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LETTERS

A mild and efficient method for chemoselective deprotection of acetonides by bismuth(III) trichloride[†]

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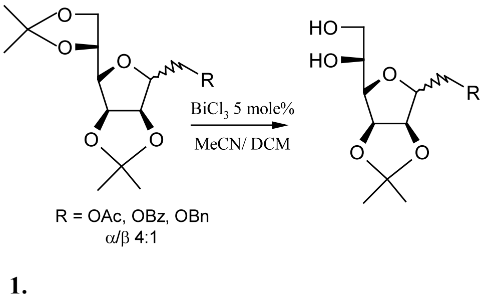
Abstract—Acetonides undergo chemoselective deprotection to afford the corresponding 1,2-diols in excellent yields using bismuth trichloride in acetonitrile/dichloromethane at ambient temperature. © 2002 Elsevier Science Ltd. All rights reserved.

Selective reactions on hydroxyl groups of polyhydroxyl compounds are extremely useful in organic synthesis especially in the field of carbohydrate and nucleoside chemistry. Indirect methods involve the use of protective groups.[1] Acetonides are the most frequently used protecting groups for 1,2-diols in carbohydrates in organic synthesis. The selective deprotection of acetonide groups is an important transformation in the synthesis of biologically active natural products and in the field of drugs and pharmaceuticals. They have also been used as chiral auxiliaries in the chiron approach.[2] A variety of reagents have been employed to effect this transformation including acids such as aq. HCl,[3a] aq. HBr,[3b] 60% aq. acetic acid[3c] and 0.8% H_2SO_4 in MeOH.[3d] Other Lewis acid base reagents such as $FeCl_3\cdot 6H_2O/SiO_2$,[4] $CuCl_2\cdot 2H_2O$ in ethanol,[5] $Zn(NO_3)_2\cdot 6H_2O$,[6] and $CeCl_3\cdot 7H_2O$ $(COOH)_2$[7] are also known to deprotect acetonides. However, many of these procedures suffer from disadvantages such as strong oxidizing conditions, high acidity, long reaction times, unsatisfactory yields, low chemoselectivity and large amounts of reagent or catalyst.



Scheme 1.

In this paper, we report that bismuth trichloride is as an efficient and selective deprotecting agent for acetonides (Scheme 1). The selective cleavage of acetonides in the presence of other acid-labile protective groups such as *tert*-butyldimethylsilyl ethers (TBDMS) and tetrahydropyranyl ethers (THP) proceeded smoothly. Bismuth, the heaviest stable element, is by far the least toxic of the heavy metals,[8–10] and consequently, an 'ecofriendly' element. Numerous bismuth compounds are commercially available at relatively low cost. The main industrial uses of bismuth are in metallurgy,[11] pharmaceutical products[8c,12] and as catalysts for the manufacture of acrolein[13a] and acrylonitrile.[13b]

Recently the catalytic activity of bismuth(III) derivatives as Lewis acids has been utilized in deprotections of ketoximes,[14] cleavage of epoxides,[15] oxidation of alkenes, acyloins, epoxides, α-hydroxy acids, and α-glycols or ketols,[14a,16] and in cyanation and allylation of carbonyl compounds.[17] They are also used in Knoevenagel condensations, Friedel–Crafts acylation, sulfonylation,[18] carbonyl and aza-Diels–Alder reactions,[19] carbonyl-ene reactions,[19c,20] Mukaiyama-aldol reactions, Michael reactions[21] and Ferrier rearrangements.[22]

In view of the current interest in catalytic processes there is a merit in developing a truly catalytic deprotection of acetonides using an inexpensive and non-polluting reagent. Herein, we wish to report the bismuth trichloride catalyzed acetonide deprotection. The reaction proceeds efficiently at ambient temperature and the products are obtained in excellent yields without by-products. Furthermore, other functionalities such as OMe, OBn, OBz, NHBOC, TBDMS, THP and OAc

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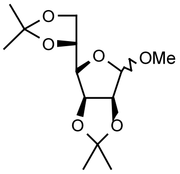
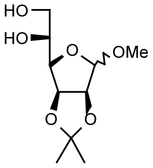
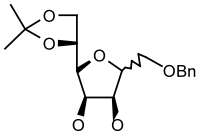
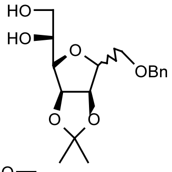
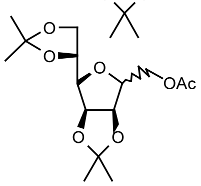
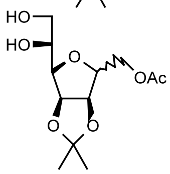
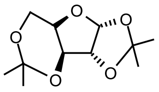
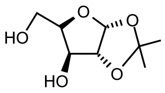
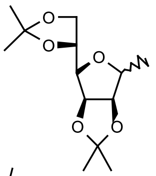
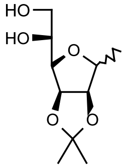
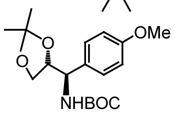
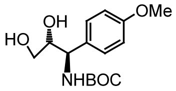
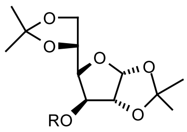
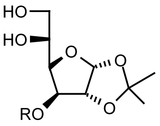
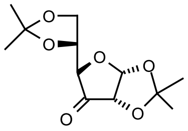
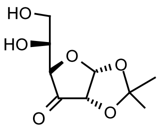
Table 1. Bismuth trichloride catalyzed acetonide deprotection

S.No	Substrate	Product	Solvent	Time (min)	%Yield*
a			CH_3CN	30	89[23a]
b			CH_3CN	30	92[23b]
c			CH_3CN	30	88[23b]
d			CH_3CN	30	93[23c]
e			CH_3CN	30	85
f			CH_3CN	30	88
					
g	R=Bn		CH_2Cl_2	30	93[23d]
h	R=Ac		CH_2Cl_2	20	90[23e]
i	R=Bz		CH_2Cl_2	20	92[23c]
j	R=THP		CH_2Cl_2	10	79
k	R=TBDMS		CH_2Cl_2	10	90
l			CH_3CN	30	89[23f]

* Isolated yields of pure products. All compounds were consistent with IR and ^{1}H NMR spectroscopic data and gave satisfactory analytical data.

are compatible with the reaction conditions. We first examined the reaction of 3-*O*-(*tert*-butyldimethylsilyl)-1,2:5,6-*O*-isopropylidene-α-D-glucofuranose in the presence of bismuth trichloride in acetonitrile at ambient temperature which afforded the corresponding 3-*O*-(*tert*-butyldimethylsilyl)-1,2-*O*-isopropylidene-α-D-glucofuranose in 90% yield (Table 1, entry l). This success has encouraged us to extend the generality of the reaction. The deprotection of acetonides of other substrates proceeded smoothly (see Table 1).

In conclusion the present procedure for the synthesis of 1,2-diols has the advantages of mild reaction conditions, high chemoselectivity, short reaction times, an inexpensive catalyst, high yields of products and a simple experimental work-up procedure. $BiCl_3$ catalyzed acetonide deprotection has been developed to produce 1,2-diols, and will be an important addition to present procedures.

Experimental Section

General procedure for the generation of 1,2-diols from acetonides: A solution of the acetonide (1 mmol) in MeCN (10 mL) was treated with bismuth trichloride (5 mol%) and two drops of water and stirred for an appropriate time (Table 1) at rt. After completion of the reaction, $NaHCO_3$ was added and the solvent was removed under reduced pressure, water was added and the mixture extracted into EtOAc, washed with brine, dried over anhydrous Na_2SO_4 and concentrated to give the crude product, which was purified on silica gel column to provide the pure 1,2-diol in high yields (Table 1).

3,6-Anhydro-6-methyl 4,5-*O*-isopropyl-D-glycero-D-galacto-heptitol (**e**): $\alpha/\beta = 4:1$ ratio ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.17 (d, $J = 7$ Hz, 3H), 1.28 (s, 3H), 1.50 (s, 3H), 3.61 (dd, $J = 5.4$ Hz, 1H), 3.72–3.85 (m, 2H), 3.90–3.97 (m, 1H), 4.22 (q, $J = 6$ Hz, 1H), 4.41 (d, $J = 6$ Hz 1H), 4.8 (m, 1H). FAB MS (*m*/*z*): 219 (*M*+1).

3-*tert*-Butoxycarbonylamino-3-(4-methoxyphenyl)-1,2-propanediol (**f**): mp 125–128°C, $[\alpha]_D^{25}$ 1.091 (*c* 1, $CHCl_3$),^{1}H NMR ($CDCl_3$, 200 MHz), δ 1.41 (s, 9H), 3.20 (d, $J = 7$ Hz, 2H), 3.61 (m, 1H), 3.77 (s, 3H), 3.82–3.89 (m, 1H), 6.8 (d, $J = 8$ Hz, 2H), 7.24 (d, $J = 8$ Hz, 2H). FAB MS (*m*/*z*): 320 (*M*+Na).

3-*O*-Tetrahydropyranyl-1,2-isopropylidene-α-D-glucofuranose (**j**): ^{1}H NMR ($CDCl_3$, 200 MHz), δ 1.35 (s, 3H), 1.48 (s, 3H), 1.54–1.62 (m, 2H), 1.77–1.90 (m, 2H), 3.47–3.62 (m, 2H), 3.64–3.79 (m, 2H), 3.73–3.81 (m, 1H), 4.01 (m, 3H), 4.22–4.32 (m, 1H), 4.0–4.51 (m, 1H), 4.6–4.69 (m, 1H), 5.91 (d, $J = 7.5$ Hz, 1H).

3-*O*-(*tert*-Butyldimethylsilyl)-1,2-*O*-isopropylidene-α-D-glucofuranose (**k**): IR 1250 cm^{-1}, ^{1}H NMR ($CDCl_3$, 200 MHz), δ 0.16 (s, 6H), 0.83 (s, 9H), 1.32 (s, 3H), 1.50 (s, 3H), 2.0 (br s, 1H), 2.51 (br s, 1H), 3.75–4.40 (m, 6H), 5.93 (d, $J = 3.7$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz), δ −5.14, −4.86, 17.94, 25.63, 26.23, 64.43, 68.71, 75.72, 80.85, 85.28, 104.93, 111.74; FAB MS (*m*/*z*): 335 (*M*+1) Anal. calcd for $C_{15}H_{30}O_6Si$: C, 53.86; H, 9.04. Found: C, 53.80; H, 8.97.

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References

1. (a) Green, T. W.; Wuts, P. G. M. *Protecting Groups in Organic Synthesis*, 2nd ed.; Wiley: New York, 1991; (b) Kocienski, P. J. *Protecting Groups*; Thieme: Stuttgart, New York, 1994.
2. Hanessian, S. *Total Synthesis of Natural Products*: *The Chiron Approach*; Pergamon: Oxford, 1984.
3. (a) Fleet, G. W. J.; Smith, P. W. *Tetrahedron Lett.* **1985**, *26*, 1469; (b) Gerspacher, M.; Rapoport, H. *J. Org. Chem.* **1991**, *56*, 3700; (c) Yadav, J. S.; Chander, M. C.; Reddy, K. K. *Tetrahedron Lett.* **1992**, *33*, 135; (d) Sukumar, M.; Jacques, V.; Pendri, Y.; Falck, J. R. *Tetrahedron Lett.* **1986**, *27*, 2679.
4. Kim, K. S.; Song, Y. H.; Lee, B. H.; Hahn, C. S. *J. Org. Chem.* **1986**, *51*, 404.
5. Iwata, M.; Ohrui, H. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 2837.
6. Vijayasaradhi, S.; Singh, J.; Aidhen, I. S. *Synlett* **2000**, *1*, 110.
7. Xiao, X.; Bai, D. *Synlett* **2001**, *4*, 535.
8. (a) Irwing-Sax, N.; Bewis, R. J. *Dangerous Properties Of Industrial Materials*; Van Nostran Reinhold: New York, 1989; pp. 283–284; (b) Irwing-Sax, N.; Bewis, R. J. *Dangerous Properties Of Industrial Materials*; Van Nostran Reinhold: New York, 1989; pp. 522–523; (c) Wormser, U.; Nir, I. In *The Chemistry Of Organic Arsenic*, *Antimony and Bismuth Compounds*; Patai, S., Ed.; Wiley: New York, 1994; pp. 715–723.
9. Dill, K.; McGown, E. L. In *The Chemistry Of Organic Arsenic*, *Antimony and Bismuth Compounds*; Patai, S., Ed.; Wiley: New York, 1994; pp. 695–713.
10. Maeda, S. In *The Chemistry Of Organic Arsenic*, *Antimony and Bismuth Compounds*; Patai, S., Ed.; Wiley: New York, 1994; pp. 725–759.
11. (a) Carapella, S. C., Jr.; Howe, H. E. *Encyclopedia of Chemical Technology*, 3rd ed.; Wiley: New York, 1978; Vol. 3, pp. 912–921; (b) Kruger, J.; Winkler, P.; Luderitz, E.; Luck, M. In *Ullman's Encyclopedia of Industrial Chemistry*; Gerhartz, W. E., Ed.; VCH: Weinheim, 1985; Vol. A4, pp. 171–189.
12. Reglinski, J. In *Chemistry Of Organic Arsenic*, *Antimony and Bismuth*; Norman, N. C., Ed; Blackie Academic and Professional: London, 1998; Chapter 8, pp. 403–440.
13. (a) Ohara, T.; Sato, T.; Shimizu, N. In *Ullman's Encyclopedia of Industrial Chemistry*; Gerhartz, W. E., Ed.; VCH: Weinhem, 1985; Vol. A1, pp. 149–160; (b) Langvardt, P. W. In *Ullman's Encyclopedia of Industrial Chemistry*; Gerhartz, W., Ed.; VCH: Weinhem, 1985; Vol. A1, pp. 177–184.

14. (a) Suzuki, H.; Ikegami, T.; Matano, Y. *Synthesis* **1997**, 251 and references cited therein; (b) Eash, K. J.; Pulia, M. S.; Wieland, L. C.; Mohan, R. S. *J. Org. Chem.* **2000**, *65*, 8399; (c) Nattier, B. A.; Eash, K. J.; Mohan, R. S. *Synthesis* **2001**, 1010.
15. (a) Anderson, A. M.; Blazek, J. M.; Garg, P.; Payne, B. J.; Mohan, R. S. *Tetrahedron Lett.* **2000**, *41*, 1527; (b) Mohammadpoor-Baltork, I.; Tangestaninejad, S.; Aliyan, H.; Mirkhani, V. *Synth. Commun.* **2000**, *30*, 2365; (c) Oussaid, A.; Boukherroub, R.; Dejean, V.; Garrigues, B. *Phosphorus Sulfur Silicon Relat. Elem.* **2000**, *167*, 81; (d) Bassett, M. R.; Bedard, T. C.; Christensen, S. P.; Keen, B. T.; Sleadd, B. A. US Patent Application 343767, 1999. *Chem. Abstr.* **2001**, *134*, 71304y.
16. (a) Tymonoko, S. A.; Nattier, B. A.; Mohan, R. S. *Tetrahedron Lett.* **1999**, *40*, 7657; (b) Coin, C.; Le Boisslier, V.; Favier, I.; Postel, M.; Dunach, E. *Eur. J. Org. Chem.* **2001**, 735.
17. Komatsu, N.; Uda, M.; Suzuki, H.; Takahashi, T.; Domae, T.; Wada, M. *Tetrahedron Lett.* **1997**, 7215.
18. Le Roux, C.; Dubac, J. *Synlett* **2002**, *2*, 181.
19. (a) Garrigues, B.; Gonzaga, F.; Robert, H.; Dubac, J. *J. Org. Chem.* **1997**, *62*, 4880; (b) Robert, H.; Garrigues, B.; Dubac, J. *Tetrahedron Lett.* **1998**, *39*, 1161; (c) Laurent-Robert, H.; Le Roux, C.; Dubac, J. *Synlett* **1998**, 1138; (d) Motorina, I. A.; Grierson, D. S. *Tetrahedron Lett.* **1999**, *40*, 7215; (e) Laurent-Robert, H.; Garrigues, B.; Dubac, J. *Synlett* **2000**, 1160.
20. Peidro, L.; Le Roux, C.; Laporterie, A.; Dubac, J. *J. Organomet. Chem.* **1996**, *521*, 397.
21. (a) Wada, M.; Takeichi, E.; Matsumoto, T. *Bull. Chem. Soc. Jpn.* **1991**, *69*, 990; (b) Le Roux, C.; Gaspardiloughmane, H.; Dubac, J.; Jaud, J.; Vignaux, P. *J. Org. Chem.* **1993**, *58*, 1835; (c) Le Roux, C.; Gaspardiloughmane, H.; Dubac, J. *Bull. Soc. Chim. Fr.* **1993**, *130*, 832; (d) Le Roux, C.; Gaspardiloughmane, H.; Dubac, J. *J. Org. Chem.* **1994**, *59*, 2238.
22. Swamy, N. R.; Venkateswarlu, Y. *Synthesis* **2002**, 598.
23. (a) Evans, M. E.; Parrish, F. W. *Carbohydr. Res.* **1977**, *54*, 105; (b) Frechou, C.; Dheilly, G.; Beaupere, D.; Uzanet, R.; Demailly, G. *Tetrahedron Lett.* **1992**, *33*, 5061; (c) Nair, V.; Emanuel, J. D. *J. Am. Chem. Soc.* **1977**, 1571; (d) Meyer, A. S.; Reichstein, T. *Helv. Chim. Acta* **1946**, *29*, 152; (e) Smanathan, R.; Hellberg, L. H. *Org. Prep. Proceed. Int.* **1984**, *16*, 388; (f) Czemecki, S.; Georgoulis, C.; Stevens, C. L.; Vijaykumaran, R. *Tetrahedron Lett.* **1985**, *26*, 1699.