Pergamon

Tetrahedron Letters 40 (1999) 8919–8922

TETRAHEDRON
LETTERS

A novel reduction of alcohols and ethers with a $HSiEt_3$/catalytic $B(C_6F_5)_3$ system

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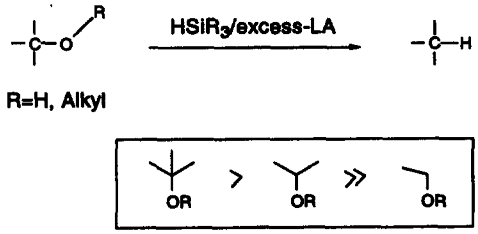
Received 29 July 1999; accepted 14 September 1999

Abstract

The primary alcohols **1a–d** and ethers **4a–b** were effectively reduced into the corresponding hydrocarbons **2** by $HSiEt_3$ in the presence of catalytic amounts of $B(C_6F_5)_3$. The secondary alkyl ethers **4g,h** underwent cleavage and/or reduction under similar reaction conditions to produce either the silyl ether **3k** or the corresponding alcohol **5b** upon subsequent deprotection with TBAF. The secondary alcohols (**1g,h**) and tertiary alcohol **1i**, as well as tertiary alkyl ether **4i**, did not react with the $HSiEt_3$/($B(C_6F_5)_3$ reducing reagent at all. The following relative reactivity order of substrates was found: primary≫secondary>tertiary. The methyl aryl ethers **4c–e** and alkyl aryl ether **4f** were smoothly deprotected to give the corresponding silyl ethers **3b,h–j** in nearly quantitative isolated yields. © 1999 Elsevier Science Ltd. All rights reserved.

It is known that hydrosilanes are able to reduce alcohols and alkyl ethers in the presence of Lewis acids (Eq. 1).[1] These methods require at least stoichiometric amounts of Lewis acid. Furthermore, the methodologies described are most effective for the reduction of a C–O bond at tertiary carbon,[1] are much less effective for the reduction of secondary substrates,[2] and absolutely ineffective for the reduction of primary alcohols and ethers (Eq. 1).[1]



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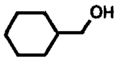
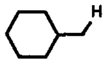
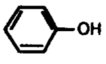
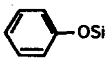
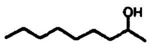
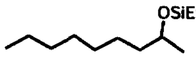
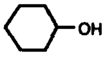
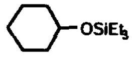
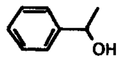
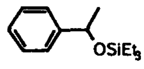
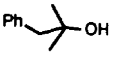
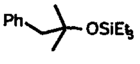
0040-4039/99/$ - see front matter
PII: S0040-4039(99)01757-8

Table 1
Reduction of alcohols **1** with $HSiEt_3$/cat.-$B(C_6H_5)_3$ system[a]

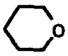
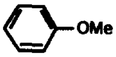
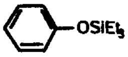
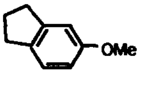
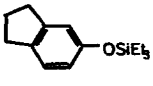
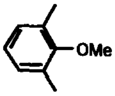
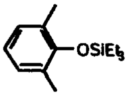
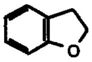
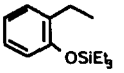
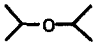
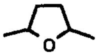
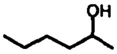
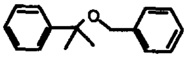
Entry	Alcohol 1		$HSiEt_3$ (eq)	Products (Yield, %)		
1	n-$C_9H_{19}OH$	**(1a)**	1.1	n-$C_9H_{19}OSiEt_3$	**(3a)**	(>95)[b]
2		**(1a)**	3.0	n-C_9H_{20}	**(2a)**	(>99)[c]
3		**(1b)**	6.0		**(2b)**	(91)[c]
4	$Ph(CH_2)_3OH$	**(1c)**	3.0	$Ph(CH_2)_3H$	**(2c)**	(>95)[b]
5	$Ph(CH_2)_2OH$	**(1d)**	3.0	$Ph(CH_2)_2H$	**(2d)**	(>95)[b]
6		**(1e)**	1.1 (or 6.0)		**(3b)**	(>99)[c]
7		**(1f)**	3.0		**(3c)**	(>95)[b]
8		**(1g)**	6.0		**(3d)**	(>95)[b]
9		**(1h)**	6.0		**(3e)**	(>95)[b]
10		**(1i)**	3.0		**(3f)**	(86)[b]

[a] $HSiEt_3$ was added under an argon atmosphere to a mixture of $B(C_6F_5)_3$ (10 mol %) and alcohol 1 (1 mmol) in hexane or CH_2Cl_2 (0.5 mL). After being stirred for 20 hours at room temperature, the appropriate internal standard was added and the mixture was analyzed by capillary GC. For NMR analysis, after completion of the reaction the mixture was quenched (Et_3N, 0.5 mL), filtered through celite and concentrated, followed by addition of internal standard (CH_3CCl_3). In the case of low b.p. products the reaction mixture was analyzed by ^1H NMR without concentration. [b] NMR yield. [c] GC yield.

We found that $HSiEt_3$ (3.0 equiv.) in the presence of catalytic amounts of $B(C_6F_5)_3$ (10 mol%) enabled us to reduce primary alcohols **1a–d** into the corresponding hydrocarbons **2a–d** in very high to quantitative yields (Eq. 2, Table 1, entries 2–5). It should be noted that employment of an equimolar amount of $HSiEt_3$ was not sufficient for the reduction of **1a**, instead alkyl silyl ether **3a** was produced quantitatively (entry 1).[3] In contrast to the primary alcohols, the more bulky secondary alcohols **1f–h**, as well as the tertiary alcohol **1i**, were stable towards reduction, and the corresponding silyl ethers **3c–f** were obtained in very high yields (entries 7–10). Phenol, as expected, did not undergo reduction even under treatment with a large excess of $HSiEt_3$ (entry 6).

$$\underset{\mathbf{1}}{\text{R-OH}} \xrightarrow{\text{HSiEt}_3\text{/cat-B(C}_6\text{F}_5)_3} \underset{\mathbf{2}}{\text{R-H}} \quad \left(\underset{\mathbf{3}}{\text{R-OSiEt}_3}\right) \qquad (2)$$

Table 2
Cleavage and reduction of ethers 4 with $HSiR_3$/cat.-$B(C_6H_5)_3$ system[a]

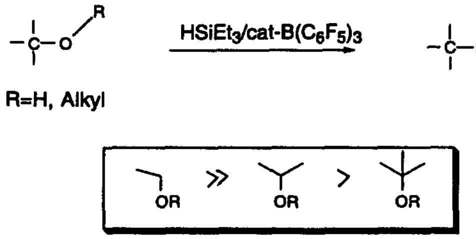
Entry	Ether 4	$HSiEt_3$ (eq)	Products (Yield, %)
1	$(n\text{-}C_{10}H_{21})_2O$ **(4a)**	1.1	$n\text{-}C_{10}H_{22}$ **(2e)** (93)[b] $n\text{-}C_{10}H_{21}OSiEt_3$ **(3g)** (95)[c]
2	**(4a)**	3.0	2 × **(2e)** (>99)[b]
3	 **(4b)**	1.1	 **(5a)** (88)[c,d]
4	**(4b)**	3.0	 **(2f)** (87)[c]
5	 **(4c)**	1.1	 **(3b)** (>99)[e,f]
6	 **(4d)**	1.1	 **(3h)** (96)[e]
7	 **(4e)**	1.1	 **(3i)** (98)[e]
8	 **(4f)**	1.1	 **(3j)** (>99)[e,f]
9	 **(4g)**	3.0	 **(3k)** (>95)[c]
10	 **(4h)**	3.0	 **(5b)** (91)[c,d]
11	 **(4i)**		no reaction[g]

[a] All reactions were carried in CH_2Cl_2. For more detailed reaction conditions, see Table 1, note a. [b] GC yield. [c] NMR yield. [d] Yields of alcohols 5 after TBAF deprotection of corresponding alkoxysilanes 3. [e] Isolated yield. [f] Reaction was performed in 5 mmol scale. [g] 97% of **4a** was recovered.

Next, we tested the $HSiEt_3$/cat.-$B(C_6F_5)_3$ reducing system for cleavage of alkyl ethers. It was found that linear primary alkyl ether **4a** could be easily cleaved in the presence of a stoichiometric amount of $HSiEt_3$/10 mol% $B(C_6F_5)_3$ to give decane (**2e**) and silylether **3g** (Eq. 3, Table 2, entry 1). Similarly, reduction of cyclic primary ether **4b** gave the corresponding ring cleaved silyl ether, which was converted into alcohol **5a** in 88% yield upon treatment with TBAF (entry 3). However, in the presence of excess amounts of $HSiEt_3$ both linear and cyclic ethers **4a,b** underwent smooth exhaustive reduction into the hydrocarbons **2e,f** in quantitative to high yields, respectively (entries 2 and 4). It was found that methyl aryl ethers **4c–e** readily underwent deprotection under the treatment of 1.1 equiv. of $HSiEt_3$ to give the corresponding silyl ethers **3b,h,i** in virtually quantitative yields (Table 2, entries 5–7). As expected, the aryl C–O bond in dehydrobenzofuran (**4e**) was tolerant towards the reduction, and consequently the cleavage product **3j** was produced quantitatively (entry 8). The secondary alkyl ether **4g** was quantitatively cleaved in the presence of 3 equivalents of $HSiEt_3$ to give the silyl ether **3k** (entry 9), thus exhibiting a striking resistance of linear secondary alkyl ethers (as well as corresponding alcohols; see also Table 1, entries 7–9) towards reduction. Cyclic secondary ether **4h** behaved similarly, producing the cleavage product **5b** in very high yield (entry 10). Sterically hindered ether **4i**, possessing both tertiary and primary alkyl units, did not undergo the reduction at all (entry 11).

$$\underset{\mathbf{4}}{\text{R-O-R}^1} \xrightarrow{\text{HSiEt}_3\text{/cat-B(C}_6\text{F}_5)_3} \underset{\mathbf{2}}{\text{R-H}} \quad \left(\underset{\mathbf{3}}{\text{R-OSiEt}_3} \right) \qquad (3)$$

In conclusion, we developed a novel effective method for reduction of primary alcohols and ethers with $HSiEt_3$ in the presence of catalytic amounts of $B(C_6F_5)_3$ (Eq. 4). In addition, this method could serve as a powerful tool for deprotection of methyl aryl and alkyl aryl ethers. Further development of this synthetic methodology, as well as mechanistic studies, are now underway in our laboratories.



(4)

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1. (a) Adlington, M. G.; Orfanopoulos, M.; Fry, J. L. *Tetrahedron Lett.* **1976**, 2955. (b) Fry, J. L.; Orfanopolous, M.; Adlington, M. G.; Dittman, W. R.; Silverman, S. B. *J. Org. Chem.* **1978**, *43*, 374. (c) Orfanopolous, M.; Smonou, I. *Synthetic Commun.* **1988**, *18*, 833. (d) Larsen, J. W.; Chang, L. W. *J. Org. Chem.* **1979**, *44*, 1168. (e) Yato, M.; Ishida, A. *Heterocycles* **1995**, *41*, 17. (e) Smonou, I. *Synthetic Commun.* **1994**, *24*, 1999.
2. For a report on the reduction of secondary benzyl alcohols in the presence of primary alkyl alcohols with $HSiEt_3/BF_3$ system, see Ref. 1c.
3. During the preparation of this manuscript, a method for silyl protection of alcohols with hydrosilanes in the presence of $B(C_6F_5)_3$ was reported, see: Blackwell, J. M.; Foster, K. L.; Beck, V. H.; Piers, W. E. *J. Org. Chem.* **1999**, *64*, 4887.