Vanadium(III) chloride: A mild and efficient catalyst for the chemoselective deprotection of acetonides ☆

Gowravaram Sabitha *, G.S. Kiran Kumar Reddy, K. Bhaskar Reddy,
N. Mallikarjuna Reddy, J.S. Yadav

Organic Chemical Sciences, Indian Institute of Chemical Technology, Hyderabad 500 007, India

Abstract

Acetonides are selectively cleaved at room temperature by a catalytic amount of VCl$_3$ in methanol to furnish the corresponding diols under mild conditions. Other hydroxyl protecting groups such as TBDMS, TBDPS, Ac, THP, Bn, prenyl, allyl present in the substrate were intact under the reaction conditions.
© 2005 Elsevier B.V. All rights reserved.

Keywords: Acetonides; Vanadium chloride; Chemoselective; Diols

1. Introduction

The selective deprotection of substituted hydroxyl groups is one of the most active research topics in synthetic organic chemistry especially in polyhydroxy natural products, carbohydrates and in nucleosides chemistry [1]. Cyclic isopropylidene acetals, also known as acetonides are the most popular for the protection of 1,2 or 1,3-diols in carbohydrates in organic synthesis [2]. The deprotection of acetonides is usually carried out with aq. HCl [3a], aq. HBr [3b], aq. AcOH [3c], 0.8% H$_2$SO$_4$ in MeOH [3d], Dowex-H$^+$ in MeOH:H$_2$O [3e], CSA [4a], CF$_3$COOH [4b], TsOH [4c], NaHSO$_4$–SiO$_2$ [4d] and clay-catalysed [4e]. In addition, some Lewis acids have also been employed to effect this transformation which include FeCl$_3$·6H$_2$O/SiO2 [5], CuCl$_2$·2H$_2$O in ethanol [6], BiCl$_3$ [7], Zn(NO$_3$)$_2$ [8] and CeCl$_3$·7H$_2$O–(COOH)2 [9]. However, many of these reported procedures suffer from disadvantages like high acidity, longer reaction times, high temperatures, use of more than a stoichiometric amounts of catalyst, requiring the control of pH and more importantly failed to cleave acetonide group selectively. Selective cleavage of acetonides in the presence of other functional groups is a useful synthetic reaction in organic synthesis. Therefore, there is still continuing interest in developing a new selective method which has a good compatibility with other protecting groups.

2. Results and discussion

In continuation of our recent findings on the use of VCl$_3$ [10] as a mild Lewis acid in organic synthesis, herein, we report a mild and efficient method for the selective cleavage of acetonide in the presence of other functional groups with a catalytic amount of VCl$_3$ in methanol at room temperature (Scheme 1).

Thus, when a compound **1c** containing both isopropylidene group and TBDMS ether linkage was treated with a catalytic amount of VCl$_3$ in methanol, the terminal 5,6-*O*-isopropylidene group was regioselectively cleaved at room temperature to afford the corresponding diol in 86% yield. The reaction was found to be complete in 20 min leaving 1,2-isopropylidene and TBDMS groups intact, which was confirmed by ^{1}H NMR spectroscopy. On the other hand
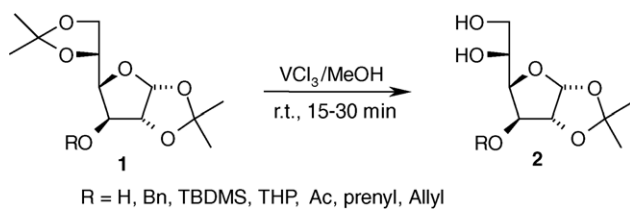
Scheme 1.

H_2SO_4 or acetic acid are reported to hydrolyse both iso-propylidene group and the TBDMS ether to afford a mixture of products. Monoisopropylidene-D-mannose and -glucose are useful starting materials for the preparation of numer-

ous derivatives and chiral natural products [11]. Similarly, a number of substrates were used for the cleavage of ace-tonide group and the results are summarized in Table 1, which reveal the scope and selectivity of the reaction. In all cases, the acetonide group was selectively cleaved and reactions were complete in just 15–30 min, hydrolysing cleanly only the terminal acetonide group, affording the corresponding products in good to excellent yields. Other hydroxyl protect-ing groups such as TBDMS, TBDPS, Bn, THP, prenyl, allyl ethers and OAc esters present in the substrate were survived under present reaction conditions. The cleavage of acetonide group in chiral compounds was achieved under mild condi-tions without disturbing its stereochemistry. No racemization

Table 1
VCl_3 catalyzed selective cleavage of acetonides

Entry	Substrate 1	Product[a] 2	Time (min)	Yield (%)[b]	Optical rotation
a	R = H		30	85	−10.9 (c = 2 H$_2$O)
b	R = Bn		20	83	−46.2 (c = 1.5 CHCl$_3$)
c	R = TBDMS		20	86	−1.9 (c = 0.2 CHCl$_3$)
d	R = THP		20	80	−40.3 (c = 1.0 CHCl$_3$) [12]
e	R = Ac		30	90	+2.0 (c = 0.2 CHCl$_3$)
f	R = Prenyl		30	92	−40.13 (c = 1.0 CHCl$_3$) [12]
g	R = Allyl		15	88	−30.2 (c = 1.0 CHCl$_3$)
h	R = Bn		25	80	+81.0 (c = 1.0 CHCl$_3$) [6]
I	R = TBDPS		30	85	+41.1 (c = 1.0 CHCl$_3$)
j	R = Ac		30	82	+11.5 (c = 1.0 CHCl$_3$) [8]
k			30	87	−18.4 (c = 1.0 H$_2$O)
l	R = H		15	85	
m	R = TBDMS		20	84	+0.9 (c = 1.0 CHCl$_3$) [14]
n	R = Bn		20	90	+4.7 (c = 1.0 CHCl$_3$)
o	R = TBDPS		25	88	+1.2 (c = 1.0 CHCl$_3$) [15]
p	R = TBDMS		20	78	+20.7 (c = 1.0 CHCl$_3$)
q	R = TBDPS		25	82	+5.7 (c = 1.0 CHCl$_3$)
r	R = THP		20	54[c]	+1.57 (c = 1.0 CHCl$_3$)

[a] All products were characterized by IR and ^{1}H NMR spectral data.
[b] Isolated yields after column chromatography.
[c] Triol isolated.
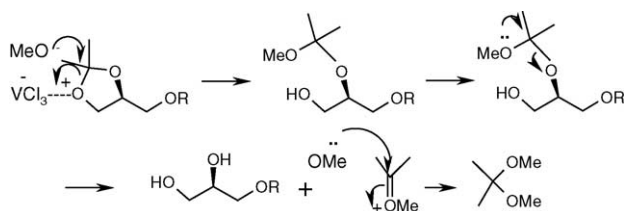
Scheme 2.

was observed under our reaction conditions, which was confirmed by the comparison of optical rotation of compound **2f** ([α]$_D$ −40.3 (c 1.0, CHCl$_3$)) with an authentic sample ([α]$_D$ −40.1 (c 1.0, CHCl$_3$)) [12]. Therefore, it is important to mention that the stereochemistry of the product was retained during deprotection. It was also observed that prolonged reaction time in entry **d** resulted in the cleavage of both the groups such as THP and isopropylidene group. Whereas in the case of entry **r**, monodeprotected compound has been obtained as a major, and the compound with deprotection of both THP and isopropylidene groups as a minor. The monodeprotection of the acetonide group in the presence of THP reveals the mild Lewis acid nature of the VCl$_3$ [13]. All the reactions are very efficient, and a catalytic amount of the reagent is sufficient to drive the reaction to completion at room temperature. The products were characterized by spectral data such as ^{1}H NMR, IR and also by comparison with authentic samples. The spectroscopic data was identical with the data reported in the literature.

In this reaction, we assume that the Lewis acidity of vanadium(III) ion plays a role on removing the acetonide, and a possible mechanism is envisioned in Scheme 2.

3. Conclusions

In conclusion, we have developed a novel, and efficient method for the selective cleavage of acetonide group with a catalytic amount of VCl$_3$. The advantages of the present method are shorter reaction times, mild reaction conditions, operational simplicity, regioselectivity and good compatibility with other acid labile groups and high yields of the products.

4. Experimental

To a solution of compound **1** (1 mmol) in methanol (5 mL), was added VCl$_3$ (5 mol%) and stirred for a specified time (Table 1). Upon completion of the reaction, as indicated by TLC, the reaction mixture was concentrated using rotary evaporator in vacuo and the residue was taken up into dichloromethane. The organic layer was washed with water, brine and dried over Na$_2$SO$_4$. Evaporation of the solvent and purification by silica gel column chromatography using ethyl acetate/hexane as eluent afforded the corresponding

diol **2** in good yields. Selected spectroscopic data: entry **1d**: ^{1}H NMR (CDCl$_3$, 200 MHz): δ 1.08–1.95 (m, 6H), 1.30 (s, 3H), 1.35 (s, 3H), 1.38 (s, 3H), 1.55 (s, 3H), 3.50 (m, 2H), 3.70–4.80 (m, 6H), 4.55 (t, 1H, J = 2.60, 6.22 Hz), 5.80 (d, 1H, J = 4.5 Hz). Entry **2d**: ^{1}H NMR (CDCl$_3$, 200 MHz): δ 0.65–1.65 (m, 6H), 1.20 (s, 3H), 1.35 (s, 3H), 3.40–4.40 (t, 1H, J = 2.60, 6.20 Hz), 5.85 (d, 1H, J = 4.5 Hz). Entry **1g**: ^{1}H NMR (CDCl$_3$, 200 MHz): δ 1.22 (s, 3H, –CH$_3$), 1.30 (s, 3H, –CH$_3$), 1.40 (s, 3H, CH$_3$), 1.45 (s, 3H, CH$_3$), 3.85–4.15 (m, 6H), 4.25 (m, 1H), 4.45 (d, 1H, J = 4.0 Hz), 5.20 (dd, 2H, J = 8.2, 14 Hz), 5.80 (d, 1H, J = 4.0 Hz), 5.84 (m, 1H). Entry **2g**: ^{1}H NMR (CDCl$_3$, 200 MHz): δ 1.22 (s, 3H, −CH$_3$), 1.40 (s, 3H, –CH$_3$), 3.30–4.10 (m, 7H and 2-OH), 4.45 (d, 1H, J 4.0 Hz), 5.20 (dd, 2H, J 8, 14 Hz), 5.80 (d, 1H, J 4.0 Hz), 5.84 (m, 1H). Entry **1m**: ^{1}H NMR (CDCl$_3$, 200 MHz): δ 0.02 9s, 6H), 0.82 (s, 9H), 1.25 (s, 3H), 1.30 (s, 3H), 3.50 (dd, 1H, J = 6.2, 8.5 Hz), 3.60 (dd, 1H, J = 7.5, 12.2 Hz), 3.73 (dd, 1H, J = 6.2, 8.0 Hz), 3.94 (dd, 1H, J = 7.5, 12.5 Hz), 4.20 (m, 1H). Entry **2m**: ^{1}H NMR (CDCl$_3$, 200 MHz): δ 0.0 (s, 6H), 0.85 (s, 9H), 3.50–3.65 (m, 4H), 3.70–3.75 (m, 1H). Entry **1q**: ^{1}H NMR (CDCl$_3$, 200 MHz): δ 0.85 (d, 3H, J = 6.6 Hz), 1.05 (d, 3H, J = 6.6 Hz), 1.30 (s, 9H), 1.36 (d, 3H, J = 6.7 Hz), 1.58 (s, 3H), 1.62 (s, 3H, 2.00–2.45 (m, 3H), 3.60–3.95 (m, 4H), 4.05–4.18 (m, 2H), 4.85 (dd, 2H, J = 7.5, 14.5 Hz), 7.45–7.80 (m, 11H), 7.90–8.00 (m, 4H). Entry **2q**: ^{1}H NMR (CDCl$_3$, 200 MHz): δ 0.72 (d, 3H, J = 6.6 Hz), 0.98 (d, 3H, J = 6.6 Hz), 1.05 (s, 9H), 1.10 (d, 3H, J = 6.8 Hz), 1.75–2.18 (m, 3H), 3.45–4.02 (m, 6H), 4.58 (dd, 2H, J = 4.0, 9.2 Hz), 6.98–7.80 M, 15H).

References

[1] (a) T.W. Greene, P.G.M. Wuts, Protective Groups in Organic Synthesis, 2nd ed., Wiley, New York, 1991;
(b) P.J. Kocienski, Protecting Groups, Georg Thieme, Stuttgart, New York, 1994.
[2] (a) D.M. Clode, Chem. Rev. 79 (1979) 491;
(b) K.C. Nicolaou, R.A. Daines, J. Uenishi, W.S. Li, D.P. Papahatjis, T.K. Chakraborthy, J. Am. Chem. Soc. 110 (1988) 4672;
(c) Y. Kim, R.A. Singer, E.M. Carreira, Angew. Chem. Int. Ed. 37 (1998) 1261.
[3] (a) G.W.J. Fleet, P.W. Smith, Tetrahedron Lett. 26 (1985) 1469;
(b) M. Gerspacher, H. Rapoport, J. Org. Chem. 56 (1991) 3700;
(c) J.S. Yadav, M.C. Chander, K.K. Reddy, Tetrahedron Lett. 33 (1992) 135;
(d) M. Sukumar, V. Jacques, Y. Pendri, J.R. Falck, Tetrahedron Lett. 27 (1986) 2679;
(e) K.H. Park, Y.J. Yoon, S.G. Lee, Tetrahedron Lett. 35 (1994) 9737.
[4] (a) S. Baurle, S. Hoppen, U. Koert, Angew. Chem. Int. Ed. 38 (1999) 1263;
(b) Y. Leblanc, B.J. Fitzsimmons, J. Adams, F. Perez, J. Rokach, J. Org. Chem. 51 (1986) 789;

(c) A. Ichihara, M. Ubukata, S. Sakamura, Tetrahedron Lett. (1977) 3473;

(d) G. Mahender, R. Ramu, C. Ramesh, B. Das, Chem. Lett. 32 (2003) 734;

(e) N.S. Shaik, S.S. Bhor, A.S. Gajare, V.H. Deshpande, R.D. Wakharkar, Tetrahedron Lett. 45 (2004) 5395.

[5] K.S. Kim, Y.H. Song, B.H. Lee, C.S. Hahn, J. Org. Chem. 51 (1986) 404.

[6] M. Iwata, H. Ohrui, Bull. Chem. Soc. Chim. Jpn. 54 (1981) 2837.

[7] N. Raghavendraswamy, Y. Venkateshwarlu, Tetrahedron Lett. 43 (2002) 7549.

[8] S. Vijayasaradhi, J. Singh, I.S. Aidhen, Synlett 1 (2000) 110.

[9] X. Xiao, D. Bai, Synlett 4 (2001) 535.

[10] (a) G. Sabitha, G.S. Kiran Kumar Reddy, K. Bhaskar Reddy, J.S. Yadav, Tetrahedron Lett. 44 (2003) 6497;

(b) G. Sabitha, G.S. Kiran Kumar Reddy, K. Bhaskar Reddy, J.S. Yadav, Synthesis 15 (2003) 2298.

[11] W.A. Szabo, H.T. Lee, Aldrichim. Acta 13 (1980) 13.

[12] G.V.M. Sharma, I. Srinivas Reddy, V. Govardhan Reddy, A.V. Rama Rao, Tetrahedron: Asymmetry 10 (1999) 229.

[13] S. Kobayashi, T. Busujima, S. Nagayama, Chem. Eur. J. 19 (2000) 3491.

[14] J. Balint, G. Egri, C. Dianoczky, E. Fogassy, L. Novak, L. Poppe, Tetrahedron: Asymmetry 10 (1999) 4017.

[15] E.I. Victor, P. Mark, Syn. Comm. 28 (1998) 3727.