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REDUCTION OF OXIMES WITH HYDROSILANE/H^+ REAGENT

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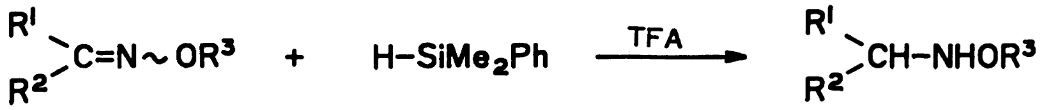
Hydrosilane/H^+ reagent reduced oximes in good yields. Stereospecific reduction of (2-acetoxy-1-phenylpropylidene)benzyloxyazane (**3**) was observed: the (*E*)-isomer gave *erythro*-1-phenyl-1-benzyloxyamino-2-propanol (**4**) in 99% selectivity, whereas (*Z*)-**3** afforded the threo isomer of **4** in 76% selectivity.

Reduction of ketones with hydrosilane/H^+ reagent is shown to be a powerful and reliable method for the synthesis of *erythro*-isomers of 2-amino alcohols, 1,2-diols, and 3-hydroxyalkanoic acid derivatives.[1)] Reported herein is the reduction of oximes[2,3)] with the same reagent, in which amines, particularly 2-amino alcohols of biological interest, are readily produced under high stereocontrol.

When benzylidenebenzyloxyazane (**1a**) was treated with dimethylphenylsilane (1.2 mol-equiv) in trifluoroacetic acid (TFA) at room temperature, the reduction proceeded smoothly and *N*-benzyloxybenzylamine (**2a**) was isolated in 75% yield after workup and purification. *O*-Protected oximes of benzaldehyde, acetophenone, and cyclohexanone (**1a-d**) were easily reduced, whereas an acyclic aliphatic derivative **1e** was reduced only in 23% yield even under forcing conditions (50 °C, 5 d, with 2 mol of $HSiMe_2Ph$), as summarized in Table 1.



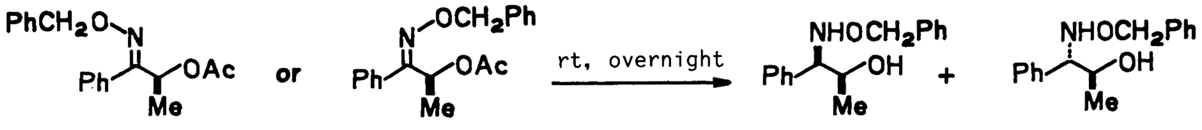
1 **2**

Table 1. Reduction of Oximes with $PhMe_2SiH/H^+$ Reagent [a)]

Oxime	R^1	R^2	R^3	Conditions	Yield/%
1a	Ph	H	CH_2Ph	rt, overnight	75
1b	Ph	Me	COMe	rt, overnight	67
1c	Ph	Me	COPh	rt, overnight	78
1d	$-(CH_2)_5-$		CH_2Ph	rt, 24 h[b)]	65
1e	C_7H_{15}	Me	CH_2Ph	50 °C, 5 d[c)]	23

a) Carried out with $HSiMe_2Ph$ (1.2 mol) in TFA or TFA-CH_2Cl_2 (1:1)(1-2 cm^3/mmol).
b) KF (1 mol) was added. c) $HSiMe_2Ph$ (2 mol) was employed.

It is noteworthy that stereospecificity was observed in the hydrosilane/H^+ reduction of (2-acetoxy-1-phenylpropylidene)benzyloxyazane (**3**). When the (*E*)-isomer[4,5] **3a** was allowed to react with $PhMe_2SiH$ in CF_3COOH (rt, overnight), *erythro*-1-phenyl-1-benzyloxyamino-2-propanol (**4a**) was obtained in 99% selectivity[6] (77% yield). In contrast, the (*Z*)-isomer[4,5] **3b** gave the threo isomer **4b** preferentially[6] (**4a** : **4b** = 24 : 76). These results contrast to lithium aluminum hydride reduction[9] wherein no stereospecificity was observed. Lithium aluminum hydride reduction of **4a** affords naturally occurring *erythro*-1-phenyl-1-amino-2-propanol (norisoephedrine).



3a or **3b** → **4a** + **4b**

Starting material	Reducing agent (solvent)	Yield/%	**4a** : **4b**
3a	$HSiMe_2Ph/TFA$	73	99 : 1
3a	$LiAlH_4$ (Et_2O)	46	82 : 18
3b	$HSiMe_2Ph/TFA$	77	24 : 76
3b	$LiAlH_4$ (Et_2O)	39	58 : 42

References

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3) Hydrosilylation of imines catalyzed by $RhCl(PPh_3)_3$ or $PdCl_2$: I. Ojima and T. Kogure, Tetrahedron Lett., 1973, 2475.
4) Stereochemical assignment of oximes by ^1H NMR spectroscopy: G. J. Karabatsos and N. Hsi, Tetrahedron, 23, 1079 (1967).
5) A mixture of **3a** and **3b** was prepared from 2-acetoxy-1-phenyl-1-propanone and *O*-benzylhydroxylamine by a conventional method. Both isomers were easily separated by silica gel column chromatography.
6) The high erythro selectivity obtained in the reduction of (*E*)-isomer **3a** should be ascribed to the proton bridged Cram's cyclic model[7] like the reduction of α-acyloxy ketones.[1] On the other hand, the same transition state model is not applicable to the (Z)-isomer **3b**. The threo selectivity for **3b** may be attributed to nucleophilic attack of the hydrosilane molecule to $>C=N^{\pm}OCH_2Ph$ moiety through the Felkin transition state model.[8]
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