The Reduction of *O*-(*tert*-Butyldimethylsilyl) Aldoximes and Ketoximes and Electronic Effect Studies on the Novel Rearrangement that occurs with a Borane–Tetrahydrofuran Complex

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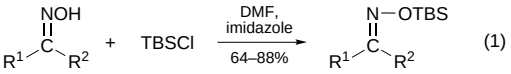
The reduction of aromatic and cyclic *O*-(*tert*-butyldimethylsilyl) oximes with various reducing reagents, such as $NaBH_4$, $LiAlH_4$, 9-BBN, $Li(Me_3Si)_2NBH_3$ and BH_3–THF, was investigated.

Since the fundamental work of Feuer and Vincent,[1] it has been well established that borane and boron hydrides reduce oximes, oxime ethers and acyl oximes affording *N*-monosubstituted hydroxylamines or primary amines, depending on the structure and reaction conditions. In 1985, Itsuno *et al.*[16] first enantioselectively reduced *O*-trimethylsilylacetophenone oxime with borane complexed to 1,3,2-oxazaborolidine formed *in situ* by the reaction of the chiral amino alcohol, (*S*)-(−)-2-amino-3-methyl-1,1-diphenylbutan-1-ol and borane. Although the *O*-(trimethylsilyl)oximes are readily prepared,[19] they are very susceptible to hydrolysis.[20] We developed a new and convenient method for the large scale synthesis of *O*-(*tert*-butyldimethylsilyl) oximes,[21] that were also envisioned as novel intermedites for the synthesis of chiral primary amines,[22] and other organic compounds.[23,24] Tillyer *et al.*[27] reported the enantioselective reduction of keto *O*-TBS oxime ethers by Corey's reagent,[28] for the synthesis of cyclic amino alcohols. However, they observed a lower yield for the 6-methoxy-substituted aromatic ring. Similarly, Liu and co-workers[29] found recently only 5% of hydroxylamine along with an unidentified compound, when 6-benzyloxy-2,3-dihydrobenzofuran 3-*O*-trimethylsilyloxime was reduced with borane and norephedrine. For the *O*-TBS analogue, it was reported that no reaction took place. In this paper, we describe our studies on the reduction of *O*-(*tert*-butyldimethylsilyl) oximes with various reducing reagents and the role that electronic effects play on the reaction pathways.

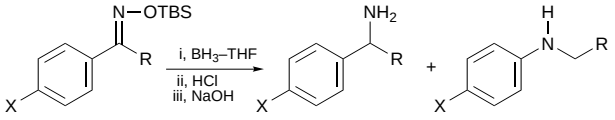
Representative aromatic and aliphatic *O*-TBS oximes were prepared in excellent yield by the reaction of the corresponding oxime with *tert*-butyldimethylchlorosilane, DMF and imidazole, [eqn. (1)], using a modification of our previously reported method.[21]



(1)

Initially, we found that the *O*-TBS moiety hinders the aromatic oximes from reduction with $NaBH_4$, $LiAlH_4$, 9-BBN, $Li(Me_3Si)_2NBH_3$ nd BH_3–THF at room temperature.[24] Afterwards, we investigated the reduction of *O*-TBS oximes with BH_3–THF under more vigorous reaction conditions. The results of the reductions of the corresponding silylated aryl oximes are summarized in Table 1. Benzylamine (**2a**) was obtained in excellent yield from the reduction of the *O*-TBS benzaldoxime (**1a**) with BH_3–THF complex after 3 h under reflux conditions. Borane reduction of the acetophenone *O*-TBS oxime at reflux temperature for 4 h afforded 21% of the expected α-methylbenzylamine (**2b**), 49% yield of *N*-ethylaniline (**3b**) and a minor amount of *N*-monosubstituted

Table 1 Reduction of aryl *O*-TBS ketoximes with borane



1 **2** **3**

Starting material					
1	X	R	Reaction conditions	Yield (%)[a]	**2**:**3**[b]
a	H	H	2BH_3–THF, heat, 5 h	83[c]	>99:1
a	H	H	2BH_3–THF, 1 $MgBr_2$–Et_2O, 5 h	80	97:3
a	H	H	3BH_3–THF, 1.5 $MgBr_2$–Et_2O, 5 h	88	90:10
b	H	Me	1BH_3–THF, heat, 6 h	65	45:55[d]
b	H	Me	2BH_3–THF, heat, 4 h	86	31:69
b	H	Me	2BH_3–THF, heat, 4 h, $MgBr_2$–Et_2O	88	43:57
c	Me	Me	2BH_3–THF, 25 °C, 9 days	24(12)[e]	21:79
c	Me	Me	2BH_3–THF, heat, 4 h	80	36:64[d]
c	Me	Me	3BH_3–THF, heat, 4 h	70	30:70
d	MeO	Me	2BH_3–THF, heat, 8 h	75	25:75
e	NO_2	Me	2BH_3–THF, heat, 8 h	74	>99:1
f	Cl	Me	2BH_3–THF, heat, 8 h	55	63:36

[a]Isolated overall yields. Product purity determination by GC–MS and by 300 MHz ^1H and ^{13}C NMR. [b]Determined by capillary GC. [c]Comparison with authentic samples. [d]Ratio of isolated products by column chromatography. [e]Isolated hydroxylamine.

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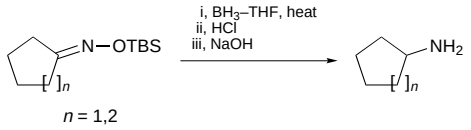
hydroxylamine. Reduction with 3 mol. equiv. of or a longer reaction time gave no hydroxylamine. Only the isomeric amines **2b** and **3b** were isolated and characterized by their spectroscopic data.

As illustrated in entries 2, 3 and 6, the addition of magnesium bromide–diethyl ether promotes the rearrangement of the silylated benzaldoxime and acetophenone oxime, probably owing to the coordination of magnesium to the oxygen, making the silyloxy moiety a better leaving group. Moreover, entries 8 and 10 clearly show that the yield of the reductive rearranged product increases with an increase in the electron-releasing ability of the *para*-substituent, while a strong electron-withdrawing group such as NO_2 (entry 11) favours formation of the primary amine. Although the formation of secondary anilines from the borane reduction of aromatic oximes and oxime ethers is unprecedented in the literature, borane can act as a Lewis acid promoting a reductive type of rearrangement for *O*-TBS oximes.



(2)

In the case of aliphatic cyclic *O*-TBS oximes, [eqn. (2)], we observed that *O*-TBS cyclopentanone and cyclohexanone oximes, when treated with BH_3–THF under reflux, generated only cyclopentyl- and cyclohexyl-amine in a 70 and 68% yield, respectively.

Techniques used: IR, ^{1}H NMR, ^{13}C NMR, GC–MS

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