Pergamon

Tetrahedron Letters 43 (2002) 2777–2780

TETRAHEDRON LETTERS

Chemoselective deprotection of primary *tert*-butyldimethylsilyl ethers on carbohydrate molecules in the presence of secondary silyl ethers

Ming-Yi Chen,[a,*] Kuo-Cheng Lu,[b] Adam Shih-Yuan Lee[c,*] and Chun-Cheng Lin[b,d,*]

[a]*Department of General Education, Taipei Nursing College, Taipei 112, Taiwan*
[b]*Institute of Chemistry, Academia Sinica, Nankang, Taipei 115, Taiwan*
[c]*Department of Chemistry, Tamkang University, Tamsui 251, Taiwan*
[d]*Department of Chemistry, National Changhua University of Education, Changhua 500, Taiwan*

Received 14 December 2001; revised 13 February 2002; accepted 21 February 2002

Abstract—The primary silyl ethers of TBDMS-protected saccharides were regioselectively cleaved in excellent yields (71–95%) by treating the silyl ethers with a catalytic amount of CBr_4 in methanol under photochemical reaction conditions.

Although many studies have reported selective deprotection of protected hydroxyl groups,[1,2] there remains a great need to explore a simple and effective selective deprotecting method for carbohydrate chemistry. Silyl ethers have attained a position of prominence in the area of hydroxyl group protection due to their ease of formation and removal and their stability to a wide range of reagents and reaction conditions.[1,2] However, the selective deprotection of a particular silyloxy functionality requires the use of different silyl protecting groups for the various OH groups[3–8] present in saccharides. Such methodology demands many synthetic steps and tedious deprotection work, resulting in low overall yields. Thus, we found it necessary to develop a method using one trialkyl silyl group to protect hydroxyl functionalities on a saccharide and then regioselectively deprotecting the requisite silyloxy group without affecting the other silyloxy groups.

Among silyl ethers, *tert*-butyldimethylsilyl (TBDMS) is the most popular and commonly used protecting group because it can be easily installed in high yields under mild conditions and is robust to a variety of reaction conditions.[9–11] Although numerous methods for deprotecting TBDMS groups have been reported,[1,2] only a few selective deprotections of silyl ethers[12–16] on carbohydrate molecules have been achieved.[17–20] In our previous studies,[21] we have successfully deprotected trialkylsilyl ethers by using CBr_4/MeOH under refluxing conditions. Herein, we report a mild, highly efficient and selective desilylating method for *tert*-butyldimethylsilyl protected carbohydrate molecules by modifying our previous method.

The TBDMS-protected saccharides starting materials **1**, **3**–**9**, and **17**–**25** were obtained in high yields by treating the corresponding saccharides with *tert*-butyldimethylsilyl trifluoromethane sulfonate (TBDMSOTf) in the presence of 2,6-lutidine.[22] Our initial investigations of regioselective deprotection of primary TBDMS ethers in the presence of secondary TBDMS ethers are shown in Table 1. The desilylation of compound **1** proceeded smoothly by treatment with a catalytic amount of CBr_4 in MeOH or EtOH under either ultrasonic or photochemical reaction conditions.[23] The results showed that the starting material persisted after sonication for 4 h (entry 1) whilst compound **2** was obtained in high yield under photo-irradiation reaction conditions (entries 2–4). It was found that under photochemical reaction conditions solvents played an important role, and that methanol was a more effective solvent for regioselective deprotection than ethanol. Only a small amount of diol was obtained under photochemical reaction conditions.

Encouraged by these promising results, we then proceeded with different types of TBDMS-protected saccharides using 5 mol% of CBr_4 in MeOH. As shown in

* Corresponding authors. Tel.: +886-2-27898648; fax: +886-2-27831237; e-mail: cclin@chem.sinica.edu.tw

0040-4039/02/$ - see front matter
PII: S0040-4039(02)00385-4

Table 1.

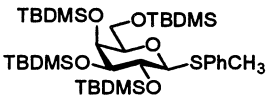
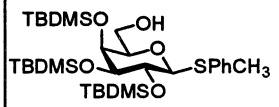
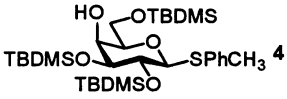
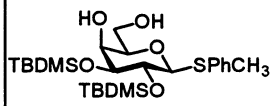
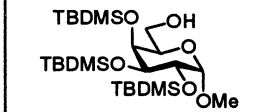
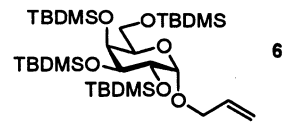
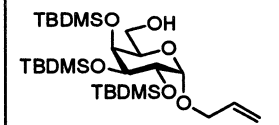
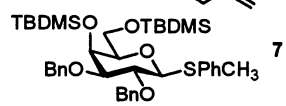
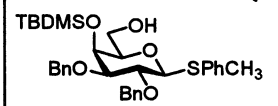
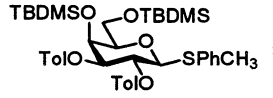
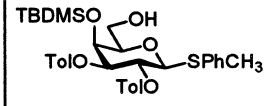
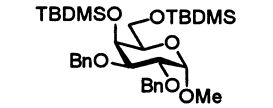
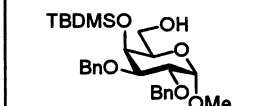
1 2

Entry	Reaction Conditions	Yield(%)	Recovery of starting material(%)	Diol(%)
1	CCl_4 / MeOH (1:1),))) (39 kHz), 4 h	73	25	
2	CBr_4 / MeOH (5 mol% / 5mL), *hν* 0.5 h then rt 10 h	92		<3
3	CBr_4 / EtOH (5 mol% / 5mL), *hν* 0.5 h then rt 52 h	56	39	
4	CBr_4 / EtOH (10mol% / 5mL), *hν* 0.5 h then rt 24 h	87		8

Tol = *p*-methylbenzoyl

Table 2, the regioselective deprotections of primary TBDMS ethers of galactosides were achieved in high yields (71–94%).[24] The results showed that the deprotection rates were influenced by other protecting groups on the saccharides. In general, the desilylation rates of primary silyl ethers of methyl glycosides were faster than those of saccharides with other substituents at their anomeric centers (Table 2, entries 1, 3–5 and 7). In the presence of ether protecting groups at secondary hydroxyls, the desilylation rates were faster than those of saccharides with ester protecting groups at the same positions (Table 2, entries 5 and 6). The longer reaction time needed for deprotection of **8** may be due to its low solubility in MeOH. Interestingly, the presence of a free hydroxyl group near the primary silyl ether accelerated the deprotection rate (Table 2, entries 1 and 2). It should be noted that no silyl group migration was observed in any cases. More diversified examples are illustrated in Table 3.[25] The results showed that regardless of the various orientations of the hydroxyl groups on the saccharides, the primary TBDMS ethers were successfully deprotected in high yields (82–95%). It was

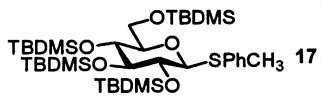
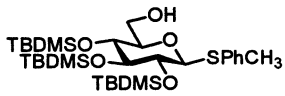
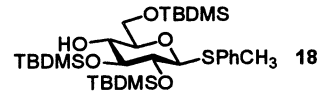
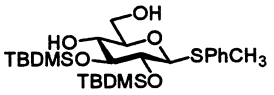
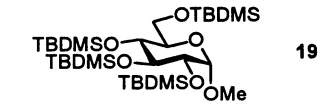
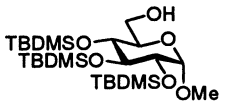
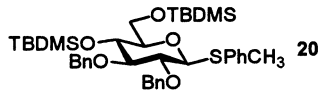
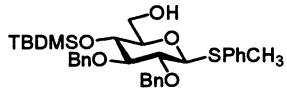
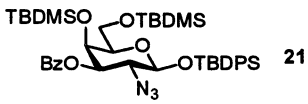
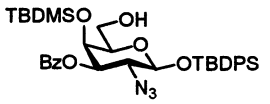
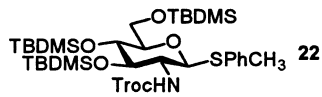
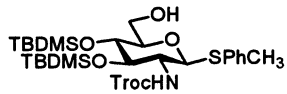
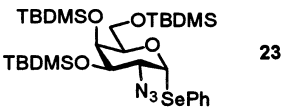
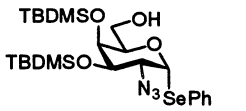
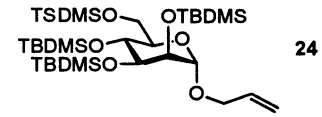
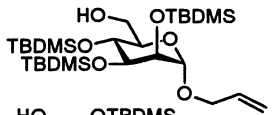
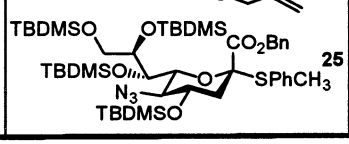
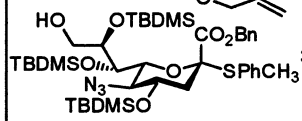
Table 2.

Entry	Substrate[a]	Time[b] (h)	Product	Yield (%)
1	 3	20	 10	75
2	 4	1	 11	87
3	 5	4	 12	94
4	 6	28	 13	90
5	 7	12	 14	93
6	 8	39	 15	71
7	 9	5	 16	85

[a]TBDMS = *tert*-butyldimethylsilyl; Tol = *p*-methylbenzoyl

[b]Irradiated for 0.5 h then stirred at room temperature

Table 3.

Entry	Substrate[a]	Time[b] (h)	Product	Yield (%)
1	 17	28	 26	83
2	 18	2	 27	95
3	 19	23	 28	87
4	 20	19	 29	90
5	 21	12	 30	89
6	 22	6	 31	82
7	 23	20	 32	90
8	 24	13	 33	83
9	 25	11	 34	86

[a]TBDMS = *tert*-butyldimethylsilyl; Tol = *p*-methylbenzoyl; Troc = 2,2,2-trichloroethoxycarbonyl
[b]Irradiated for 0.5 hthen atirred at room temperature

also observed that the trend in deprotection rates of glucosides was similar to that of galactosides except for entry 2 of Table 1 and entry 4 of Table 3.

The typical procedure for deprotection of a primary *tert*-butyldimethylsilyl ether is as follows: A solution of saccharide (1.0 equiv.), CBr_4 (0.05 equiv.) and anhydrous MeOH (10 mL/1.0 mmol saccharide) in a Pyrex round flask was irradiated by a TLC lamp (Uvltec Limited, 245 nm, 8 W) for 0.5 h, followed by stirring without irradiation at room temperature. After the reaction was complete (TLC), the organic solvent was removed under reduced pressure. Further purification was achieved by flash chromatography on silica gel with ethyl acetate/hexane.

In conclusion, our present studies achieved highly regioselective deprotections of primary TBDMS ethers in the presence of secondary TBDMS ethers on saccharides. This highly selective deprotection method could have a wide application in organic synthesis, particularly in carbohydrate chemistry.[26] Further application of this selective desilylation method for the synthesis of glucan is in hand.

Acknowledgements

We thank the Academia Sinica, National Science Council in Taiwan, Tamkang University and National Taipei College of Nursing for their financial support.

References

1. Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 2nd ed.; John Wiley & Sons: New York, 1999; pp. 17–292.

2. Kocienski, P. J. *Protecting Groups*; Georg Thieme: New York, 1994; pp. 21–117.
3. Nelson, T. D.; Crouch, R. D. *Synthesis* **1996**, 1031–1069.
4. Hattori, K.; Sajiki, H.; Hirota, K. *Tetrahedron* **2001**, *57*, 2109–2114.
5. Higashibayashi, S.; Shinko, K.; Ishizu, T.; Hashimoto, K.; Shirahama, H.; Nakata, M. *Synlett* **2000**, 1306–1308.
6. Hunter, R.; Hinz, W.; Richards, P. *Tetrahedron Lett*. **1999**, *40*, 3643–3646.
7. Ramasamy, K. S.; Averett, D. *Synlett* **1999**, 709–712.
8. Farras, J.; Serra, C.; Vilarrasa, J. *Tetrahedron Lett*. **1998**, *39*, 327–330.
9. Bartoli, G.; Bosco, M.; Marcantoni, E.; Sambri, L.; Torregiani, E. *Synlett* **1998**, 209–211.
10. Muzart, J. *Synthesis* **1993**, 11–27.
11. Lalonde, M.; Chan, T. H. *Synthesis* **1985**, 817–845.
12. De Groot, A. H.; Dommisse, R. A.; Lemière, G. L. *Tetrahedron* **2000**, *56*, 1541–1549.
13. Firouzabadi, H.; Etemadi, S.; Karimi, B.; Jarrahpour, A. A. *Synth. Commun*. **1999**, *29*, 4333–4339.
14. Maiti, G.; Roy, S. C. *Tetrahedron Lett*. **1997**, *38*, 495–498.
15. Tandon, M.; Begley, T. P. *Synth. Commun*. **1997**, *27*, 2953–2959.
16. Feixas, J.; Capdevila, A.; Guerrero, A. *Tetrahedron* **1994**, *50*, 8539–8550.
17. Yang, Y.-Y.; Yang, W.-B.; Teo, C.-F.; Lin, C.-H. *Synlett* **2000**, 1634–1636.
18. Cormier, J. F. *Tetrahedron Lett*. **1991**, *32*, 187–188.
19. Kawai, A.; Hara, O.; Hamada, Y.; Shioiri, T. *Tetrahedron Lett*. **1988**, *29*, 6331–6334.
20. McInnes, A. G. *Can. J. Chem*. **1965**, *43*, 1998–2003.
21. Lee, A. S.-Y.; Yeh, H.-C.; Shie, J.-J. *Tetrahedron Lett*. **1998**, *39*, 5249–5252.
22. Corey, E. J.; Cho, H.; Rucker, C.; Hua, D. H. *Tetrahedron Lett*. **1981**, *22*, 3455–3458.
23. NMR data for compound **2**: ^{1}H NMR: δ −0.20 (s, 3H), 0.05 (s, 3H), 0.75 (s, 9H), 2.33 (s, 3H), 2.34 (s, 6H), 2.69 (br, 1H), 3.54 (m, 1H), 3.77 (m, 1H), 3.93–3.99 (m, 2H), 4.90 (d, J=9.9 Hz, 1H), 5.26 (dd, J=9.7, 9.7 Hz, 1H), 5.58 (dd, J=9.7, 9.7 Hz, 1H), 7.09–7.13 (m, 6H), 7.32–7.35 (m, 2H), 7.76–7.81 (m, 4H).
24. Selective data for compound **12**: ^{1}H NMR: δ 0.05 (s, 3H), 0.07 (s, 3H), 0.08 (s, 3H), 0.09 (s, 3H), 0.11 (s, 6H), 0.87 (s, 9H), 0.88 (s, 9H), 0.89 (s, 9H), 3.39 (s, 3H), 3.58–3.62 (m, 2H), 3.76–3.82 (m, 3H), 4.14 (m, 1H), 4.65 (d, J=2.9 Hz, 1H). For compound **13**: ^{1}H NMR: δ 0.05 (s, 3H), 0.06 (s, 3H), 0.07 (s, 3H), 0.10 (s, 3H), 0.12 (s, 3H), 0.13 (s, 3H), 0.90 (s, 9H), 0.91 (s, 9H), 0.94 (s, 9H), 1.94 (br, 1H), 3.62 (d, J=6.3 Hz, 1H), 3.86–3.91 (m, 2H), 3.94–3.99 (m, 4H), 4.22 (dd, J=13.2, 4.9 Hz, 1H), 4.85 (d, J=1.8 Hz, 1H), 5.1 (dd, J=10.4, 1.0 Hz, 1H), 5.31 (d, J=13.8, 1.3 Hz, 1H), 5.91 (m, 1H). For compound **14**: ^{1}H NMR: δ 0.05 (s, 3H), 0.07 (s, 3H), 0.90 (s, 9H), 2.33 (s, 3H), 3.45 (dd, J=9.4, 2.5 Hz, 1H), 3.48 (dd, J=7.8, 4.3 Hz, 1H), 3.60 (dd, J=11.1, 4.3 Hz, 1H), 3.80 (t, J=9.4 Hz, 1H), 3.91 (dd, J=11.1, 7.8 Hz, 1H), 4.04 (d, J=2.5 Hz, 1H), 4.55 (d, J=9.4 Hz, 1H), 4.71 (s, 2H), 4.72 (d, J=10.3 Hz, 1H), 4.76 (d, J=10.3 Hz, 1H), 7.09 (d, J=8.0 Hz, 2H), 7.26–7.40 (m, 8H), 7.48 (d, J=8.0 Hz, 2H). For compound **16**: ^{1}H NMR: δ 0.09 (s, 3H), 0.11 (s, 3H), 0.92 (s, 9H), 2.66 (br, 1H), 3.40 (s, 3H), 3.72–3.89 (m, 5H), 4.06 (m, 1H), 4.67–4.86 (m, 5H), 7.28–7.42 (m, 10H).
25. Selective data for compound **26**: ^{1}H NMR: δ 0.06 (s, 3H), 0.08 (s, 3H), 0.10 (s, 3H), 0.11 (s, 3H), 0.13 (s, 6H), 0.88 (s, 9H), 0.89 (s, 9H), 0.91 (s, 9H), 2.32 (s, 3H), 3.68–3.79 (m, 3H), 3.80–3.89 (m, 3H), 4.90 (d, J=6.7 Hz, 1H), 7.09 (d, J=8.1 Hz, 2H), 7.37 (d, J=8.1 Hz, 2H). For compound **30**: ^{1}H NMR: δ −0.18 (s, 3H), −0.08 (s, 3H), 0.91 (s, 9H), 1.14 (s, 9H), 3.20 (dd, J=7.6, 6.1 Hz, 1H), 3.27 (dd, J=10.9, 6.1 Hz, 1H), 3.50 (dd, J=10.8, 7.6 Hz, 1H), 3.99 (dd, J=10.9, 7.6 Hz, 1H), 4.06 (d, J=2.7 Hz, 1H), 4.68 (d, J=7.6 Hz, 1H), 4.75 (dd, J=10.8, 2.7 Hz, 1H), 7.36–7.50 (m, 8H), 7.59 (m, 1H), 7.70–7.80 (m, 4H), 8.05–8.08 (m, 2H). For compound **32**: ^{1}H NMR: δ 0.08 (s, 3H), 0.17 (s, 3H), 0.19 (s, 3H), 0.22 (s, 3H), 0.90 (s, 9H), 0.98 (s, 9H), 3.53 (dd, J=11.3, 4.2 Hz, 1H), 3.73 (dd, J=11.3, 7.9 Hz, 1H), 3.86 (dd, J=9.8, 2.1 Hz, 1H), 3.94 (d, J=2.1 Hz, 1H), 4.12–4.18 (m, 2H), 6.01 (d, J=4.8 Hz, 1H), 7.24–7.29 (m, 2H), 7.61–7.64 (m, 2H). For compound **34**: ^{1}H NMR: δ 0.00 (s, 6H), 0.01 (s, 3H), 0.07 (s, 3H), 0.13 (s, 3H), 0.20 (s, 3H), 0.87 (s, 9H), 0.88 (m, 1H), 0.88 (s, 9H), 0.98 (s, 9H), 1.73 (dd, J=11.6, 9.2 Hz, 1H), 2.34 (s, 3H), 2.69 (dd, J=7.6, 3.5 Hz, 1H), 3.09 (dd, J=9.5, 1.8 Hz, 1H), 3.30 (dd, J=7.2, 1.8 Hz, 1H), 3.51–3.59 (m, 3H), 3.83 (m, 1H), 4.03 (br, 1H), 5.03 (d, J=2.2 Hz, 2H), 7.10 (d, J=7.8 Hz, 2H), 7.23–7.27 (m, 3H), 7.34–7.38 (m, 4H).
26. Bosques, C. J.; Tai, V. W.-F.; Imperiali, B. *Tetrahedron Lett*. **2001**, *42*, 7207–7210.