Available online at www.sciencedirect.com

SCIENCE DIRECT®

Tetrahedron Letters 46 (2005) 7439–7441

Tetrahedron Letters

A mild and efficient method for the chemoselective deprotection of acetonides with lanthanum(III) nitrate hexahydrate☆

S. Malla Reddy, Y. Venkat Reddy and Y. Venkateswarlu*

Natural Products Laboratory, Organic Chemistry Division-I, Indian Institute of Chemical Technology, Hyderabad 500 007, India

Received 14 July 2005; revised 8 August 2005; accepted 17 August 2005
Available online 9 September 2005

Abstract—Acetonides are hydrolyzed selectively and efficiently with lanthanum(III) nitrate hexahydrate in acetonitrile. The method has good compatibility with other sensitive hydroxyl protecting groups such as trityl, TBDMS, THP, OAc, OBz and OBn.

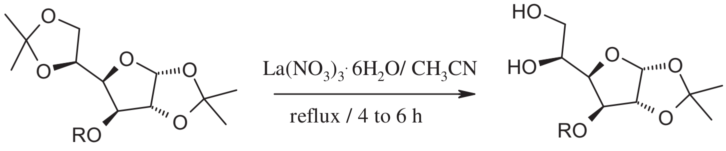
1. Introduction

Protecting groups in organic synthesis, particularly in multi-step synthesis of structurally complicated natural products, are very important. However many syntheses have failed because the protecting groups could not be removed at the appropriate step.[1] Acetonides are commonly used to mask hydroxyl groups in polyhydroxylated natural products, nucleosides and oligosaccharides.[2] As a consequence, many methods have been developed for their formation and removal.[3] Typically, deprotection of acetals requires the use of protic or Lewis acids.[3,4] More recently alternative methods that include the use of DDQ, aqueous DMSO, lithium halides, silanes and insoluble acidic matrices have been developed.[5]

However, many of these methods suffer from disadvantages such as high acidity, long reaction times, unsatisfactory yields, inconvenient handling and low chemoselectivity. In view of the current interest in catalytic processes, there is merit in developing a truly catalytic deprotection of acetonide groups using an inexpensive and non-polluting reagent.

In this letter (Scheme 1), we describe an efficient method for the chemoselective deprotection of acetonide groups using lanthanum(III) nitrate hexahydrate in acetonitrile which gives the corresponding diols in high yields. This method does not need expensive reagents or special care to exclude moisture from the reaction medium. It is evident from Table 1, that a wide range of hydroxyl protecting groups such as trityl, TMS, THP, TBDMS, Bz, Bn, prenyl, methyl and Ac groups, including acid labile hydroxyl protecting groups, are left intact under the reaction conditions. A primary acetonide group is selectively hydrolyzed in the presence of a secondary acetonide and other hydroxyl protecting groups. No by-products were obtained.

We first examined the reaction of 3-*O*-(*tert*-butyldimethylsilyl)-1,2:5,6-*O*-isopropylidene-α-D-glucofuranose



Scheme 1.

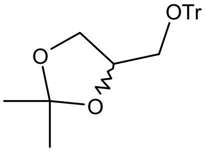
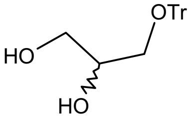
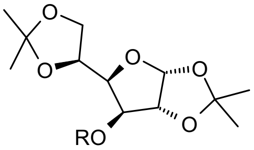
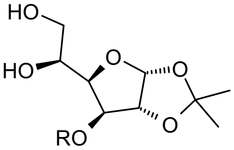
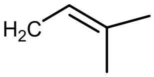
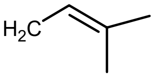
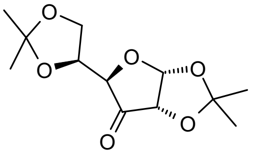
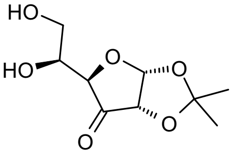
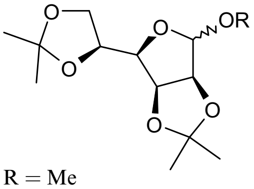
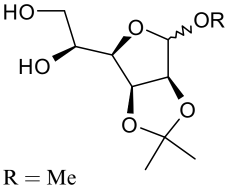
Keywords: Lanthanum nitrate hexahydrate; Chemoselective deprotection; Acetonides.

☆ IICT Communication No. 050805.

* Corresponding author. Tel.: +91 40 27193167; fax: +91 40 27160512; e-mail: luchem@iict.res.in

0040-4039/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2005.08.081

Table 1. Chemoselective deprotection of acetonides with lanthanum(III) nitrate hexahydrate

Entry	Compound	Product[a]	Time (h)	Yield[b] (%)
1			5	82[6]
				
2	R = TMS	R = TMS	6	81[8]
3	R = TBDMS	R = TBDMS	6	96[7]
4	R = THP	R = THP	5	94[7]
5	R = Ac	R = Ac	5	94[7]
6	R = Bz	R = Bz	5	90[7]
7	R = Bn	R = Bn	5	96[7]
8	R = Me	R = Me	5	90[8]
9	R = 	R = 	5	92[10a]
10			6	88[7]
				
11	R = Me	R = Me	5	88[7]
12	R = Ac	R = Ac	6	89[9]
13	R = Bn	R = Bn	6	92[10b]
14	R = Bz	R = Bz	6	94[9]

[a] All the products were characterized by ^{1}H NMR, ^{13}C NMR, IR and mass spectral analysis.

[b] Yields refer to isolated yields after column chromatography.

(Table 1, entry **3**), with lanthanum(III) nitrate hexahydrate in acetonitrile at room temperature for 24 h, which gave the corresponding diol in 76% yield. In order to improve the yield of the reaction, it was carried out at reflux in acetonitrile for 4 h to give the corresponding diol in 96% yield. This result encouraged us to carry out the reaction in the presence of several different hydroxyl protecting groups at reflux in acetonitrile, the corresponding products were obtained in excellent yields (Table 1).

In conclusion, the present method for acetonide removal has advantages in addition to an easy work-up procedure.

2. General experimental procedure for the synthesis of diols

A mixture of acetonide (1 mmol) and lanthanum nitrate hexahydrate (5 mol %) in acetonitrile (15 mL) was heated under reflux for the appropriate time (Table 1). After completion of the reaction as monitored by TLC, the solvent was evaporated under reduced pressure, water was added and the product was extracted into ethyl acetate. The organic layer was dried over anhydrous sodium sulfate and concentrated. The crude product was purified over silica gel to yield the corresponding diol (Scheme 1).

Acknowledgements

S.M.R. thanks the CSIR, India, for financial assistance.

References and notes

1. (a) Schkeryantz, J. M.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1995**, *117*, 4722–4723; (b) Masters, J. J.; Link, J. T.; Snyder, L. B.; Young, W. B.; Danishefsky, S. J. *Angew.*

Chem., Int. Ed. Engl. **1995**, *34*, 1723–1726; (c) Boyce, R. J.; Pattenden, G. *Tetrahedron Lett.* **1996**, *37*, 3501–3504.

2. (a) Clode, D. M. *Chem. Rev.* **1979**, *79*, 491–513; (b) Nicolaou, K. C.; Daines, R. A.; Uenishi, J.; Li, W. S.; Papahatjis, D. P.; Chakraborthy, T. K. *J. Am. Chem. Soc.* **1988**, *110*, 4672–4685; (c) Kim, Y.; Singer, R. A.; Carreira, E. M. *Angew. Chem., Int. Ed.* **1998**, *37*, 1261–1263.
3. Green, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*; John Wiley and Sons: New York, 1991.
4. (a) Barbot, F.; Miginiac, P. *Synthesis* **1983**, 651–654; (b) Sterzycki, R. *Synthesis* **1979**, 724–725; (c) Kantam, M. L.; Swapna, V.; Santhi, P. L. *Synth. Commun.* **1995**, *25*, 2529–2532; (d) Ma, S.; Venanzi, L. M. *Tetrahedron Lett.* **1993**, *34*, 8071–8074; (e) Ford, K. L.; Roskamp, E. J. *J. Org. Chem.* **1993**, *58*, 4142–4143; (f) Chang, C.; Chu, K. C.; Yue, S. *Synth. Commun.* **1992**, *22*, 1217–1220; (g) Sarmah, P.; Barua, N. C. *Tetrahedron Lett.* **1989**, *30*, 4703–4704; (h) Lipshutz, B. H.; Pollart, D.; Monforte, J.; Kotsuki, H. *Tetrahedron Lett.* **1985**, *26*, 705–708; (i) Lipshutz, B. H.; Harvey, D. F. *Synth. Commun.* **1982**, *12*, 267–277.
5. (a) Tanemura, K.; Suzuki, T.; Horaguchi, T. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 290–292; (b) Kametani, T.; Kondoh, H.; Honda, T.; Ishizone, H.; Suzuki, Y.; Mori, W. *Chem. Lett.* **1989**, 901–904; (c) Maiti, G.; Roy, S. C. *J. Org. Chem.* **1996**, *61*, 6038–6039; (d) Chen, Y.-H.; Tseng, Y.-T.; Luh, T.-Y. *Chem. Commun.* **1996**, 327–328; (e) Elmory, S. S.; Bhatt, M. V.; Pelter, A. *Tetrahedron Lett.* **1992**, *33*, 1657–1660; (f) Rao, M. N.; Kumar, P.; Singh, A. P.; Reddy, R. S. *Synth. Commun.* **1992**, *22*, 1299–1305; (g) Hoyer, S.; Laszlo, P. *Synthesis* **1986**, 655–657; (h) Otera, J.; Nozaki, H. *Tetrahedron Lett.* **1986**, *27*, 5743–5746; (i) Coppola, G. M. *Synthesis* **1984**, *61*, 6646–6650.
6. Kim, K. S.; Song, Y. H.; Lee, B. H. *J. Org. Chem.* **1986**, *51*, 404–407.
7. Swamy, N. R.; Venkateswarlu, Y. *Tetrahedron Lett.* **2002**, *43*, 7549–7552.
8. Chary, M. A.; Syamasunder, K. *Synthesis* **2005**, 708–710.
9. Vijayasaradhi, S.; Singh, J.; Aidhen, I. S. *Synlett* **2000**, *1*, 110–112.
10. (a) Spectral data for the product in entry 9 (Table 1): Viscous liquid, $[\alpha]_D^{25}$ −27.8 (*c* 1.28, $CHCl_3$): ^1H NMR (300 MHz, $CDCl_3$): δ 5.82 (1H, d, $J = 3.9$ Hz), 5.30 (1H, t, $J = 7$ Hz), 4.49 (1H, d, $J = 3.9$ Hz), 4.00–4.13 (3H, m), 3.93 (2H, dd, $J = 10, 7$ Hz), 3.61–3.8 (2H, m), 3.04 (2H, br s), 1.75 (3H, s), 1.69 (3H, s), 1.45 (3H, s) and 1.28 (3H, s); EIMS *m/z*: 288 (M^+); HRMS, obsd *m/z* 288.1564, $C_{14}H_{24}O_6$ requires *m/z* 288.1573; (b) Spectral data for the product in entry 13 (Table 1): Viscous liquid, $[\alpha]_D^{25}$ −51.6 (*c* 2, $CHCl_3$): ^1H NMR (300 MHz, $CDCl_3$): δ 7.23–7.33 (5H, m), 4.82 (1H, d, $J = 12.6$Hz), 4.73–4.77 (2H, m), 4.54–4.60 (2H, m), 4.02 (1H, m), 3.82 (1H, dd, $J = 11.9, 3$ Hz), 3.67 (2H, m), 1.52 (3H, s), 1.35 (3H, s); EIMS *m/z*: 310 (M^+); HRMS, obsd *m/z* 310.1424, $C_{16}H_{22}O_6$ requires *m/z* 310.1416.