Journal of Sulfur Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713926081

Lanthanum(III) nitrate hexahydrate catalyzed chemoselective thioacetalization of aldehydes

M. Srinivasulu[a]; K. Rajesh[a]; N. Suryakiran[a]; J. Jon Paul Selvam[a]; Y. Venkateswarlu[a]
[a] Natural Products Laboratory, Organic Chemistry Division-I, Indian Institute of Chemical Technology, Hyderabad, India

To cite this Article Srinivasulu, M. , Rajesh, K. , Suryakiran, N. , Selvam, J. Jon Paul and Venkateswarlu, Y.(2007) 'Lanthanum(III) nitrate hexahydrate catalyzed chemoselective thioacetalization of aldehydes', Journal of Sulfur Chemistry, 28: 3, 245 — 249
To link to this Article: DOI: 10.1080/17415990701344710
URL: http://dx.doi.org/10.1080/17415990701344710

Journal of Sulfur Chemistry
Vol. 28, No. 3, June 2007, 245–249

Taylor & Francis
Taylor & Francis Group

COMMUNICATION

Lanthanum(III) nitrate hexahydrate catalyzed chemoselective thioacetalization of aldehydes†

M. SRINIVASULU, K. RAJESH, N. SURYAKIRAN, J. JON PAUL SELVAM, and Y. VENKATESWARLU*

Natural Products Laboratory, Organic Chemistry Division-I, Indian Institute of Chemical Technology, Hyderabad, India

(Received 14 December 2006; in final form 14 March 2007)

A wide variety of cyclic and acyclic dithioacetals have been prepared chemoselectively from their corresponding aldehydes with 1,3-dithiol and ethanethiol using catalytic amounts of lanthanum(III) nitrate hexahydrate as a catalyst at room temperature.

Keywords: $La(NO_3)_3 \cdot 6H_2O$; Aldehydes; 1,3-dithianes; Thioacetals

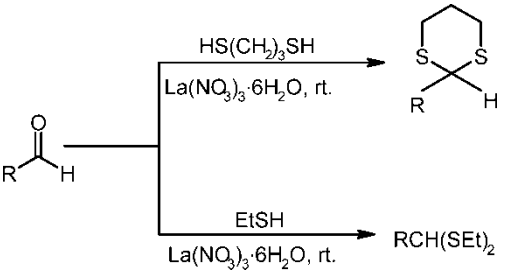
1. Introduction

Natural products being the main target in synthetic organic chemistry, selective protection and deprotection of carbonyl functionality as an 1,3-dithiane plays an important role in the multi-step organic synthesis of complex natural products due to its inherent stability under both acidic and basic conditions [1]. 1,3-Dithiane as a protecting group has been used in the synthesis of azasugars such as 1,4-dideoxy-1,4-imino-D-galactiol,an inhibitor of mycobacterial galactan biosynthesis [2], in the synthesis of azadirachtin [3], a strong anti-feedant isolated from the seeds of an Indian Neem tree, and 2-lithio-1,3-dithiane derivatives [4], starting materials for the synthesis of natural products, such as serriconin [5], compactin [6], pinellic acid [7], manzamine [8], discodermolide [9] and prostaglandinA_2 [10]. 1,3-Dithanes are generally obtained by Brönsted acid or Lewis acid [11] catalyzed condensation of carbonyl compounds with thiols or dithiols. Further, the other acids such as HCl [12], $BF_3 \cdot OEt_2$ [13], *p*-TSA [14], $InCl_3$ [15], SO_2 [16], $TiCl_4$ [17], CAN [18], $ZrCl_4$ [19], triflates [20], oxidizing agents such as NBS [21] and DDQ [22] and heterogeneous catalysts such as heteropoly acids [23] were employed to carry out the reaction.

*Corresponding author. Tel.: +91 40 27193167; Fax: +91 40 27160512; Email: luchem@iict.res.in
†IICT Communication # 061103.

Journal of Sulfur Chemistry
ISSN 1741-5993 print/ISSN 1741-6000 online
http://www.tandf.co.uk/journals
DOI: 10.1080/17415990701344710

However, several of these reported methods are associated with drawbacks such as low chemoselectivity [24], incompatible with other protecting groups [25], strong acidic conditions [26], long reaction times [27], tedious procedure for the preparation of catalyst and demand dry reaction conditions under nitrogen atmosphere. Thus, there is further scope to explore suitable mild and selective alternative reagent for thioacetalization of carbonyl compounds (Scheme 1).



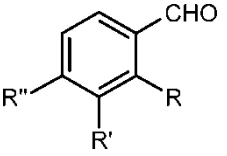
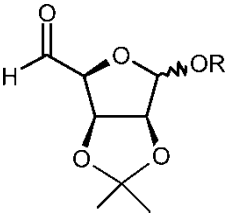
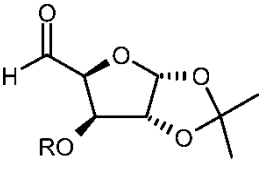
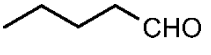
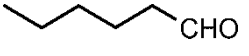
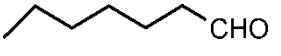
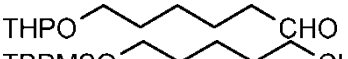
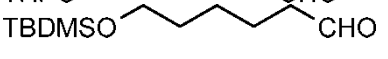
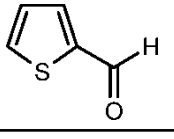
SCHEME 1

Organic reactions using mild and water tolerant catalysts received much attention in recent years. They can be conveniently handled and removed from the reaction mixture, making the experimental procedure simple and eco-friendly. Recently, we explored $La(NO_3)_3{\cdot}6H_2O$ as a mild and efficient acid catalyst in various organic transformations, such as chemoselective deprotection of primary acetonides [28], tetrahydropyranylation of primary alcohols [29], acetylation of alcohols, phenols and amines [30], in the synthesis of α-amino nitriles [31], benzodiazepines [32] and *N-tert*-butoxycarbonylation, *N*-benzyloxycarbonylation of amines [33, 34]. $La(NO_3)_3{\cdot}6H_2O$ is mild, inexpensive, non-toxic, readily available, easy to handle and insensitive to air. In the course of study in above transformations, it has been observed that the substrates containing other acid labile functional groups such as acetonides, TBDMS ethers, some isopropylidene protected diols and *N-tert*-Boc protected amines were intact in the presence of $La(NO_3)_3{\cdot}6H_2O$. Now, we envisaged for chemoselective thioacetalization of aldehydes using catalytic amounts of lanthanum(III) nitrate hexahydrate with 1,3-dithiol under solvent free conditions.

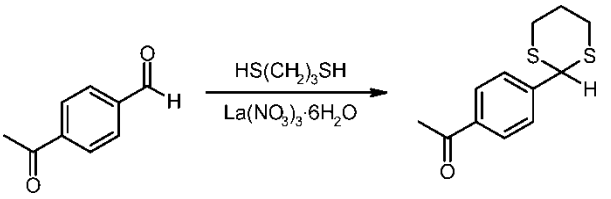
2. Results and discussion

This method does not require special care to exclude moisture from the reaction medium. Initially, we reacted benzaldehyde with ethanethiol in the presence of catalytic amounts of lanthanum(III) nitrate hexahydrate to yield corresponding thioacetal in 90% yield. Encouraged by the yields of the reaction, we further explored this thioacetalization reaction on various aldehydes in excellent yields (table 1). It is evident from the table 1 that a large number of acid-sensitive groups remain unchanged during thioacetalization (table 1). Further, aldehydes only underwent protection as thioacetals under this reaction conditions, and ketones are unaffected (scheme 2). The reaction is compatible to the substrates having acid sensitive groups such as TBDMs and THP. (table 1, entries 7, 13, 19, 20).

Table 1. Thioacetalization of aldehydes using lanthanum(III) nitrate hexahydrate.

Entry	Substrate	Thiol	Time (min)[a]	Yield (%)[b]
				
1	R=H, R′=H, R″=OH	CH_3CH_2SH	60	90
2	R=H, R′=NO_2, R″=H	CH_3CH_2SH	75	92
3	R=NO_2, R′=H, R″=H	CH_3CH_2SH	60	86
4	R=H, R′=H, R″=Cl	CH_3CH_2SH	60	84
5	R=H, R′=H, R″=NO_2	CH_3CH_2SH	90	90
6	R=H, R′=NO_2, R″=OMe	CH_3CH_2SH	60	92
7	R=H, R′=OMe, R″=OTBDMS	CH_3CH_2SH	60	85
8	R=H, R′=H, R″=OMe	CH_3CH_2SH	60	80
9	R=H, R′=H, R″=NMe_2	CH_3CH_2SH	60	90
				
10	R=OMe	$HS(CH_2)_3SH$	90	92
11	R=Bz	$HS(CH_2)_3SH$	90	82
12	R=Ac	$HS(CH_2)_3SH$	90	90
13	R=TBDMS	$HS(CH_2)_3SH$	90	90
				
14	R=Bn	$HS(CH_2)_3SH$	90	80
15	R=Bz	$HS(CH_2)_3SH$	90	80
16		$HS(CH_2)_3SH$	60	90
17		$HS(CH_2)_3SH$	60	95
18		$HS(CH_2)_3SH$	60	95
19		$HS(CH_2)_3SH$	60	92
20		CH_3CH_2SH	60	85
21		CH_3CH_2SH	60	93

[a]All compounds were characterized by ^{1}H NMR and EIMS spectral data.
[b]Isolated yields after column chromatography.



SCHEME 2

3. Conclusion

In conclusion, we have developed a mild and efficient reagent lanthanum(III) nitrate hexahydrate for the protection of aldehydes as thioacetals using 1,3-dithiol and ethanethiol under solvent-free condition at room temperature. The catalyst is inexpensive, commercially available and the reaction conditions do not require dry conditions.

4. Experimental section

4.1 *Typical experimental procedure*

To a mixture of aldehyde (1 mmol) and 1,3-dithiol (1.1 mmol) or ethanethiol (2.2 mmol) was added finely powdered $La(NO_3)_3 \cdot 6H_2O$ (5 mol%) and the reaction was stirred under solvent-free conditions at room temperature for an appropriate time (table 1). After completion of the reaction as monitored by TLC, water (10 mL) was added to the reaction mixture and the product was extracted into ethyl acetate (3×20 mL). The combined organic layer was washed with brine solution, dried over anhydrous sodium sulphate and concentrated under reduced pressure to give crude product, which was purified over silica gel column to afford corresponding thioacetals.

Entry 10. ^{1}H NMR (300 MHz, $CDCl_3$) $\delta = 1.35$ (s, 3H), 1.45 (s, 3H), 1.80–2.00 (m, 2H), 2.60–2.90 (m, 4H), 3.35 (s, 3H), 3.85 (dd, 1H), 4.00 (d, 1H), 4.48 (d, 1H), 4.75 (dd, 1H), 4.85 (s, 1H); EIMS: m/z 203 ($M^{+\cdot} + 1$).

Entry 11. ^{1}H NMR (300 MHz, $CDCl_3$) $\delta = 1.34$ (s, 3H), 1.44 (s, 3H), 1.82–2.05 (m, 2H), 2.65–2.90 (m, 4H), 3.85 (dd, 1H), 4.00 (d, 1H), 4.48 (d, 1H), 4.76 (dd, 1H), 4.86 (s, 1H), 7.40 (d, 2H, $J = 8.42$ Hz), 7.50 (m, 1H), 8.00 (m, 2H, $J = 8.42$ Hz); EIMS: m/z 293 ($M^{+\cdot} + 1$).

Entry 12. ^{1}H NMR (300 MHz, $CDCl_3$) $\delta = 1.35$ (s, 3H), 1.45 (s, 3H), 1.80–2.00 (m, 2H), 2.60–2.90 (m, 4H), 2.10 (s, 3H), 3.85 (dd, 1H), 4.00 (d, 1H), 4.48 (d, 1H), 4.75 (dd, 1H), 4.85 (s, 1H); EIMS: m/z 231 ($M^{+\cdot} + 1$).

Entry 13. ^{1}H NMR (300 MHz, $CDCl_3$) $\delta = 0.20$ (s, 6H), 0.90 (s, 9H), 1.30 (s, 3H), 1.40 (s, 3H), 1.75–2.00 (m, 2H), 2.62–2.92 (m, 4H), 3.85 (dd, 1H), 4.05 (d, 1H), 4.50 (d, 1H), 4.75 (dd, 1H), 4.85 (s, 1H); EIMS: m/z 247 ($M^{+\cdot} + 1$).

Entry 15. ^{1}H NMR (300 MHz, $CDCl_3$) $\delta = 1.40$ (s, 3H), 1.50 (s, 3H), 1.85–2.00 (m, 2H), 2.65–2.95 (m, 4H), 4.25 (m, 1H), 4.62 (d, 1H), 4.80 (s, 1H), 5.45 (d, 1H), 5.80 (d, 1H), 7.40 (d, 2H, $J = 8.52$ Hz), 7.50 (m, 1H), 8.00 (m, 2H, $J = 8.52$ Hz); EIMS: m/z 277 ($M^{+\cdot} + 1$).

Acknowledgements

The authors are thankful to CSIR, DOD and DBT New Delhi, India, for the financial support and to the Director of Indian Institute of Chemical Technology for his encouragement.

References

[1] T.W. Greene, P.G.M. Wuts. *Protective Groups in Organic Synthesis*, 3rd ed. p. 329, Wiley, New York (1999).
[2] E.R. Lee, D.M. Smith, J.R. Nash, C.R. Griffiths, M. Mc Neil, K.R Grewal, W. Yan, S.G. Besra, J.P. Brennan, W.J.G. Fleet. *Tetrahedron Lett*., **38**, 6733 (1997).
[3] S.V. Ley, A.A. Denholm, A. Wood. *Nat. Prod. Rep*., **10**, 109 (1993)
[4] Y. Miguel, N. Carmen, F. Francisco. *Tetrahedron*, **59**, 6147 (2003).
[5] N.H. Andersen, A.P. Denniston, D.A. Mcre. *J. Org. Chem*., **47**, 1145 (1982).
[6] N. Iwasawa, J. Sugimori, Y. Kawase, K. Narasaka. *Chem. Lett*., **18**, 1947 (1989).
[7] T. Sunazuka, T. Shirahata, K. Yoshida, D. Yamamoto, Y. Harigaya, T. Nagai, H. Kihoyara, H. Yamada, I. Kuwajima, S. Omura. *Tetrahedron Lett*., **43**, 1265 (2002).
[8] I. Coldham, K.M. Crapnell, J.C. Fernandez, J.P. Moseley, R. Rabot. *J. Org. Chem*., **67**, 6181 (2002).
[9] A.B. Smith III, M.D. Kaufman, Y. Qiu, H. Arimoto, D.R. Jones, K. Kobayashi. *J. Am. Chem. Soc*., **122**, 8654 (2000).
[10] G.H. Schmid, D.G. Garratt. *Tetrahedron Lett*., **16**, 399 (1975).
[11] D. Seebach. *Angew. Chem. Int. Ed. Engl*., **18**, 329 (1979).
[12] J.W. Ralls, R.M. Dobson, B. Reigel. *J. Am. Chem. Soc*., **71**, 3320 (1949).
[13] T. Nakata, S. Nagao, S. Mori, T. Osihi. *Tetrhaedron Lett*., **26**, 6461 (1985).
[14] C. Djerassi, M. Gorman. *J. Am. Chem. Soc*., **75**, 3704 (1953).
[15] S. Madhuswamy, S. Arulananda Babu, C. Gunathan. *Tetrahedron Lett*., **42**, 359 (2001).
[16] B. Burezyk, Z. Kortylewicz. *Synthesis*, 831 (1982).
[17] B.S. Ong. *Tetrahedron Lett*., **21**, 4225 (1980).
[18] M.P. Kumar, S.C. Roy. *Tetrahedron*, **51**, 7823 (1995).
[19] Y. Kamitori, M. Hojo, R. Masuda, T. Kimura, T. Yoshida. *J. Org. Chem*., **51**, 1427 (1986).
[20] D. Suryakanta. *Synthesis*, **17**, 2837 (2004).
[21] B. Karimi, H. Ebrahimian, H. Seradj. *Org. Lett*., **1**, 1737 (1999).
[22] B. Karimi, A.M. Ashtiani. *Chem. Lett*., **28**, 1199 (1999).
[23] F. Habib, N. Iranpoor, K. Amani. *Synthesis*, **1**, 59 (2002).
[24] R.V. Anand, P. Sarvanan, V.K. Singh. *SynLett*., 413 (1999).
[25] J.S. Yadav, B.V.S. Reddy, S.K. Pandey. *SynLett*., 338 (2001).
[26] G.R. Pettit, E.E. Van Tamden. *Org. React*., **12**, 352 (1962).
[27] T. Srikanth Reddy, K. Ravinder, N. Suryakiran, M. Narasimhulu, K. Chinni Mahesh, Y. Venkateswarlu. *Tetrahedron Lett*., **47**, 2341 (2006).
[28] S. Malla Reddy, Y. Venkat Reddy, Y. Venkateswarlu. *Tetrahedron Lett*., **46**, 7439 (2005).
[29] M. Narasimhulu, K. Chinni Mahesh, T. Srikanth Reddy, K. Rajesh, Y. Venkateswarlu. *Tetrahedron Lett*., **47**, 4381 (2006).
[30] T. Srikanth Reddy, M. Narasimhulu, N. Suryakiran, K. Chinni Mahesh, Y. Venkateswarlu. *Tetrahedron Lett*., **47**, 6825 (2006).
[31] M. Narasimhulu, T. Srikanth Reddy, K.C. Mahesh, S. Malla Reddy, Y. Venkateswarlu. *J. Mol. Cat. A. Chem*., **264**, 288 (2006).
[32] N. Suryakiran, K. Rajesh, P. Prabhakar, J. Jon Paul Selvam and Y. Venkateswarlu. *Cat. Commun*., **8**, 1635 (2007).
[33] N. Suryakiran, P. Prabhakar, T. Srikanth Reddy, K. Rajesh, Y. Venkateswarlu. *Tetrahedron Lett*., **47**, 8039 (2006).
[34] K.C. Mahesh, M. Narasimhulu, T. Srikanth Reddy, Y. Venkateswarlu. *Tetrahedron Lett*., **48**, 55 (2007).