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Fluoride Activated Stereoinformation Transfer from a C-Si Bond of a Chiral Benzyl Silane to C-C Bonds

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Abstract: Reactions of (*S*)-*N,N*-diisopropyl-*o*-(1'-trimethylsilyl)ethyl benzamide (**1**) with benzaldehyde, *p*-anisaldehyde, and acetophenone activated by fluoride provide diastereomers of *N,N*-diisopropyl-*o*-(2'-alkyl-2'-aryl-2'-hydroxy)ethyl benzamides **2**, **3**, and **4** with retention of configuration at the benzylic position in enantiomeric ratios of up to 90:10. Reactions of **1** with allyl bromide and allyl iodide in the presence of fluoride provides (*R*)-*N,N*-diisopropyl-*o*-(1'-methyl)but-3'-enylbenzamide (**5**) with modest enantiomeric ratios. The results are interpreted as involving collapse of a siliconate complex. © 1997 Elsevier Science Ltd.

Recent developments of methodologies for syntheses of enantioenriched compounds have provided enantioenriched benzyl silanes.[1,2] However, except for allyl silanes,[3] there are relatively few cases of the stereoselective synthetic transformations of formally sp^3 carbon-silicon bonds to carbon-carbon bonds. Sauvetre has provided fluoride initiated conversions of C-Si bonds of epoxysilanes to C-C bonds for additions to aldehydes or ketones with retention of stereochemistry.[4] Stereoselective insertions into strained carbon-silicon bonds have been reported recently by Woerpel.[5] Hiyama has reported palladium catalyzed conversions of chiral trifluoro benzyl silanes to chiral diaryl silanes occurs with retention or inversion depending on the reaction conditions.[6] Corey has provided a diastereoselective intramolecular reaction in which a benzyl silane is used as a benzyl anion equivalent activated by fluoride ion.[7] Activation of achiral trialkyl benzyl silanes using fluoride to afford formal nucleophiles which provide carbon-carbon bonds is established methodology.[8]

In this paper we report transfers of stereoinformation from a C-Si bond to a C-C bond in the reactions of (*S*)-*N,N*-diisopropyl-*o*-(1'-trimethylsilyl)ethyl benzamide (**1**) with electrophiles to give **2**-**5** in the presence of fluoride sources. To the best of our knowledge, there is no previous report of a fluoride ion activated transfer of enantioselectivity from a C-Si bond to a C-C bond at the same carbon in an intermolecular reaction.

Treatment of (*S*)-**1** with *tetra*-butyl ammonium fluoride (1 M in THF which had been dried over molecular sieves) and the carbonyl electrophiles, acetophenone, benzaldehyde, and *p*-anisaldehyde provided the products **2**, **3**, and **4** with the diastereomeric ratios (drs) and enantiomeric ratios (ers) shown in Table 1. The enantiomeric ratios show low to moderate fidelity of stereoinformation transfer with retention. Similar reactions of **1** with allyl bromide and allyl iodide provide (*R*)-**5** in low yields with enantiomeric ratios from 60:40 to 80:20 as shown in Table 1. The assignments of absolute configurations were made by comparision to established compounds.[9]

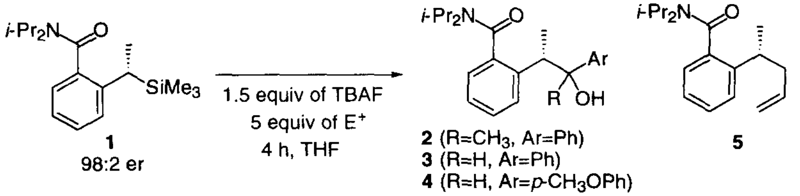

Table 1. Reactions of **1** with TBAF and Electrophiles.

E^+	Temperature	Yield (%)[a]	dr[b,d]	er[c,d]
$C_6H_5C(=O)CH_3$	-78 °C	25 (**2**)[e]	2 : 1	90:10, 81:19
$C_6H_5C(=O)CH_3$	-0 °C	68 (**2**)	2 : 1	86:14, 81:19
$C_6H_5C(=O)CH_3$	ambient	56 (**2**)	2 : 1	84:16, 79:21
C_6H_5CHO	0 °C	87 (**3**)	1 : 1	75:25, 50:50
C_6H_5CHO	ambient	86 (**3**)	1 : 1	69:31, 50:50
p-CH_3O C_6H_5CHO	ambient	89 (**4**)	1 : 1	75:25, 50:50
$CH_2=CHCH_2Br$	0 °C	37 (**5**)	-	80:20
$CH_2=CHCH_2Br$	ambient	42 (**5**)	-	76:24
$CH_2=CHCH_2I$	ambient	27 (**5**)[e]	-	60:40

(a) The desilylated product was the major side product in all reactions. (b) The drs were determined by GC. (c) The ers were determined by CSP-HPLC. (d) er=enantiomeric ratio, dr=diastereomeric ratio (e) The starting material **1** is recovered in *ca.* 50% yields.

We investigated the effect of reaction variables on the reaction of **1** with *p*-anisaldehyde as shown in Table 2.[11] The results show that the er of one diastereomer can be improved with DMF or methylene chloride as solvent but changes in temperature and fluoride source have little effect on ers of products. The crown ether of the last three entries was required to achieve the reaction with potassium fluoride at or below room temperature. The change in solvent from THF to DMF also resulted in lower yields.

Substitutions similar to these reactions have been reported for analogous laterally lithiated benzamides.[2b,10] In that case, reactions with carbonyl electrophiles gave products with very low enantioselectivities, so the current methodology provides access to these products with somewhat better enantiomeric ratios. Clayden has shown that reactions via laterally lithiated benzamides and naphthamides exhibit atropisomerism and has used those systems to establish that tin-lithium exchange can proceed with retention as well as loss of stereoinformation with different diastereomers.[12]

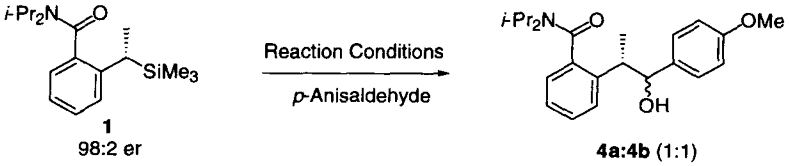

Table 2. Reactions of **1** with Fluoride and *p*-Anisaldehyde.

Reaction Conditions	Yield (%)	er of **4a**	er of **4b**
TAS-F / THF / RT / 12 h	54	82:18	53:47
TAS-F / DMF / RT / 12 h	67	78:22	75:25
CsF / CH_3CN / reflux / 12 h	43	76:24	74:26
CsF /DMF / RT / 17 h	63	79:21	77:23
CsF / DMF / 130 °C	54	75:25	71:29
KF / DMF / 130 °C	28	74:26	73:27
KF / 18-crown-6 / DMF / RT / 12 h	39	74:26	77:23
KF / 18-crown-6 / DMF / 0 °C / 12 h	39	79:21	77:23
KF / 18-crown-6 / CH_2Cl_2 / RT / 12 h	39	74:26	70:30

An interesting aspect of the conversion of **1** to **2-5** is the retentive transfer of enantioinformation in the absence of a second stereogenic center or strong complexation with a metal ion.[13] The two limiting possibilities are reaction via an atropisomeric benzylic carbanion which maintains its configuration and exhibits facial selectivity or formation and collapse of a siliconate complex. The former possibility seems inconsistent with the lability of the corresponding lithiated species. We favor the latter pathway for the fluoride activated reactions of **1** with the ketone and aldehydes.[2b,5,10,12] Further work will be needed to develop the potential and gain understanding of these and related benzylic silanes for asymmetric syntheses.

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9. The absolute configuration of **1** was assigned by ananlogy to the absolute configuration of the corresponding phenyldimethylsilyl product which was converted to (*S*)-3-methylphthalide by Tamao-Fleming oxidation and cyclization. The optical rotation of the product was compared to that of authentic (*S*)-3-methylphthalide. The absolute configuration of the benzylic carbon of **4** was established by converting into (*R*)-*N*,*N*-diisopropyl-*o*-(2'-(*p*-methoxyphenyl)-1'-methyl)ethylbenzamide using modified Barton's deoxygenation procedure . The absolute configurations of deoxygenated product of **4** and **5** were assigned by analogy to (*R*)-*N*,*N*-diisopropyl-*o*-(1'-methylbutyl)benzamide, which was synthesized independently from (*R*)-2-phenylbutane. The relative configuartions of **2**, **3**, and **4** were not determined.[2d,10]

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11. The diastereomer **4a** is the non-polar diastereomer and **4b** is the polar diastereomer, as eluted in the CSP-HPLC.

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