203. High *Syn* Selectivity of a S_E' Reaction: Acylation of an Optically Active 1,1-Disilyl-2-alkene

Preliminary communication

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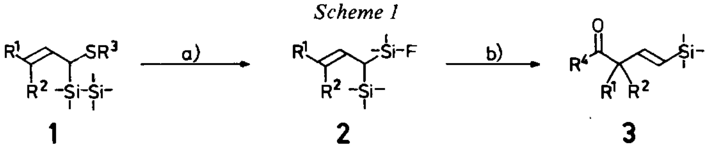
Summary

The disilane/disilylmethane rearrangement of an optically active disilanyl sulfide **9B** was used to prepare an optically active disilylalkene **10** whose absolute configuration was established by X-ray analysis of the bromo derivative **13** ($P2_1$, $a = 7.847\,(3)$ Å, $b = 9.487\,(3)$ Å, $c = 20.010\,(8)$ Å, $\beta = 82.28°\,(3)$, $Z = 2$). Acylation of **10** furnished an optically active ketone **14**, which was degraded to **16**, a compound of known absolute configuration. The enantiomeric excess of **10** was determined by alkylation with an optically active lithium compound and that of **14** by an optically active NMR.-shift reagent. The S_E' reaction **10**→**14** was thus shown to proceed with 94% (97% *syn*/3% *anti*) stereoselectivity.

We recently reported the preparation of α-(alkylthio)allyl disilanes **1** and their rearrangement to disilylalkenes **2** [1]. When the disilylalkenes **2** were acylated (R-COCl/$AlCl_3$) highly selective substitution of the dimethylfluorosilyl group occurred and vinyl silanes **3** were formed with exclusive (*E*)-configuration *(Scheme 1)*. This specificity might result from an allylic electrophilic substitution (S_E'), whereby the electrophile attacks the double bond selectively *syn* or *anti* with respect to the leaving dimethylfluorosilyl substituent. In order to determine the *syn* or *anti* selectivity an optically active disilylalkene **2** of known absolute configuration would have to be prepared, acylated to **3** and then degraded to a compound of known absolute configuration. Qualitative theoretical interpretations of the S_E' reaction predict *anti*

Scheme 1



a) $(CH_3)_3O^+BF_4^-$; b) R^4-COCl/$AlCl_3$.

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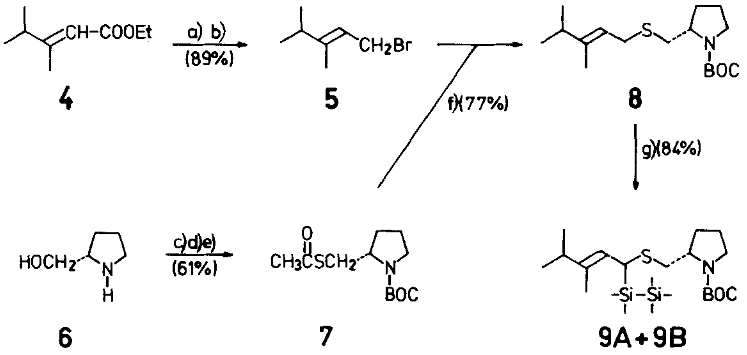
[2], but examples of both *syn* [3] and *anti* [4] stereoselectivity have been reported for cyclic allyl silanes. However, the approach of the electrophile is clearly guided by steric interactions in these examples.

The preparation of an optically active disilane derivative is outlined in *Scheme 2.* Isopropyl methyl ketone was converted to a 6:1 mixture[3]) of (*E*)- and (*Z*)-ester **4** [5a] ($(EtO)_2PO-CH_2COOEt$, NaOEt in EtOH, RT.; 82% yield). Distillation[4]) of the (*E*/*Z*)-mixture of **4** resulted in pure[5]) (*E*)-ester **4**[6]) in 50% overall yield based on isopropyl methyl ketone. (*E*)-**4** was reduced to the corresponding alcohol ($LiAlH_4$ in Et_2O, RT.; 90% yield) which on treatment with PBr_3 (Et_2O, $T < 0°$ [6]) produced **5** in 95% crude yield. (−)-(*S*)-Prolinol **6**[7]) was converted in a three-step sequence to the thioprolinol derivative **7** ($(BOC)_2O$ in dioxane, RT. [8]; $PhSO_2Cl$ in pyridine; CH_3COSK in EtOH, 50° [9]; 61% overall yield). The thioacetate **7** was then hydrolyzed (KOH in CH_3OH, reflux) and the soformed potassium salt of *N*-BOC-thioprolinol treated with bromide **5** to yield optically active sulfide **8** in 77% yield. Metallation of **8** with LDA in THF at −40° and capture of the anion with chloropentamethyldisilane [10] (−70° to RT.) produced a 1:1 mixture of two diastereomeric disilane derivatives **9A** and **9B** in 84% yield. **9A** and **9B** could be separated by flash chromatography on silica gel [11].

One isomer was treated with trimethyloxonium tetrafluoroborate (CH_2Cl_2, RT.) to furnish pure (*E*)-disilylalkene **10**[8]) in 81% yield *(Scheme 3).* The optical purity of **10** was determined in the following way: fluorosilane **10** was alkylated with optically

Scheme 2



a) $LiAlH_4$; b) PBr_3; c) $(BOC)_2O$; d) $PhSO_2Cl$; e) $CH_3COS^-K^+$; f) KOH, then **5**; g) LDA, then $(CH_3)_3Si-Si(CH_3)_2Cl$.

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[3]) According to integration of the $CH_3-C(3)$ ^1H-NMR. signal of the two isomers[5]).

[4]) The mixture was separated in a *Fischer* 'Spaltrohr' column HMS 500 at 10 Torr; b.p. (*Z*)-**4**: 73°/10 Torr, (*E*)-**4**: 78°/10 Torr.

[5]) Purity >99.5% (*E*)-**4** according to GC. analysis (17 m glass capillary coated with *Pluronic* 64 as stationary phase).

[6]) The (*E*)-configuration was confirmed by the chemical shift in the ^1H-NMR. of the $CH_3-C(3)$ at 2.10 ppm, vs. 1.78 ppm of (Z)-**4** [5b].

[7]) Prepared according to [7]; supplied by *Aldrich-Europe.*

[8]) In another series with a racemic 6:1 (*E*/*Z*)-mixture **10** the ^1H-NMR. signal of $CH_3-C(3)$ of the (*Z*)-isomer appeared at 1.55 ppm. Pure (*E*)-**10** shows the $CH_3-C(3)$ as only one signal at 1.42 ppm.

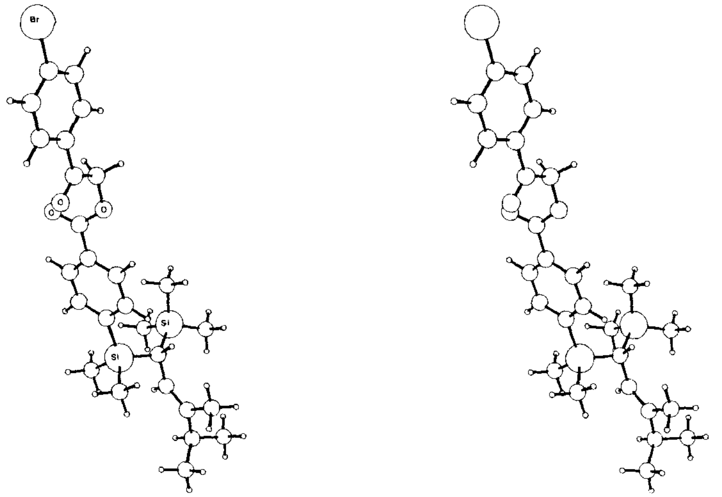

Figure. *Stereoview of molecule* **13**[12]

active 2-methylbutyllithium (99% ee)[9] (THF, −70°) in 95% yield to **11**. GC.-Analysis[10] showed **11** to be a 95:5 mixture of two diastereomers. Diastereoselective formation of **11** being excluded[11] this result proves: a) the enantiomeric excess of **10** (and all preceeding optically active intermediates) is 92%; and b) the disilane/disilylmethane rearrangement **9B** → **10** occurred with a stereoselectivity of at least 92%. The absolute configuration of **10** could not be determined by chemical degradation. Consequently, a crystalline derivative was prepared: **10** was treated with 4-bromophenyllithium [15] (THF, −70° to RT.) to furnish **12** (an oil) in 96% yield; bromide **12** was lithiated with *t*-butyllithium (THF, −70°) [16] and the reaction mixture quenched with solid CO_2 to yield the corresponding acid in 90% crude yield; *p*-bromophenacylester **13** (*p*-bromophenacyl bromide, DBU in benzene, reflux [17]) was obtained in 80% yield and recrystallized from hexane, m.p. 121-122°.

X-ray intensities for **13** were collected on an automated CAD-4 Enraf-Nonius diffractometer with graphite-monochromatized MoK_α radiation. The structure was solved by the *Patterson* method and refined by full-matrix least-squares analysis[13]. Br, Si and methyl C atoms were refined anisotropically, H positions were estimated from stereochemical assumptions; final R-factor 0.094. Intensities of *Friedel* pairs were measured for ϑ between 17° and 21°. When anomalous dispersion corrections for Br and Si were made, all significant *Friedel* differences (14 pairs with $|I_{hkl}-I_{\bar{h}\bar{k}\bar{l}}| > 0.2 \cdot I_{mean}$, $I > 3\sigma_I$) were in agreement with the (*S*)-configuration *(Fig.)*.

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[9] (−)-(*S*)-2-Methylbutanol *(Fluka)* was treated with PBr_3 [12], the bromide $[\alpha]_D = +4.06$ (neat) (99% ee) [13] was lithiated [14] and assumed to have 99% enantiomeric excess.

[10] 40 m glass capillary, *Pluronic* 64 as stationary phase: $t_R = 58.35$ min (95%), $t_R = 59.09$ min (5%).

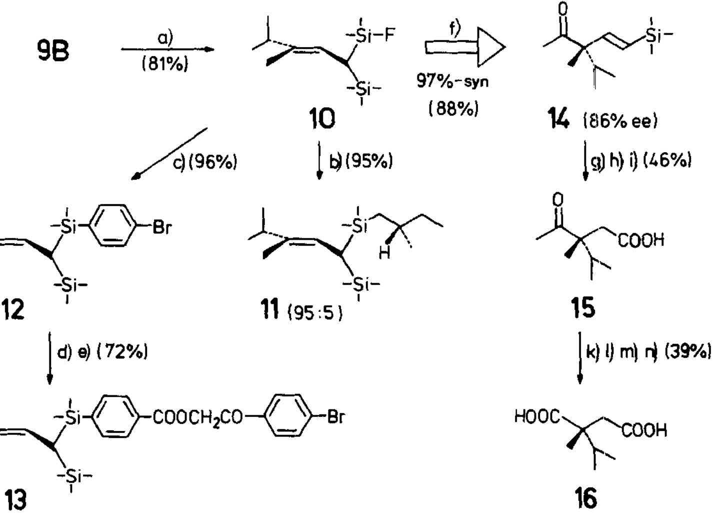
[11] Alkylation of racemic **10** with optically active lithium reagent produced **11** as a 1:1 mixture: $t_R = 58.32$ min (50.3%), $t_R = 59.36$ min (49.7%).

[12] Program PLUTO. *Crystallographic Data Centre*, University Chemical Laboratory, Cambridge, England.

[13] *G. M. Sheldrick.* SHELX 76. Program for Crystal Structure Determination, University of Cambridge, England.

Acylation ($CH_3COCl/AlCl_3$ in CH_2Cl_2, $-70°$) of **10** furnished vinyl silane **14**[14]) in 88% yield. The ^{1}H-NMR. spectrum of **14** in presence of the optically pure shift reagent Eu(tfc)$_3$ showed an enantiomeric excess of at least 86%[15]). This indicates that acylation had occurred with a stereoselectivity of 94%. To establish whether the reaction had proceeded in a *syn* or *anti* fashion, vinyl silane **14** was degraded to ketoacid **15** in 46% yield: desilylation with HI in benzene at RT. [18], $BH_3 \cdot S(CH_3)_2$ in Et_2O at RT. [19], followed by CrO_3-oxidation of the borane intermediate [20]. Ketoacid **15** was esterified (CH_3OH, H_2SO_4, reflux; 90% yield) and converted to the corresponding enol triethylsilyl ether (LDA in THF, $-70°$, then Et_3SiCl; 87% yield). Ozonization in CH_3OH at $-70°$ to the corresponding α-hydroxyketone and cleavage with $Pb(OAc)_4$ in 90% aq. AcOH at 50° [21] furnished the acid **16** in 50% yield, $[\alpha]_D = -10.6°$ ($c = 3.4$ in 95% EtOH). Comparing the sign of the optical rotation of **16** with that of 2-isopropyl-2-methylsuccinic acid of known absolute configuration[16]) establishes (*R*)-configuration of **16** as drawn in *Scheme 3.*

Scheme 3



a) $(CH_3)_3O^+BF_4^-$; b) $CH_3CH_2CH(CH_3)CH_2Li$ (opt. active); c) BrC_6H_4Li; d) *t*-BuLi, then CO_2; e) $BrCH_2COC_6H_4Br$, DBU; f) $CH_3COCl/AlCl_3$; g) HI; h) $BH_3 \cdot S(CH_3)_2$; i) CrO_3; k) CH_3OH/H_2SO_4; l) LDA, then Et_3SiCl; m) O_3; n) $Pb(OAc)_4$.

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[14]) (*E*)-configuration is based on ^{1}H-NMR. evidence: $J = 19$ Hz between the olefinic protons. We thank Prof. *I. Fleming* for personally communicating his findings that (*Z*)-vinylsilanes show ^{1}H-NMR. coupling constants of up to 14 Hz for the olefinic protons.

[15]) Eu(tfc)$_3$ (tfc = 3-(trifluoromethylhydroxymethylene)-*d*-camphorato) shift experiments with racemic **14** revealed shift differences between the *AB*-systems of the olefinic proton signals of 3 and 4 Hz and between the CH_3CO-R signals of 7 Hz. In presence of Eu(tfc)$_3$ optically active **14** showed only a single *AB*-system for the olefinic protons. Because the chemical shift of the CH_3CO-R group is very close to the chemical shift of $H{-}C(CH_3)_2$ up to 7% (peak hight) of the minor enantiomer **14** could be hidden under the septet of the methine proton.

[16]) The rubidium salt of (+)-3,4-dimethyl-3-methoxycarbonylpentanoic acid was determined by X-ray analysis to have (*S*)-configuration [22] and was correlated to the diacid **16** *via* 2-isopropyl-2-methylglutaric acid [23]. $[\alpha]_D$ of (+)-**16** = +19.1° ($c = 1.6$ in EtOH) [24].

The present work shows that disilylalkene **10** is acylated with 94% (97% *syn*/3% *anti*) stereoselectivity to **14**. The influence of stereoelectronic control remains to be shown by varying solvents, electrophiles and silylalkenes. The *syn* S_E' pathway from **10** to **14** assumes that the reactive conformation of the disilyl compound is that shown in **10** *(Scheme 3)*. However, an alternative possibility exists for the production of **14**: this would involve rotation of the disilylmethyl group by 180° with respect to the double bond, then an *anti* S_E' reaction giving the (*Z*)-isomer of **14** and finally isomerization of the olefin (under reaction condition) to **14**. This alternative seems unlikely, considering the stereoselective nature of the substitution of (*Z*)-vinyl silanes with retention of configuration of the double bond [25].

The disilane/disilylmethane rearrangement might turn out to be of synthetic value to prepare tetrasubstituted carbon atoms of known absolute configuration in high enantiomeric excess.

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