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On the stereochemistry of β-elimination of β-silyl azides

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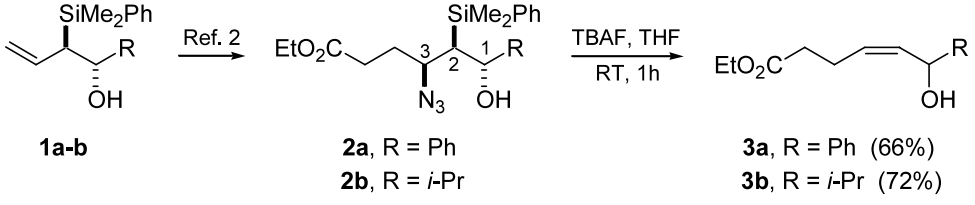
Abstract—Fluoride-mediated elimination of *syn* and *anti* β-silyl azides was shown to afford the corresponding (*Z*)- and (*E*)-olefins, respectively, demonstrating that β-elimination of β-silyl azides is stereospecifically *anti*.

β-Silyl azides are useful intermediates for organic synthesis which have yet received little attention.[1] We recently reported a stereocontrolled carbo-azidation of chiral allylsilanes such as **1a**–**b** which led to the formation of β-silyl azides **2a**–**b** having up to three contiguous stereogenic centers (Scheme 1).[2] While the C1–C2 relative configuration of **2a**–**b** could be assigned without ambiguities, the relation between C2 and C3 centers was found to be more difficult to determine. ^{1}H NMR studies provided no conclusive information regarding this relative configuration and we were unable to produce crystals for X-ray diffraction studies. It was thus decided to convert **2a**–**b**, using a transformation of known stereochemical course, into compounds which structures would be more amenable to simple ^{1}H NMR structure determination. We thus envisioned carrying out a fluoride-ion mediated β-elimination of the silicon and the azido group.[3] It was anticipated, based on the known stereochemistry of β-silyl halide elimination in similar conditions,[4] that this transformation would proceed in an *anti* fashion. Treatment of the major diastereomers **2a**–**b** using tetrabutylammonium fluoride (TBAF) led to (*Z*)-alkenes **3a**–**b**, as a unique stereoisomer, suggesting that β-silyl azides **2a**–**b** had the C2–C3–*syn* relative configuration.[5]

In order to formerly establish the stereochemistry of this reaction,[3] we initiated a study on the fluoride-mediated elimination of β-silyl azides of known relative configuration. We report here our conclusions regarding the stereochemistry of the β-elimination of β-silyl azides.

As mentioned above, there are few efficient methods to prepare configurationally defined β-silylazides.[1] One of the most straightforward methods relies on the electrophilic azidation of β-silylester enolates using trisyl azide (triisopropylsulfonyl azide).[6] As shown by the pioneering studies of Panek, this transformation produce *anti*-β-silyl azides with high stereocontrol.[1a,b,7] β-silylesters **4a** and **4b** were thus prepared through silyl-cupration of the corresponding unsaturated esters,[8] and their enolate (generated using LDA) treated with trisyl azide, eventually leading to β-silyl azides **5a**–**b** in reasonable yield as a unique diastereomer in each case (Scheme 2).



1a-b

2a, R = Ph
2b, R = *i*-Pr

3a, R = Ph (66%)
3b, R = *i*-Pr (72%)

Scheme 1.

Keywords: β-elimination reaction; silicon and compounds; azides.
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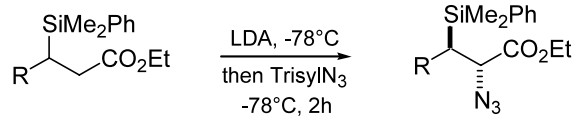
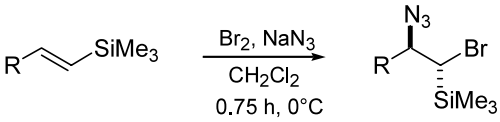


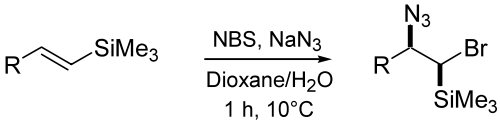
4a, R = Ph — **5a**, R = Ph (64%) *anti/syn* > 98 : < 2

4b, R = Me — **5b**, R = Me (58%) *anti/syn* > 98 : < 2

Scheme 2.



6a, R = Ph — **7a**, R = Ph (58%) *anti/syn* 99 : 1



6a, R = Ph — **8a**, R = Ph (25%) *syn/anti* > 98 : < 2

6b, R = n-C_5H_{11} — **8b**, R = n-C_5H_{11}(53%) *syn/anti* > 98 : < 2

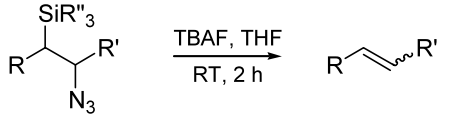
Scheme 3.

In order to obtain unambiguous answer regarding the stereospecificity of the process, it was essential to carry out the β-elimination, independently, on pure *syn* and *anti*-β-silyl azides. As no method was available to access rapidly to the *syn*-isomers of **5a**–**b**, we turned our attention to β-silyl azides such as **7a** and **8a**–**b**, the preparation of which has recently been described and their relative configurations well secured.[9] Addition of BrN_3 onto *E*-vinylsilanes[10] **6a** was thus shown to afford the corresponding *syn* and *anti*-β-silyl azides **7a** and **8a**, depending on the method used to generate BrN_3. Treatment of **6a** using method **A** (Br_2, NaN_3, CH_2Cl_2, HCl) led to the *anti*-isomer **7a** with a 99:1 ratio (GC), while treatment using method **B** (NBS, NaN_3, dioxane–H_2O) produced the *syn*-isomer **8a** with a >98:<2 ratio (^{1}H NMR) (Scheme 3). With non-styrenic substrates, only the *syn*-isomer was produced as shown by the transformation of **6b** into **8b** (method **B**).

The above *anti*- and *syn*-β-silyl azides were then submitted to fluoride-mediated elimination and led to the corresponding olefins **10a**–**e** in high yield and in most cases, in a stereospecific fashion (Scheme 4, Table 1). As most olefins were quite volatile, the isolated yields did not always match those estimated through GC analysis, which therefore provide a more accurate picture about the efficiency of the elimination process.

Our results are summarized in Table 1. Some interesting features emerge from these data. First, configurationally pure *anti*-β-silyl azide **5b** produces exclusively the corresponding (*E*)-olefin **10b** (entry 2), while *syn*-β-silyl azides **8a**–**b** furnished (*Z*)-olefins **10d**–**e** (entries 4–5). As shown in entry 3, starting from a 99:1 *anti*/*syn* isomeric mixture of β-silyl azide **7a** led to the corresponding olefin **10c** with the same ratio. Similarly, a 54/46 mixture of *anti* and *syn*-β-silyl azides **7a** and **8a** led, in the same conditions, to the formation of a 55:45 mixture of (*E*)/(*Z*)-β-bromostyrenes **10c**–**d** (entry 6). These few examples demonstrate that, *syn*- and *anti*-isomers affording (*Z*)- and (*E*)-olefins respectively, *the β-elimination of β-silyl azides is an anti-stereospecific process* (Scheme 5).

However, although all these data point towards an *anti* process, β-elimination of diastereomerically pure *anti*-β-silyl azide **5a** unexpectedly produced a 90:10 *E*/*Z* mixture of the corresponding olefin **10a** (entry 1). This indicates that when the silicon group is located on a benzylic centre, the reaction probably follows a different pathway from that observed for alkyl analogues. Similar observations have been made recently by Porter[3] and earlier on by Fleming on related compounds.[4a] A $E1_{CB}$ mechanism was proposed instead, which may be rationalized by the stabilization of a carbanion thus generated at the benzylic position. Partial configurational inversion of this benzylic anion (R^1 = Ph in **A**, Scheme 5), followed by azide elimination would then overall result in a *syn*-elimination, thus



5a-b
7a
8a-b

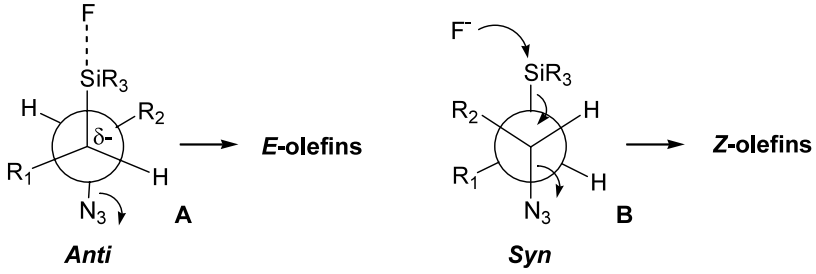
10a-e

Scheme 4.

Table 1. β-Elimination of β-silyl azides (Scheme 4).

Entry	β-Silyl azides	*anti*/*syn*	Olefins	*E*/Z (%)	Yield (%)
1	**5a**	>98:<2[a]	**10a**	90:10[a]	88[c]
2	**5b**	>98:<2[a]	**10b**	>98:<2[a]	64[d]
3	**7a**	99/1[b]	**10c**	98:2[b]	97[d]
4	**8a**	<2:>98[a]	**10d**	<2:>98[b]	95[d]
5	**8b**	<2:>98[a]	**10e**	<2:>98[b]	99[d]
6	**7a**/**8a**	54:46[b]	**10c**/**10d**	55:45[b]	94[d]

[a] Estimated ratio by ^{1}H NMR.
[b] Estimated ratio by GC analysis.
[c] Isolated yield.
[d] Estimated yield by GC analysis.



Scheme 5.

explaining the minor amount of (*Z*)-olefin formed during elimination of **5a**.[11] Such a stabilization is not present with analogue **5b**, and the elimination in this case follows a pure E2 pathway as indicated by the stereospecificity of the process.

In conclusion, except in the particular case of benzylic β-silyl azides (i.e. **5a**), elimination of β-silyl azides induced by fluorine-ion proceeds in an *anti* fashion. The formation of less stable (*Z*)-olefins and the precedent in the literature[3,4] for *anti*-elimination of β-silyl acetates and halides provide a strong support for this *anti*-stereospecificity. This study finally confirms our assumption that β-silyl azides **2a**–**b**, prepared through carbo-azidation of allylsilanes **1a**–**b**, have the *syn*-configuration.[2] This result should be helpful for the unambiguous determination of the relative configuration of β-silyl azides, through simple ^{1}H NMR determination of the geometry of the olefins issued from their β-elimination.

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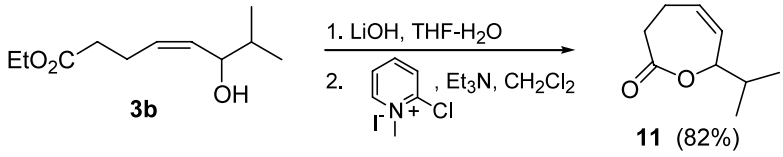
5. The (*Z*)-stereochemistry of olefins **3a**–**b** was determined using NOE experiments and was confirmed by the easy preparation of the seven-membered ring lactone **11** from **3b**.



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