

## *N*-Iodosuccinimide (NIS) as a mild and highly chemoselective catalyst for deprotection of *tert*-butyldimethylsilyl ethers

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**Abstract**—A variety of alcoholic TBDMS (*t*-butyldimethylsilyl) ethers are easily removed in excellent yields by treatment with a catalytic amount of *N*-iodosuccinimide (NIS, 5 mol%) in methanol. This method is able to deprotect TBDMS ethers of alcohols in the presence of TBDMS ethers of phenols.

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Silyl groups are important in organic chemistry, especially in the synthesis of complex natural products.<sup>1</sup> *tert*-Butyldimethylsilyl (TBDMS) ethers are among the most frequently used protective groups for alcohol, because they can be easily installed in high yields and can withstand a wide variety of reaction conditions.<sup>2</sup> Although, the major goal of such a protection is usually to prevent unfavorable reactions of hydroxyl groups, in many cases it is often necessary to selectively convert the silyl ethers to their corresponding parent alcohols.<sup>3</sup> Thus, many alternative and mild protocols have been reported for the deprotection of silyl ethers including some examples of recent Lewis-acid-based protocols such as TMSOTf,<sup>4</sup> BF<sub>3</sub>·OEt<sub>2</sub>,<sup>5</sup> BCl<sub>3</sub>,<sup>6</sup> Sc(OTf)<sub>3</sub>,<sup>7</sup> InCl<sub>3</sub>,<sup>8</sup> ZnBr<sub>2</sub>,<sup>9</sup> Zn(BF<sub>4</sub>)<sub>2</sub>,<sup>10</sup> Ce(OTf)<sub>4</sub>,<sup>11</sup> CeCl<sub>3</sub>·7H<sub>2</sub>O/NaI,<sup>12</sup> BiBr<sub>3</sub>,<sup>13</sup> BiOClO<sub>4</sub>,<sup>14</sup> SbCl<sub>5</sub>,<sup>15</sup> and LiCl.<sup>16</sup> Other reagents such as carboxylic acid resins,<sup>17</sup> organotin reagents,<sup>18</sup> I<sub>2</sub>,<sup>19</sup> Br<sub>2</sub> in methanol,<sup>20</sup> and CBr<sub>4</sub> in methanol<sup>21</sup> have also been developed to desilylate TBDMS ethers under mild reaction conditions. There are also several reductive methods for deprotecting TBDMS ethers including catalytic transfer hydrogenation with palladium<sup>22</sup> and cleavage using DIBAL-H<sup>23</sup> and LiAlH<sub>4</sub>.<sup>24</sup> Although, many of these methods promote selective deprotection of bis-silyl ethers,<sup>3b</sup> some are strongly reducing and others are oxidizing, thereby restricting their use. More-

over, many of these methods suffer from limitations such as harsh reaction conditions, the use of expensive reagents and cumbersome work-up procedures. Therefore, it seems that there is much room to develop new selective methods for desilylation of TBDMS ethers under mild reaction conditions.

We report herein a new, mild, and highly selective method for the deprotection of a variety of alcoholic TBDMS ethers that employs a catalytic amount of NIS (5 mol%) in absolute methanol furnishing the corresponding alcohols in good to excellent yields (Scheme 1).

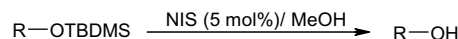
Methanol is a low-boiling solvent that can be easily removed from the reaction mixture. Moreover, due to the nonaqueous nature of the protocol, no *t*-BuMe<sub>2</sub>-SiOH was produced during the course of the reaction.

Various types of structurally diverse TBDMS ethers were deprotected using this procedure and the results are summarized in Table 1.

The method was found to be general for the cleavage of TBDMS ethers of primary (Table 1, entries 1–4), secondary (entries 5–10), allylic (entry 12), and tertiary

**Keywords:** Silyl ethers; Deprotection; *N*-Iodosuccinimide; TBDMS ethers; Protecting groups.

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R = alkyl, aryl

Scheme 1.

**Table 1.** Selective deprotection of TBDMS ethers to the corresponding alcohols using NIS in methanol at room temperature

Entry	Substrate	Product	Time (h)	Yield % <sup>a,b</sup>
1	PhCH <sub>2</sub> OTBDMS	PhCH <sub>2</sub> OH	17	95
2	4- <i>i</i> -PrC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OTBDMS	4- <i>i</i> -PrC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH	24	96
3	PhCH <sub>2</sub> CH <sub>2</sub> OTBDMS	PhCH <sub>2</sub> CH <sub>2</sub> OH	18	92
4	PhCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> OTBDMS	PhCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> OH	18	100 <sup>c</sup>
5	Ph <sub>2</sub> CHOTBDMS	Ph <sub>2</sub> CHOH	24	91
6			24	85
7			24	91
8			19	95
9			24	80
10			18	100 <sup>c</sup>
11			24	NR
12			24	84 <sup>c</sup>
13			24	69
14			24	72

<sup>a</sup> Yields refer to isolated pure products unless otherwise stated.

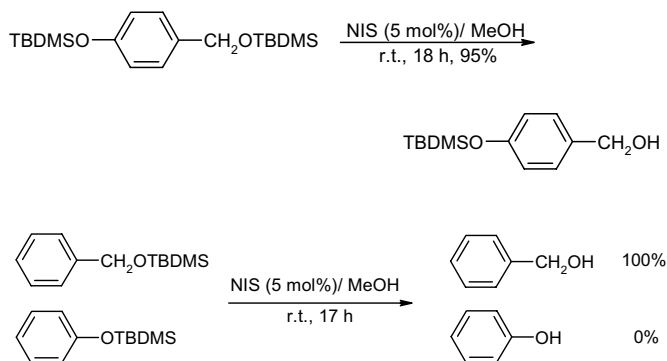
<sup>b</sup> The ratio of TBDMS ether:NIS:MeOH was 1:0.05:3 mL, respectively, and the reactions were performed at room temperature.

<sup>c</sup> GC yield.

(entries 13 and 14) alcohols. The results in Table 1 also show that the reaction conditions are mild enough to allow a C=C double bond to remain unaffected. Moreover, no elimination product was detected in the course of deprotection of tertiary TBDMS ethers (Table 1, entry 14). It is also noteworthy that phenolic TBDMS ethers (entry 11) are quite stable under these reaction conditions even after lengthy reaction times. This observation encouraged us to study the possibility of chemo-

selective deprotection of alcoholic versus phenolic TBDMS ethers in a competitive experiment. Indeed, our results show that this method is useful for the selective cleavage of alcoholic TBDMS ethers in the presence of TBDMS-protected phenols (Scheme 2).

A typical procedure for deprotection of TBDMS ethers to the corresponding alcohol is as follows: To a solution of TBDMS ether (1 mmol) in methanol (3 mL) was

**Scheme 2.**

added NIS (0.05 mmol). The mixture was stirred at room temperature for the period of time indicated in Table 1. Reaction progress was monitored by GC or TLC. After completion of the reaction, the product was isolated by rapid filtration through a short pad of silica gel. Evaporation of the solvent under reduced pressure gave the corresponding alcohol in good to excellent yields (Table 1).

In conclusion, we have established a mild, simple, and highly selective method for deprotection of alcoholic TBDMS ethers using a catalytic amount of NIS in methanol at room temperature. The reaction is selective for alkyl silyl ethers and the yields of product are very good to excellent.

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### References and notes

- (a) Greene, G. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*; John Wiley & Sons: New York, 1991; (b) Lalonde, M.; Chan, T. H. *Synthesis* **1985**, 817–845; (c) Kocienski, P. J. In *Protective Groups*; Enders, R., Noyori, R., Trost, B. M., Eds.; Thieme: Stuttgart, 1994.
- (a) Corey, E. J.; Vankateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190–6191; (b) Chaudhury, S. K.; Hernandez, O. *Tetrahedron Lett.* **1979**, *20*, 99–102; (c) Corey, E. J.; Cho, H.; Rucker, C.; Hua, D. H. *Tetrahedron Lett.* **1981**, *22*, 3455–3458; (d) Lombord, L. *Tetrahedron Lett.* **1984**, *25*, 227–228.
- (a) Colvin, E. W. *Silicon Reagents in Organic Synthesis*; Academic: New York, 1998; (b) Nelson, T. D.; Crouch, R. D. *Synthesis* **1996**, 1031–1069.
- Hunter, R.; Hinz, W.; Richards, P. *Tetrahedron Lett.* **1999**, *40*, 3643–3646.
- Jackson, S. R.; Johnson, M. G.; Mikami, M.; Shiokawa, S.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2001**, *40*, 2694–2697.
- Yang, Y. Y.; Yang, W. B.; Teo, C. F.; Lin, C. H. *Synlett* **2000**, 1634–1636.
- Oriyama, T.; Kobayashi, Y.; Noda, K. *Synlett* **1998**, 1047–1048.
- Yadav, J. S.; Reddy, B. V. S.; Madan, C. *New J. Chem.* **2000**, *24*, 853–854.
- Crouch, R. D.; Polizzi, J. M.; Cleiman, R. A.; Yi, J.; Romany, C. A. *Tetrahedron Lett.* **2002**, *43*, 7151–7153.
- Ranu, B. C.; Jana, U.; Majee, A. *Tetrahedron Lett.* **1999**, *40*, 1985–1988.
- Bartoli, G.; Cupone, G.; Dalpozzo, R.; De Nino, A.; Maiuolo, L.; Procopio, A.; Sambri, L.; Tararelli, A. *Tetrahedron Lett.* **2002**, *43*, 5945–5947.
- Bartoli, G.; Bosco, M.; Marcantoni, E.; Sambri, L.; Torregiani, E. *Synlett* **1998**, 209–211.
- Bajwa, J. S.; Vivel, J.; Slade, J.; Repic, O.; Blacklock, T. *Tetrahedron Lett.* **2000**, *41*, 6021–6024.
- Crouch, R. D.; Romany, C. A.; Kreshock, A. C.; Menconi, K. A.; Zile, J. L. *Tetrahedron Lett.* **2004**, *45*, 1279–1281.
- Gloria, P. M. C.; Prabhakar, S.; Lobo, A. M.; Gomes, M. J. S. *Tetrahedron Lett.* **2003**, *44*, 8819–8821.
- Farras, J.; Serra, C.; Vilarrasa, J. *Tetrahedron Lett.* **1998**, *39*, 327–330.
- Corey, E. J.; Ponder, J. W.; Ulrich, P. *Tetrahedron Lett.* **1980**, *21*, 137–140.
- Scheidt, K. A.; Chen, H.; Follows, B. C.; Chemler, S. R.; Coffey, D. S.; Roush, W. R. *J. Org. Chem.* **1998**, *63*, 6436–6437.
- (a) Lipshutz, B. H.; Keith, J. *Tetrahedron Lett.* **1998**, *39*, 2495–2498; (b) Vaino, A. R.; Szarek, W. A. *J. Chem. Soc., Chem. Commun.* **1996**, 2351–2352.
- (a) Barros, M. T.; Maycock, C. D.; Sineriz, F.; Thomassigny, C. *Tetrahedron* **2000**, *56*, 6511–6516; (b) Barros, M. T.; Maycock, C. D.; Thomassigny, C. *Synlett* **2001**, 1146–1148.
- Lee, A. S.-Y.; Yeh, H.-C.; Shie, J.-J. *Tetrahedron Lett.* **1998**, *39*, 5249–5252.
- Cormier, J. F. *Tetrahedron Lett.* **1991**, *32*, 187–188.
- Corey, E. J.; Jones, G. B. *J. Org. Chem.* **1992**, *57*, 1028–1029.
- de Vries, E. F. J.; Brussee, J.; van der Gen, A. *J. Org. Chem.* **1994**, *59*, 7133–7137.