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Oxidation of an α,β-(Epoxyalkyl)trimethylsilane with Pyridine Oxides in the Presence of Silylating Agents. A Facile Enantioselective Synthesis of Glyceraldehyde Derivatives

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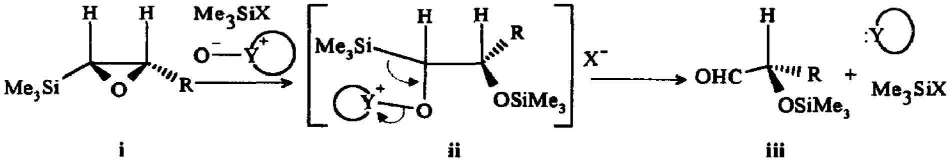
Abstract: Trimethylsilyl glycidol derivatives 1 were oxidized with pyridine N-oxides in the presence of silylating agents to give the corresponding glyceraldehyde derivatives 3. Reaction of (α,β-epoxyalkyl)silanes with N-oxides was studied.

Trimethylsilyloxiranes (α,β-epoxysilanes) are well-know synthetic precursors of geometrically defined olefins[1], various vinylic heteroatoms and metal derivatives[2], allylic alcohols[3] and some other compounds[4]. In view of the availability of optically active epoxysilanes by the Katsuki-Sharpless asymmetric epoxidation[5] it was challenging to develop a method for direct and stereospecific chemical oxidation of the epoxysilane to the hydroxy aldehyde moiety. Recently, anodic oxidation of protected β-hydroxy-α-methoxysilanes (obtained from α,β-epoxysilanes) to β-hydroxy aldehydes has been described[6]. Oxidation of all-carbon epoxides to the corresponding hydroxy aldehydes has been studied only scarcely. Cohen and Tsuji[7] have reported that epoxides treated with dimethylsulfoxide (DMSO) and boron trifluoride etherate and then with a base afford in moderate yields the corresponding α-hydroxy carbonyl compounds. The Kornblum-type oxidation is, most likely, involved in this transformation[8]. Recently, Trost and Fray[9] have successfully applied oxidation of an epoxide with DMSO in the presence of trifluoromethanesulfonic acid as the catalyst and diisopropylethylamine as the base. Our experiments aimed at oxidation of epoxysilanes to hydroxy aldehydes under conditions suitable for oxidation of all-carbon oxiranes failed so far. The oxidation could be carried out, however, on the basis of a somewhat different principle. Our concept is illustrated in Scheme 1. Nucleophilic addition of the dipolar oxidant RY$^+$-O$^-$ (where Y = N, S or similar atoms) to (trimethylsilyl)oxirane i in the α-position with respect to silicon atom[10] is assisted by complexing the epoxide oxygen with the trimethylsilyl cation derived from Me$_3$SiX (where X = leaving group). The adduct ii undergoes fragmentation to afford the carbonyl compound iii and oxidant residue RY, and to regenerate the trimethylsilyl cation. In the depicted transformation there is

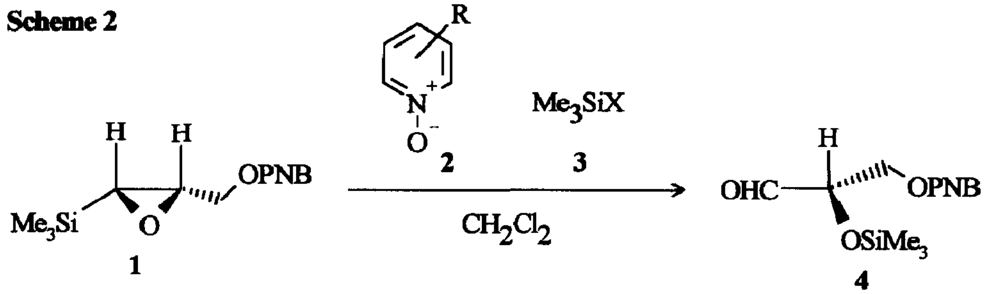
Scheme 1



no involvement of a free hydroxy group that could initiate the Peterson elimination.

We found that treatment of the trimethylsilyl glycidol 1 (Scheme 2, PNB = p-nitrobenzoyl), easily accessible from propargyl alcohol[11], with pyridine N-oxide 2 (R = H, 2 mol equiv.) and trimethylsilyl triflate (3, X = CF_3SO_2O, 1 mol equiv.) in CH_2Cl_2 affords the corresponding O-trimethylsilyl derivative of glyceraldehyde 4

Scheme 2



PNB = p-nitrobenzoyl

Table 1

No	Epoxide config.	2, R	Catalyst, X (mol eqiv.)	Reaction conditions	Yield (%)
1	*trans*	4-NO_2	OSO_2CF_3, (1)	reflux, 0.5 h	80
2	*trans*	H	OSO_2CF_3 , (1)	reflux, 13 h	76
3	*trans*	2-(MeO)-5-F	OSO_2CF_3, (1)	reflux, 8 h	67
4	*trans*	4-^{t}Bu	OSO_2CF_3, (1)	reflux, 13 h	49
5	*trans*	4-NO_2	$B(OSO_2CF_3)_4$, (0.35)	r. t., 3 h	69
6	*cis*	4-NO_2	$B(OSO_2CF_3)_4$, (0.35)	r. t., 3 h	69

in good yield (Table 1, entry 2). The reaction was examined with respect to selected amine N-oxides and silylating agents. In standard experiments the labile aldehydes were isolated as their respective 2,4-dinitrophenylhydrazones. As may be seen in Table 1, in the series of experiments with trimethylsilyl triflate, the highest yield within the shortest reaction time was obtained with the N-oxide bearing the electron-withdrawing nitro group, 4-nitropyridine N-oxide (entry 1). The N-oxide with the electron-donating *tert*-butyl group, 4-*tert*-butylpyridine N-oxide, gave the product in the lowest yield (entry 4). Comparison of the oxidation yields and the reaction times recorded in Table 1 for four selected N-oxides indicates that the nucleophilic properties of the N-oxide are not the decisive factor. The ability of the pyridine moiety to act as the leaving group in the step of adduct fragmentation (Scheme 1) appears more important. It is noteworthy that no oxidation product was obtained with the commonly used N-methylmorpholine N-oxide[12] or with highly nucleophilic N-oxides, 4-(N,N-dimethylamino)pyridine oxide[13] and 2-(N,N-dimethylamino)pyridine oxide[14]. The very recently designed[15] powerful source of the electrophilic trimethylsilyl group, $Me_3SiB(OTf)_4$ ("supersilylating agent"), efficiently promoted oxidation of *trans*-trimethylsilyl glycidol 1 (entry 5) and its *cis*-isomer (entry 6) at room temperature even when used in a catalytic amount (0.35 mol equiv.).

The described method of epoxysilane oxidation allows for rapid enantioselective synthesis of glyceraldehyde derivatives from 3-(trimethylsilyl)allyl alcohol[16].

Application of this method to oxidation of other epoxysilanes revealed side reactions which may accompany the oxidation of epoxide to hydroxy aldehyde. Treatment of *cis*-1-(trimethylsilyl)-2-butyloxirane (Scheme 3, 5, R = C_4H_9) with an excess of 4-nitropyridine N-oxide and 1 mol equiv. of trimethylsilyl triflate at room temperature afforded the corresponding hydroxyaldehyde 6, R = Bu, and methyl butyl ketone 7, R = Bu, (Table 2, entry 1). Oxidation of 5, R = C_4H_9, with the same oxidant in the presence of 0.1 mol equiv. of triflate a mixture of carbonyl compounds with higher proportion of the aldehyde (entry 2). *cis*-1-(Trimethylsilyl)-2-*iso*-propyloxirane (5, R = iso-Pr) gave, under a variety of conditions, a mixture of the corresponding aldehyde and ketone, the latter being predominat (Table 2, entries 2-6). The methyl ketones are on the same oxidation level as the starting oxiranes and should be considered as the rearrangement and desilylation products. Recently, another trimethylsilyl triflate-induced rearrangement of oxiranes has been described[17].

Scheme 3

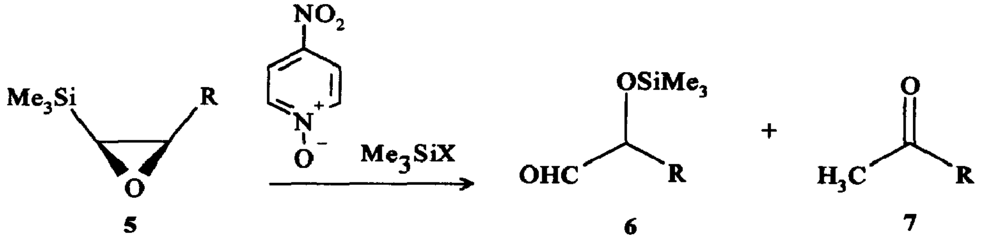


Table 2

No	5, R	Catalyst, X (mol eqiv.)	Reaction conditions	6	7 yield(%)
1	C_4H_9	OSO_2CF_3, (1)	r.t., 1 h	24	56
2	C_4H_9	OSO_2CF_3, (0.1)	r.t., 24 h	59	20
3	*iso*-C_3H_7	OSO_2CF_3, (1)	r.t., 2 h	34	56
4	*iso*-C_3H_7	OSO_2CF_3, (1)	0° C, 4.5 h	25	65
5	*iso*-C_3H_7	OSO_2CF_3, (0.1)	r. t., 4.5 h	33	66
6	*iso*-C_3H_7	$B(OSO_2CF_3)_4$, (0.1)	r. t., 3 h	26	44

Interestingly, treatment of epoxysilane 5, R = Bu with 4-(N,N-dimethylamino)-pyridine N-oxide in boiling acetonitrile afforded 1-hydroxyhexan-2-one in 51% yield. Most likely, the reaction proceeds *via* the respective α-hydroxy aldehyde.

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