even when the reaction mixtures were stirred at 60°C for 10 h, due to deactivation of the carbonyl group, and the starting materials were quantitatively recovered.

This method is highly selective for the preparation of the acylals from aldehydes. Thus, acylation of aldehyde in the presence of ketones, using solid lithium perchlorate as the catalyst under solvent-free conditions at low temperature (ca. 60°C), gave only 1,1-diacetates from aldehyde, Scheme 1. At higher temperature ketones, such as cyclohexanone, can be converted to acylals in low yields (ca. about 20% after 40 min at 100°C) (Scheme 2).

Although we have not yet studied the mechanism of the reaction in details, preliminary experiments do provide meaningful information about the catalyst. The role of LiClO_4 in catalyzing the protection of aldehydes with acetic anhydride,



Scheme 2.

maybe realized through the coordination with both of the aldehydes and acetic anhydride to Li^+ , so activating both of them under solvent-free conditions. However, when the reaction mixtures were stirred in 5 M solution of LPDE for 10 h, the starting materials were quantitatively recovered. But the reaction would proceed smoothly in solid LiClO_4 . This interesting difference in behavior of 5 M solution of LPDE and solid LiClO_4 can be referred to the Lewis acidity of lithium ion. However, in a coordinating solvent, such as ether, its Lewis acidity is moderated and it is lower in compare to solvent less condition.

In conclusion, we have shown a new clean, mild, efficient and neutral method for preparation of *geminal* diacetates from aldehydes in the presence of acetic anhydride at room temperature mediated by solid lithium perchlorate under solvent-free conditions. The most significant of this reagent is the low cost with green methodology, short reaction time, reusability and easy work up compared with the reported methods. Lithium perchlorate can be recovered and dried at 160°C and reuse it for other reactions.

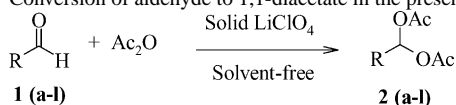
2.1. General procedure for the preparation of 1,1-diacetates from aldehyde

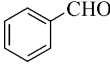
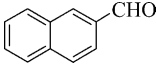
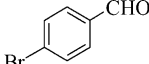
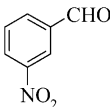
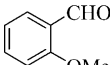
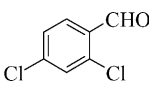
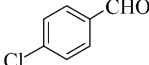

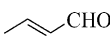
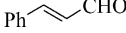
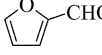

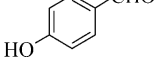
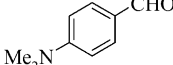
A mixture of aldehyde (3 mmol), freshly distilled acetic anhydride (5 mmol) and commercial anhydrous LiClO_4 (2 equivalents) was stirred at 60°C for an appropriate time (Table 1). After the reaction was complete (monitored by TLC), the reaction mixture was cooled and CH_2Cl_2 (10 mL) was added. The precipitated LiClO_4 was recovered by filtration. For most aromatic aldehydes, the reaction mixture solidifies and 1,1-diacetates are purified by recrystallization (cyclohexane or petroleum ether). For aliphatic aldehydes, volatile material is removed by rotary evaporation and pure 1,1-diacetates obtained by distillation in reduces pressure. All compounds were known and characterized on the basis of their spectroscopic data (IR, NMR, MS) and by comparison with those reported in the literature or compared with authentic samples [19].

2.1.1. Caution

Although we did not have any accident while using or drying LiClO_4 , it is advisable to work in a fume hood using a suitable lab-shield.

Table 1

Conversion of aldehyde to 1,1-diacetate in the presence of solid LiClO₄

Entry	Aldehyde	Time (min)	1,1-Diacetate	Isolated yield (%)
1		25	2a	92
2		30	2b	94
3		20	2c	81
4		40	2d	93
5		25	2e	87
6		25	2f	92
7		30	2g	90
8		40	2h	90
9		15	2i	92
10		20	2j	83
11		25	2k	90
12		20	2l	86
13		600 ^a	2m	95
14		600	2n	0.0

^a After 4.0 h all the starting material was consumed and ¹H NMR showed mixture of 66% 4-acetoxy-benzaldehyde and 34% of **2m**.

Acknowledgments

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References

- [1] K.S. Kochhar, B.S. Bal, R.P. Deshpande, S.N. Rajadhyaksha, H.W. Pinnick, *J. Org. Chem.* 48 (1983) 1765.
- [2] T.W. Greene, P.G.M. Wuts, *Protective Groups in Organic Synthesis*, third ed., John Wiley and Sons, New York, 1999, p. 306.
- [3] (a) B.B. Snider, S.G. Amin, *Synth. Commun.* 8 (1978) 117;
 - (b) G. Saucy, R. Marbet, H. Lindlar, O. Isler, *Helv. Chim. Acta* 42 (1959) 1945;
 - (c) H. Held, A. Rengstl, D. Mayer, in: W. Gerhartz (Ed.) *Ullman's Encyclopedia of Industrial Chemistry*, vol. A1, fifth ed., VCH, 1985, p. 68;
 - (d) L.K. Sydnes, M. Sandberg, *Tetrahedron* 53 (1997) 12679;
 - (e) M. Sandberg, L.K. Sydnes, *Tetrahedron Lett.* 39 (1998) 6361;
 - (f) B.M. Trost, C. Lee, *J. Am. Chem. Soc.* 123 (2001) 12191;
 - (g) B.M. Trost, J.M. Lee, J. Weiss, *J. Am. Chem. Soc.* 117 (1995) 7247;
 - (h) J.S. Yadav, B.V.S. Reddy, G.S.K.K. Reddy, *Tetrahedron Lett.* 41 (2000) 2695;
 - (i) F.R. Heerden, J.J. Huyser, D.B.G. Williams, C.W. Holzapfer, *Tetrahedron Lett.* 39 (1998) 5281;
 - (j) M. Sandberg, L.K. Sydnes, *Org. Lett.* 2 (2000) 687.
- [4] (a) J.G. Frick Jr., R.J. Harper Jr., *J. Appl. Polym. Sci.* 29 (1984) 1433;
 - (b) M. Sandberg, L.K. Sydnes, *Tetrahedron Lett.* 39 (1998) 6361;

- (c) F.R. Heerden, J.J. Huyser, B.D.G. Williams, C.W. Holzapfel, *Tetrahedron Lett.* 39 (1998) 5281;
- (d) J.S. Yadav, B.V. Subba Reddy, K. Kiran, G.S. Reddy, *Tetrahedron Lett.* 41 (2000) 2695;
- (e) T.-S. Li, Z.-H. Zhang, C.-G. Fu, *Tetrahedron Lett.* 38 (1997) 3285.
- [5] (a) M.J. Gregory, *J. Chem. Soc. B* (1970) 1201;
- (b) M. Tomita, T. Kikuchi, K. Bessho, T. Hori, Y. Inubushi, *Chem. Pharm. Bull.* 11 (1963) 1484;
- (c) W. Davey, J.R.G. Wilt, *J. Chem. Soc.* (1957) 1008;
- (d) F. Freeman, E.M. Karchefski, *J. Chem. Eng. Data* 22 (1977) 355;
- (e) J.A. Marshall, P.G.M. Wuts, *J. Org. Chem.* 42 (1977) 1794;
- (f) V. Kavala, B.-K. Patel, *Eur. J. Org. Chem.* 2 (2005) 441.
- [6] (a) X. Zhang, L. Li, G. Zhang, *Green Chem.* 5 (2003) 646;
- (b) T.-S. Jin, G.-L. Feng, M.-N. Yang, T.-S. Li, *Synth. Commun.* 34 (2004) 1645;
- (c) T.-S. Li, Z.-H. Zhang, Y.-J. Gao, *Synth. Commun.* 28 (1998) 4665;
- (d) Z.-H. Zhang, T.-S. Li, C.-G. Fu, *J. Chem. Res. Synop.* (1997) 174;
- (e) L. Yin, Z.-H. Zhang, Y.-M. Wang, M.-L. Pang, *Synletters* (2004) 1727.
- [7] (a) J.K. Michie, J.A. Miller, *Synthesis* (1981) 824;
- (b) J.S. Yadav, B.V. Subba Reddy, Ch. Srinivas, *Synth. Commun.* 32 (2002) 1175;
- (c) V.K. Aggarwal, S. Fonquerna, G.P. Vennal, *Synletters* (1998) 849;
- (d) K.L. Chandra, P. Saravanan, V.K. Singh, *Synletters* (2000) 359;
- (e) I. Seriabine, *Bull. Soc. Chim. Fr.* (1961) 1194.
- [8] N. Deka, D.J. Kalita, R. Borah, J.C. Sarma, *J. Org. Chem.* 62 (1997) 1563.
- [9] D.H. Aggen, J.N. Arnold, P.D. Hayes, N.J. Smoter, R.S. Mohan, *Tetrahedron* 60 (2004) 3675.
- [10] G. Smitha, S. Ch. Reddy, *Tetrahedron* 59 (2003) 9571.
- [11] D.D. Pathak, J.J. Gerald, *Synth. Commun.* 33 (2003) 1557.
- [12] A.K. Chakraborti, R. Thilagavathi, R. Kumar, *Synthesis* (2004) 831.
- [13] Y. Ishino, M. Mihara, T. Takeuchi, M. Takemoto, *Tetrahedron Lett.* 45 (2004) 3503.
- [14] M. Curini, F. Epifano, M.C. Marcotullio, O. Rosati, M. Nocchetti, *Tetrahedron Lett.* 43 (2002) 2709.
- [15] G.A. Olah, A.K. Mehrotra, *Synthesis* (1982) 962.
- [16] (a) H. Firouzabadi, N. Iranpoor, F. Nowrouzi, K. Amani, *Tetrahedron Lett.* 44 (2003) 3951;
- (b) G.P. Romanelli, H.J. Thomas, G.T. Baronetti, J.C. Autino, *Tetrahedron Lett.* 44 (2003) 1301;
- (c) P. Kumar, V.R. Hegde, T.P. Kumar, *Tetrahedron Lett.* 36 (1995) 601;
- (d) M. Katoh, T. Yamazaki, H. Kamijo, S. Ozawa, *Zeolites* 15 (1995) 597.
- [17] S. Sankara Raman, J.E. Nesakumar, *Eur. J. Org. Chem.* (2000) 2003.
- [18] (a) N. Azizi, F. Rajabi, M.R. Saidi, *Tetrahedron Lett.* 45 (2004) 9233;
- (b) N. Azizi, M.R. Saidi, *Organometallics* 23 (2004) 1457;
- (c) N. Azizi, M.R. Saidi, *Tetrahedron* 60 (2004) 383;
- (d) N. Azizi, M.R. Saidi, *Eur. J. Org. Chem.* (2003) 4630;
- (e) N. Azizi, M.R. Saidi, *J. Organomet. Chem.* 688 (2003) 283.
- [19] Selected spectral data. **2a** [8]: $^1\text{H NMR}$ (CDCl_3 , 500 MHz), $\delta_{\text{H}} = 2.16$ (s, 6H), 7.32–7.39 (m, 3H), 7.43–7.44 (m, 2H), 7.70 (s, 1H); IR (KBr): 1758, 1629, 1349, 1220, 1001 cm^{-1} . **2b** [7b]: $^1\text{H NMR}$ (CDCl_3 , 500 MHz), $\delta_{\text{H}} = 2.10$ (s, 6H), 7.50–7.62 (m, 4H), 7.74–7.75 (m, 2H), 8.02 (s, 1H), 8.27–8.29 (m, 1H); IR (KBr): 1748, 1507, 1370, 1237, 1009 cm^{-1} . **2c** [10b]: $^1\text{H NMR}$ (CDCl_3 , 500 MHz), $\delta_{\text{H}} = 2.11$ (s, 6H), 7.28–7.41 (m, 2H), 7.52–7.55 (m, 2H), 7.63 (s, 1H); IR (KBr): 1762, 1589, 1489, 1372, 1240, 1020 cm^{-1} . **2d** [10c]: $^1\text{H NMR}$ (CDCl_3 , 500 MHz), $\delta_{\text{H}} = 2.11$ (s, 6H), 7.58–7.68 (m, 1H), 7.71 (s, 1H), 7.75–7.84 (m, 1H), 8.22–8.23 (m, 1H), 8.35 (m, 1H); IR (KBr): 1764, 1535, 1431, 1352, 1012 cm^{-1} . **2e** [10d]: $^1\text{H NMR}$ (CDCl_3 , 500 MHz), $\delta_{\text{H}} = 2.12$ (s, 6H), 3.88 (s, 3H), 6.88–7.06 (m, 2H) 7.51 (m, 1H), 7.79 (m, 1H); IR (KBr): 1768, 1540, 1473, 1220, 1012 cm^{-1} . **2f** [10b]: $^1\text{H NMR}$ (CDCl_3 , 500 MHz), $\delta_{\text{H}} = 2.16$ (s, 6H), 7.32–7.34 (m, 1H), 7.45–7.53 (m, 1H), 7.67 (s, 1H), 7.89–7.93 (m, 1H); IR (KBr): 1763, 1541, 1473, 1233, 1199, 1012 cm^{-1} . **2g** [8]: $^1\text{H NMR}$ (CDCl_3 , 500 MHz), $\delta_{\text{H}} = 2.11$ (s, 6H), 7.35–7.41 (m, 2H), 7.45–7.49 (m, 2H), 7.62 (s, 1H); IR (KBr): 1762, 1580, 1358, 1230, 980 cm^{-1} . **2h** [10c]: $^1\text{H NMR}$ (CDCl_3 , 500 MHz), $\delta_{\text{H}} = 0.84$ (d, $J = 7.0$ Hz, 6H), 2.01 (s, 6H), 2.11 (m, 1H), 6.50 (d, $J = 2.5$ Hz, 1H); IR (KBr): 1762, 1471, 1375, 1241 cm^{-1} . **2i** [8]: $^1\text{H NMR}$ (CDCl_3 , 500 MHz), $\delta_{\text{H}} = 2.00$ –2.18 (m, 9H), 5.51–5.55 (m, 1H), 5.99–6.03 (m, 1H), 7.04 (m, 1H); IR (KBr): 1743, 1435, 1373, 1233 cm^{-1} . **2j** [8]: $^1\text{H NMR}$ (CDCl_3 , 500 MHz), $\delta_{\text{H}} = 2.13$ (s, 6H), 5.98 (dd, $J = 16.4$, 7.3 Hz, 1H), 6.84 (d, $J = 16.4$, 1H), 7.18–7.48 (m, 6H); IR (KBr): 1750, 1680, 1480, 1100 cm^{-1} . **2k** [8]: $^1\text{H NMR}$ (CDCl_3 , 500 MHz), $\delta_{\text{H}} = 2.12$ (s, 6H), 7.33–7.78 (m, 3H), 7.82 (s, 1H); IR (KBr): 1750, 1374, 1270, 1220, 1060 cm^{-1} . **2l** [7b]: $^1\text{H NMR}$ (CDCl_3 , 500 MHz), $\delta_{\text{H}} = 2.10$ (s, 6H), 2.11–2.15 (m, 4H), 6.63 (m, 1H), 7.35–7.62 (m, 5H). IR (KBr): 1763, 1480, 1376, 1220 cm^{-1} .