Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron Letters 45 (2004) 3031–3033
Tetrahedron Letters

Radical deoxygenation of tertiary alcohols via trifluoroacetates

Joong-Gon Kim,[c] Dae Hyan Cho[a,b] and Doo Ok Jang[a,b,*]

[a]*Department of Chemistry, Yonsei University, Wonju 220-710, South Korea*
[b]*Center for Bioactive Molecular Hybrids, Yonsei University, Seoul 120-749, South Korea*
[c]*Biotechnology Division, Hanwha Chemical R&D Center, Daejeon 305-345, South Korea*

Received 20 January 2004; revised 19 February 2004; accepted 23 February 2004

Abstract—Trifluoroacetates of tertiary alcohols undergo deoxygenation by Ph_2SiH_2 in the presence of $(^tBuO)_2$ in excellent yields of the deoxy products without affecting the stereochemistry at β-carbon.

Deoxygenation of tertiary alcohols in complicated molecules is not an easy task in organic synthesis. Dehydration/hydrogenation method affords a product that loses the original configuration of β-carbon center.[1]

Radical deoxygenation of secondary and primary alcohols via thionocarbonyl derivatives has been proven a useful synthetic method, especially for the synthesis of complex molecules.[2] However, the method is not suitable for the deoxygenation of tertiary alcohols because of the thermal instability of thionocarbonyl derivatives.[3] Although there is an example of using the thionocarbonyl derivative for the deoxygenation of tertiary alcohols, it requires special treatment and careful handling to prevent the thermal elimination.[4] The stability of thionocarbonates of tertiary alcohols depends upon the structure of the substrates.

Consequently, research efforts on radical precursors for the deoxygenation of tertiary alcohols have been reported, including the tertiary alcohol thioxoformates[5] and oxalates.[6] In spite of their potential utility, however, they involve in the use of toxic and moisture sensitive and thermally unstable reagents. Thus, there is a need to develop suitable radical precursors for the deoxygenation of tertiary alcohols. Recently, Roberts reported that tertiary alcohols were deoxygenated via their MOM ethers by refluxing in octane in the presence of a thiol.[7] It has been known that acetate derivatives of alcohols are much more stable thermally than the thionocarbonates of alcohols.[8] We have assumed that trifluoroacetate derivatives of tertiary alcohols have thermal stability and proper reactivity under radical reaction conditions. We report herein a convenient and efficient method of deoxygenating tertiary alcohols via trifluoroacetates with diphenylsilane.

We chose 1-methyl cyclododecanol trifluoroacetate as a model compound. Treatment of 1-methyl cyclododecanol trifluoroacetate with Ph_2SiH_2 in the presence of $(^tBuO)_2$ at 140 °C resulted in the formation of the deoxygenated product, methylcyclododecane quantitatively. In order to find the optimal reaction conditions, the reaction was carried out under various reaction conditions. The yield of methyl cyclododecane was measured by GLC analysis, and the results are shown in Table 1. The optimal reaction conditions were established with 3 equiv of Ph_2SiH_2 and 1 equiv of $(^tBuO)_2$ at 130 °C (entry 4). Although the reaction proceeded at below 130 °C, prolonged reaction times are needed (entries 5 and 6). We have also carried out the reaction

Table 1. Deoxygenation of 1-methylcyclododecyl trifluoroacetate with Ph_2SiH_2 under various reaction conditions

Entry	Ph_2SiH_2 (equiv)	$(^tBuO)_2$ (equiv)	Temperature (°C)	Time (h)	Yield (GC, %)[a]
1	5	1	140	15	100
2	3	1	140	15	100
3	2	1	140	15	86 (14)[b]
4	3	1	130	15	100
5	3	1	120	20	63 (35)[b]
6	3	1	125	20	89 (11)[b]
7	3	0.5	130	15	92 (8)[b]

[a] Analyzed by GC.
[b] Starting material.

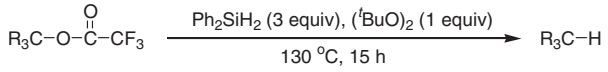
Keywords: Radical; *tert*-Alcohol; Deoxygenation; Trifluoroacetate.
* Corresponding author. Tel.: +82-33-760-2261; fax: +82-33-760-2182; e-mail: dojang@dragon.yonsei.ac.kr

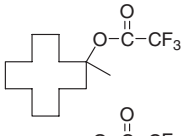
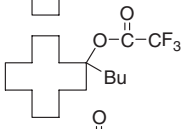
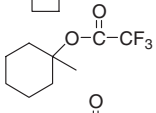
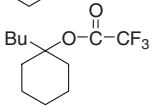
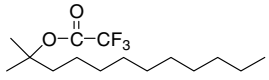
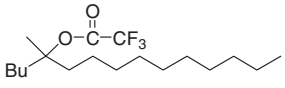
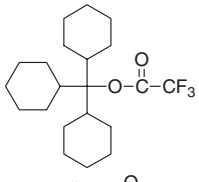
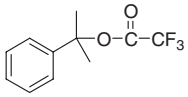
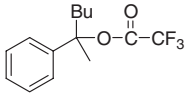
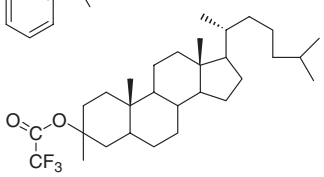
0040-4039/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2004.02.109

at 100 °C with more active other hydrides such as *n*-tributyltin hydride and triphenyltin hydride affording the corresponding alcohols in 88% and 89%, respectively. The reaction with *t*-dodecanthiol/Ph_2SiH_2 or *N*-ethylpiperidium hypophosphite at 100 °C did not proceed at all. The results implied that the reaction did not depend on the activity of hydrides, and a radical intermediate of the reaction did not break up at 100 °C to give an alkyl radical.

The procedure was applied to the deoxygenation of various tertiary alcohols to examine the scope and limitations of the reaction. The results are presented in Table 2. The reactions are clean, and there are no side reactions such as elimination reaction implying that tertiary alcohol trifluoroacetates are quite stable thermally. The experimental procedure is quite simple, and the products are obtained in high isolated yields. The results show that the method is general for the deoxygenation of tertiary alcohols.

Table 2. Deoxygenation of various tertiary alcohols with Ph_2SiH_2



Entry	Substrate	R_3C–H (%)[a]
1		90
2		90
3		84
4		86
5		88
6		82
7		87
8		89
9		93
10		85

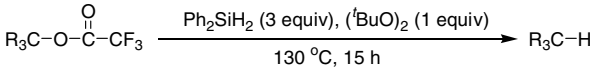
[a] Isolated yield.

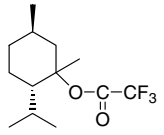
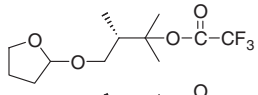
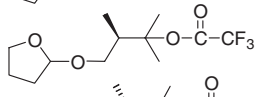
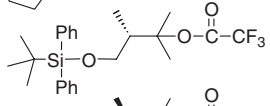
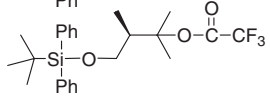
The reaction is applicable to the deoxygenation of tertiary alcohols that have a stereogenic center at β-carbon. Thus, tertiary alcohols with a stereogenic center were transformed into the deoxy products without interfering with an adjacent chiral center as shown in Table 3.

In order to prove preserving the configuration of β-position in the deoxy product, (2*S*)-1-*tert*-butyldiphenylsilyoxy-2,3-dimethylbutane was deprotected with tetrabutylammonium fluoride to obtain (2*S*)-2,3-dimethyl-1-butanol in 93% yield, which gave the identical spectroscopic data to an authentic sample (Scheme 1).[9]

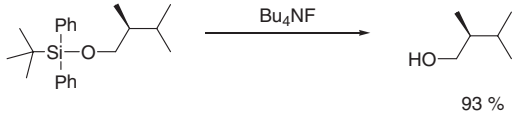
Next, we tried to utilize the present method for more complex substrates. The procedure used for the deoxygenation of a limonoid, xyloccensin K (**1**). Treatment of xyloccensin K (**1**) with trifluoroacetic anhydride in the presence of DMAP afforded trifluoroacetate **2** in 72% yield. The latter was treated with Ph_2SiH_2 in the presence of $(^tBuO)_2$ at 130 °C giving the deoxy product **3**[10] in 81% yield without epoxide ring opening.[11] The result implies that reducible functional groups such as ketones, esters, and lactones are tolerance under the reaction conditions.

Table 3. Deoxygenation of tertiary alcohols with chiral center at β-carbon with Ph_2SiH_2

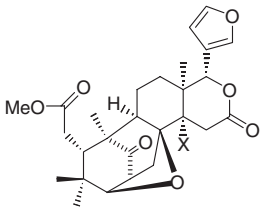


Entry	Substrate	R_3C–H (%)[a]
1		74
2		83
3		84
4		87
5		87

[a] Isolated yield.



Scheme 1.



1: X = OH
2: X = OC(O)CF_3
3: X = H

In summary, this paper describes a convenient and practical procedure for the radical deoxygenation of tertiary alcohols via their trifluoroacetates using Ph_2SiH_2. This method is compatible with acid labile acetals and silyl ethers. This procedure also provides simplicity and high yields of the deoxy products, which makes it attractive for the synthesis of complex molecules.

Typical procedure for deoxygenation of trifluoroacetates of *tert*-alcohols: (2*S*)-1-(*tert*-Butyldiphenylsilyl)oxy-2,3-dimethylbutane. A mixture of trifluoroacetate of (2*S*)-1-(*tert*-butyldiphenylsilyl)oxy-2,3-dimethylbutanol (180 mg, 0.4 mmol), diphenylsilane (220 mg, 1.2 mmol) and di-*tert*-butylperoxide (50 mg, 0.4 mmol) was sealed in an ampule under argon atmosphere. After heating at 130 °C for 15 h, the mixture was purified by silica gel column chromatography giving 157 mg (87%) of the title compound. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.78 (dd, $J = 3.2$, 11.2 Hz, 6H), 0.84 (d, $J = 6.8$ Hz, 3H), 1.06 (s, 9H), 1.51 (m, 1H), 1.69 (m, 1H), 3.34 (dd, $J = 6.8$, 9.5 Hz, 2H), 7.49–7.68 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.8, 16.8, 17.4, 19.7, 20.2, 22.5, 29.4, 60.9, 127.3, 130.4, 133.2, 134.1. Anal. Calcd for $C_{22}H_{32}OSi$: C, 83.47; H, 10.19. Found: C, 82.24; H, 10.10.

Acknowledgements

This work was supported by Korea Research Foundation Grant (KRF-2002-015-CP0214).

References and notes

1. Barton, D. H. R.; Ollis, W. D. *Comprehensive Organic Chemistry*; Pergamon: Oxford, 1979; p 579.
2. (a) Motherwell, W. B.; Crich, D. *Free Radical Chain Reactions in Organic Synthesis*; Academic: London, 1992; (b) Curran, D. P. *Synthesis* **1988**, 417; (c) Ramaiah, M. *Tetrahedron* **1987**, *43*, 3541; (d) Hartwig, W. *Tetrahedron* **1983**, *39*, 2609; (e) Graham, A. E.; Thomas, A. V.; Yang, R. *J. Org. Chem.* **2000**, *65*, 2583; (f) Jang, D. O.; Cho, D. H. *Tetrahedron Lett.* **2002**, *43*, 5921.
3. Nace, H. R. *Org. React.* **1962**, *12*, 57.
4. (a) Barton, D. H. R.; Parekh, S. I.; Tse, C. L. *Tetrahedron Lett.* **1993**, *34*, 2733; (b) Paulvannan, K.; Stille, J. R. *Tetraheron Lett.* **1993**, *34*, 6673.
5. Barton, D. H. R.; Hartwig, W.; Motherwell, R. S. H.; Motherwell, W. B.; Stange, A. *Tetrahedron Lett.* **1982**, *23*, 2019.
6. (a) Dolan, S. C.; McMillan, J. *J. Chem. Soc., Chem. Commun.* **1985**, 1588; (b) Barton, D. H. R.; Crich, D. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1603.
7. Dang, H.-S.; Franchi, P.; Roberts, B. P. *Chem. Commun.* **2000**, 499.
8. (a) Sano, H.; Taketa, T.; Migita, T. *Synthesis* **1988**, 402; (b) Sano, H.; Taketa, T.; Migata, T. *Chem. Lett.* **1988**, 119; (c) Jang, D. O.; Kim, J.; Cho, D. H.; Chung, C.-M. *Tetrahedron Lett.* **2001**, *42*, 1073.
9. Masamune, S.; Kim, B.; Petersen, J. S.; Sato, T.; Veenstra, S. *J. Am. Chem. Soc.* **1985**, *107*, 4549.
10. Spectroscopic data of compound **3**: $[\alpha]_D^{20} + 98.7$ (*c*, 0.12 $CHCl_3$); IR ($CHCl_3$): 2971, 2879, 1723, 1459, 1375, 1263, 1171, 1027 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.69 (s, 3H), 0.94 (s, 3H), 1.08 (s, 3H), 1.16 (s, 3H), 1.39–1.43 (m, 1H), 1.65–1.73 (m, 4H), 1.90–2.0 (m, 2H), 2.09–2.30 (m, 4H), 2.50 (dd, $J = 6.0$, 6.0 Hz, 1H), 2.95 (dd, $J = 2.7$, 10.5 Hz, 1H), 3.14 (t, $J = 5.7$ Hz, 1H), 3.69 (s, 3H), 4.24 (d, $J = 5.7$ Hz, 1H), 6.35 (s, 1H), 6.47 (s, 1H), 7.44 (s, 1H), 7.52 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 17.2, 19.8, 20.2, 21.6, 28.0, 32.0, 32.9, 37.3, 42.8, 48.8, 51.7, 52.0, 52.1, 53.5, 80.6, 81.2, 89.1, 110.2, 118.3, 120.3, 141.5, 143.3, 164.9, 166.2, 174.5, 215.1; Anal. Calcd. for $C_{27}H_{34}O_7$: C, 68.92; H, 7.28; O, 23.80. Found: C, 69.85; H, 7.14; O, 23.87.
11. For examples of the ring opening of an oxirane by an adjacent carbon centered radical: (a) Barton, D. H. R.; Hay-Motherwell, R. S.; Motherwell, W. B. *J. Chem. Soc. Perkin Trans. 1* **1981**, 2363; (b) Bowman, W. B.; Marples, B. A.; Zaidi, N. A. *Tetrahedron Lett.* **1989**, *30*, 3343.