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Synthesis of Optically Active 2,3-*O*-Isopropylidene-1-(trimethylsilyl)glyceraldehyde and Other Derivatives of (α-Hydroxyacyl)silane

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Summary: (α-Hydroxyacyl)silanes are prepared by oxidation of (α,β-epoxyalkyl)silanes with the system DMSO–trialkylsilyl trifluoromethanesulfonate–tertiary amine.

Since the first reports on syntheses of acylsilanes with the use of 2-(trimethylsilyl)dithiane as the precursor of the (trimethylsilyl)carbonyl group,[1] several methods of preparation of these compounds have been developed.[2] Compounds with the (trialkylsilyl)carbonyl group bearing aliphatic,[3] alicyclic,[4] aromatic or heterocyclic,[5] and vinylic[6] substituents have become relatively easily available. Useful chemical[7] and interesting spectroscopic[8] properties of acylsilanes have been revealed. Application of acylsilanes in the enantioselective synthesis is, however, limited due to the lack of methods for synthesis of chiral acylsilanes, with the chirality center in the proximity of the acylsilyl group. Until now racemic [2-(phenylthio)acyl]silane[9] and only one optically active derivative of (2-hydroxyacyl)silane[10] have been prepared. Optically active acylsilanes with an α-branched alkyl chain[11] have been synthesized and examined for the stereochemistry of addition to the carbonyl group. Even with such a narrow group of examples it has been clearly shown that acylsilanes are synthetic equivalents of aldehydes with a high potential with respect to diastereoselective transformations. We report here the first synthesis of optically active (α-hydroxyacyl)silanes, based upon Kornblum-type oxidation of (α,β-epoxyalkyl)silanes.

We found that treatment of (2*S*,3*S*)-(trimethylsilyl)-glycidol *p*-nitrobenzoate (**1a**) (95% ee, Scheme 1), easily available by the Sharpless epoxidation of 3-(trimethylsilyl)allyl alcohol[12] (*vide infra*), with DMSO and trimethylsilyl trifluoromethanesulfonate (Me_3SiOTf) in methylene chloride and then with triethylamine affords 2-*O*-(trimethylsilyl)-3-*O*-(*p*-nitrobenzyl)-1-(trimethylsilyl)-glyceraldehyde[13] (**2a**) and the corresponding alcohol **2f** in 45 and 40% yields,[14,15] respectively (Table 1, entry 1). Replacement of triethylamine with diisopropylethylamine[15] (DIEA) provided the *O*-trimethylsilyl derivative

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(13) All new compounds described in this paper exhibited the expected analytical and spectral data.

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(15) For Kornblum-type oxidation of "all-carbon" oxiranes, see: Trost, B. M; Fray, M. J. *Tetrahedron Lett.* **1988**, *29*, 2163–2166 and references cited therein.

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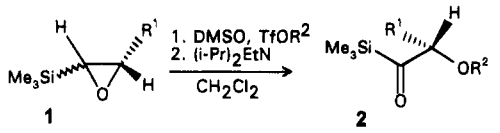
Scheme 1



1 2

a. (2S,3S) R^1 = CH_2OPNB; a. R^1 = CH_2OPNB, R^2 = $SiMe_3$
b. (2R*,3S*) R^1 = CH_2OPNB; b. R^1 = CH_2OPNB, R^2 = $SiEt_3$
c. (2R*,3R*) R^1 = i-Pr; c. R^1 = i-Pr, R^2 = $SiMe_3$
d. (2R*,3R*) R^1 = C_5H_{11}; d. R^1 = C_5H_{11}, R^2 = $SiMe_3$
e. (2R*,3R*) R^1 = Ph; e. R^1 = Ph, R^2 = $SiMe_3$
PNB = p-nitrobenzoyl f. R^1 = CH_2OPNB, R^2 = H

Table 1. Preparation of Acylsilanes According to Scheme 1

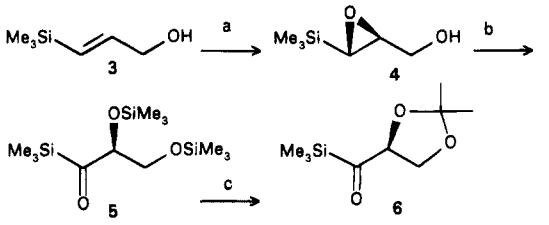
entry	epoxide	R^2 ($TfOR^2$)	acylsilane	yield (%)
1	**1a**	Me_3Si	**2a** and **2f**[a]	85
2	**1a**	Me_3Si	**2a**	82
3	**1a**	Et_3Si	**2b**	80
4	**1b**	Me_3Si	**2a**	89
5	**1c**	Me_3Si	**2c**	94
6	**1d**	Me_3Si	**2d**	92
7	**1e**	Me_3Si	**2e**	92
8	**1a**	H	**2f**	48

[a] Et_3N was used as the base.

2a in 82% yield (Table 1, entry 2). Both products **2a** and **2f** showed optical activity ($[\alpha]^{14}_D$ −2.3°, *c* 1.3, $CHCl_3$, and $[\alpha]^{22}_D$ +46.0°, *c* 1.1, $CHCl_3$, respectively).[16]

When epoxysilane **1a** was allowed to react with DMSO in the presence of Et_3SiOTf and then with DIEA, [*O*-(triethylsilyl)acyl]silane **2b** was obtained in 80% yield (Table 1, entry 3). Under similar conditions, with the use of Me_3SiOTf, (2*R**,3*S**) epoxysilane **1b** (cis-substituted oxirane) furnished acylsilane **2a** (89% yield, entry 4). Representative epoxysilanes lacking an additional oxygen function **1c**, **1d**, and **1e** were transformed into the [α-[(trialkylsilyl)oxy]acyl]silanes **2c**, **2d**, and **2e**, respectively, with excellent yields (Table 1, entries 5−7). It is noteworthy that oxidation of epoxysilane **1a** with the use of TfOH instead of Me_3SiOTf affords (α-hydroxyacyl)silane **2f**; the yield was, however, much lower (Table 1, entry 8). Having in hand a method for synthesis of chiral α-(hydroxyacyl)silanes we approached the preparation of (*S*)-2,3-*O*-isopropylidene-1-(trimethylsilyl)glyceraldehyde (**6**) which is the acylsilane analogue of one of the most important chiral building blocks in organic synthesis.[17] The synthetic route to compound **6** is presented in Scheme 2. Sharpless epoxidation[12c] of 3-(trimethylsilyl)allyl alcohol (**3**) gave (trimethylsilyl)-glycidol **4** (84% yield, 94% ee). The latter product was

Scheme 2[a]



3 4 5 6

[a] Reagents and conditions: (a) Sharpless epoxidation, 84% yield, 94% ee; (b) allyltrimethylsilane−DMSO−Me_3SiOTf/CH_2Cl_2 and then Et_3N; (c) 2,2-dimethoxypropane-TsOH cat., distillation, 72% from **4**.

transformed with allyltrimethylsilane[19] into the *O*-trimethylsilyl derivative which, without isolation, was treated with DMSO and Me_3SiOTf and subsequently with triethylamine to yield acylsilane **5**. Compound **5** was, without isolation, subjected to reaction with 2,2-dimethoxypropane in the presence of a catalytic amount of TsOH monohydrate to afford, after distillation, the required glyceraldehyde derivative **6** in 72% yield (bp 80−84 °C/15 mmHg, $[\alpha]^{22}_D$ −94.7°, *c* 1.01, $CHCl_3$). To determine the optical purity of compound **6**, its ^1H NMR spectrum was measured in the presence of tris[(3-heptafluoropropyl)hydroxymethylene)-(+)-camphorato]europium(III) [Eu(hfc)$_3$] and compared with the respective spectrum of racemic **6**. No signal corresponding to the other enantiomer could be seen.[17] This suggests that during the transformation of (trimethylsilyl)glycidols into the corresponding (trimethylsilyl)glyceraldehyde derivatives there is only a small, if any, loss of the optical purity.[16]

In conclusion, an easy and efficient method for the synthesis of (α-hydroxyacyl)silanes, including the optically active 1-(trimethylsilyl)glyceraldehyde derivatives, from (α,β-epoxyalkyl)silanes was developed. Since many (α,β-epoxyalkyl)silanes are readily available in a highly pure enantiomeric form, this method provides an access to a class of compounds of potential use in stereocontrolled synthesis.

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Supplementary Material Available: General experimental procedures and characterization data. Copies of ^1H and ^{13}C NMR spectra of **2a**−**2f** and **6** (27 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(16) We failed to prepare Mosher's esters of (α-hydroxyacyl)silanes suitable for NMR measurements. Their Mosher's esters and acetates appear to be unstable. Further experiments aimed at the determination of the optical purity of underivatized acylsilanes are in progress.

(17) Two signals corresponding to the methyl groups of the acetonide moiety δ 1.36 (br d, *J* = 0.6 Hz, 3H) and 1.47 (br d, *J* = 0.6 Hz, 3H) were selected for this measurement.

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