Asymmetric Synthesis of Tertiary and Quaternary Allyl- and Crotylsilanes via the Borylation of Lithiated Carbamates

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ABSTRACT

Tertiary allyl- or crotylsilanes have been prepared in high ee and dr via the lithiation–borylation reaction of alkyl carbamates with silaboronates. Using a related strategy, quaternary allylsilanes could be accessed in similarly high ee.

Allylsilanes are highly versatile synthetic intermediates which have been used extensively in complex molecule synthesis.1 As such, methods to generate allylsilanes in high enantiomeric and diastereomeric purity have attracted widespread attention from the synthetic community.2–8 Methods for the preparation of tertiary allylsilanes have included Cu-catalyzed allylic alkylation2,3 and carbonyl allylation.4 Methods for the preparation of the more challenging quaternary allylsilanes have included the hydroboration5 or hydrozirconation6 of allenylsilanes followed by addition to aldehydes or imines, Claisen rearrangement of vinyl silanes,7 Cu-catalyzed asymmetric allylic alkylation,2 and enantioselective allylic substitution.8

While many of these methods provide efficient pathways to specific allylsilanes, general strategies to allylsilanes in high ee and dr, particularly in the case of crotylsilanes, remain underdeveloped.


Herein, we report two general strategies for the efficient preparation of both tertiary and quaternary allylsilanes in high er and dr using our lithiation—borylation method coupled with Zweifel olefination of the derived boronate esters.9,10

We previously reported that enantioenriched lithiated alkyl carbanates could react with boranes and boronate esters to give their homologated counterparts in high er.11 This reaction could even be applied to β-silyl vinylboranes, which led to an asymmetric synthesis of β-hydroxy allylsilanes.11,12 Initial studies (Scheme 1) aimed to extend this approach to the synthesis of allylsilanes from α-silyl carbamate 1, however, proved unrewarding, because the intermediate silyl-substituted lithiated carbamate 2 was configurationally unstable and led to racemic allylsilane 4.12

We therefore considered an alternative approach: the reaction of a configurationally stable, alkyl-substituted lithiated carbamate 6 with silaborane 7. This was expected to give an intermediate ate-complex 8, which would subsequently undergo 1,2-metalate rearrangement, involving migration of the silyl group with expulsion of the nucleofugal carbamate group, to furnish the 1,1-silaboronate 9. While the migration of a carbon substituent is relatively common, there are only sporadic examples of the migration of a silyl group.15 Nevertheless, this strategy ultimately proved to be successful (Scheme 2). Lithiation of carbanates 5, followed by the addition of the commercially available boronate 7 and warming gave silaboronates 9a and 9b in 69% and 68% yield, respectively.

Conditions for the Zweifel olefination10 had to be modified to obtain good yields due to the sensitive nature of the allylsilane product toward excess I2. In fact, we found that I2/MeOH was superior to the more commonly employed conditions of I2/NaOMe/Methanol. As illustrated by the data summarized in Table 1, subsequent reaction of boronate esters 9 with the alkenylmetal reagents 10a at −78 °C, followed by the addition of iodine in methanol, gave allylsilanes 11 in excellent er (97:3 to 94:6) and good to excellent yield (60–94%). Moreover, the dr was essentially perfect for entries 2, 3, and 6, giving the respective crotylsilanes as single diastereomers by 1H NMR spectroscopy (dr > 25:1). Only in the case of the highly hindered Z-crotylsilane 11e (entry 5) was the E-diastereomer visible by NMR (85:15 dr in the crude material and 95:5 dr in the isolated product). In this case, the minor E-isomer presumably arises from the severe steric encumbrance of the conformation required for anti-elimination (leading to the Z-configuration) and so some syn-elimination occurs which leads to the small amount of the E-isomer observed (Scheme 3).17

It should be noted that, in the case of boronate ester 9a (R = PhCH2CH2), vinylmagnesium bromide was sufficiently nucleophilic to effect ate-complex formation but, for the more hindered boronate ester 9b (R = iPr), the more reactive vinylolithium was required. Propenyllithium compounds were used due to their ease of preparation from the respective propenyl bromides by halogen—metal exchange.16


(12) Our attempts to effect the lithiation—borylation reaction, shown in Scheme 1, only gave racemic allylsilane 4 (R = Ph) even when the reaction was conducted at −100 °C. The configurational instability of silyl-substituted lithiated carbanates has been noted before: (a) Simov, B. P.; Rohn, A.; Brecker, L.; Giester, G.; Hammerschmidt, F. Synthesis 2004, 26704–2710. (b) Schweifer, A.; Hammerschmidt, F. Tetrahedron 2008, 64, 7605–7610.


(14) Suginome, M.; Matsuda, T.; Ito, Y. Organometallics 2000, 19, 4647–4649. In addition to it being commercially available (and easy to make according to the Suginome procedure), the UV chromophore present makes it especially useful in determining er and therefore better than the Me3Si analogue.


Scheme 1. Proposed Synthesis of Tertiary Allylsilanes

Scheme 2. Silaboration of Lithiated Carbamates 6
We were especially interested to see if we could extend this method to the significantly more challenging quaternary allylsilanes. To achieve this, we returned to the strategy described in Scheme 1 since we recognized that secondary silyl-substituted lithiated carbamates were configurationalally stable at low temperature.\(^{18}\) Our sequence commenced with lithiation and silylation of carbamate 5\(\text{a}\) as previously described (Table 2).\(^{18}\) Subsequent deprotonation with \(\text{sBuLi/TMEDA}\) followed by the addition of a boronate ester gave intermediates 18 with a unique 1,1-silaboronate quaternary stereogenic center. These intermediates could be either isolated in excellent yield (88–94\% yield) or subjected to the next transformation in situ without prior workup. Brief optimization of the stoichiometry of the reagents, temperature, and time provided a set of conditions under which allylsilanes 19 were obtained in 62–75\% yield and very high \(\text{er} (97:3–98:2)\) from carbamates 14 in one pot over two steps.

Several points are worthy of note. (i) The one-pot reaction gave a slightly higher yield compared to the two-step procedure. (ii) The corresponding \(\text{iPr}\) substituted substrate was sterically too hindered for deprotonation with \(\text{sBuLi}\) under these conditions. (iii) For substrates 18, the more reactive vinyl lithium had to be used and the

Table 1. Olefination of Silaboronates 9\(^a\)

<table>
<thead>
<tr>
<th>R (9a,9b)</th>
<th>reagent (10)</th>
<th>product (11a-f)</th>
<th>yield (%)</th>
<th>(\text{er}^{c})</th>
<th>(\text{dr}^{f})</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Ph(CH(_2))(_2)</td>
<td>MgBr</td>
<td>10</td>
<td>81</td>
<td>97:3</td>
<td></td>
</tr>
<tr>
<td>2 Ph(CH(_2))(_2)</td>
<td>U</td>
<td>84</td>
<td>97:3</td>
<td>&gt;25:1</td>
<td></td>
</tr>
<tr>
<td>3 Ph(CH(_2))(_2)</td>
<td>U</td>
<td>94</td>
<td>97:3</td>
<td>&gt;25:1</td>
<td></td>
</tr>
<tr>
<td>4 (\text{iPr})</td>
<td></td>
<td>60</td>
<td>96:4</td>
<td>85:15</td>
<td></td>
</tr>
<tr>
<td>5 (\text{iPr})</td>
<td></td>
<td>80</td>
<td>96:4</td>
<td>95:5</td>
<td></td>
</tr>
<tr>
<td>6 (\text{iPr})</td>
<td></td>
<td>80</td>
<td>96:4</td>
<td>&gt;25:1</td>
<td></td>
</tr>
</tbody>
</table>

\(^{a}\) Reactions were performed on 0.2–1.0 mmol scales. Boronate ester (1 equiv), alkenylmetal reagent (4 equiv), and methanolic I\(_2\) (4 equiv), THF, –78 to \(0^\circ\)C. \(^{b}\) The alkenyllithium reagents were prepared from the respective alkenyl bromides using 2 equiv of \(\text{sBuLi}\) (see Supporting Information). \(^{\text{c}}\) Yield of the isolated product. \(^{d}\) The \(\text{er}\) was determined by analysis of 400 MHz \(^1\)H NMR spectra of the crude products. \(^{e}\) Absolute stereochemistry was assigned after comparison with the literature. \(^{f}\) All other assignments were made by analogy. \(^{g}\) The \(\text{dr}\) was determined after column chromatography.

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temperature raised to 0 °C for efficient ate-complex formation. The vinyl Grignard reagent only gave low conversions. (iv) Reaction of 18 with propenyllithium reagents led to incomplete formation of the ate-complex, presumably due to the severe steric bulk of these 1,1-silaboronates. (v) The absolute stereochemistry was determined by X-ray analysis of the alcohol obtained by hydroboration/oxidation of allylsilane 19b (see Figure 1 and Supporting Information). (vi) This process could be extended to the phenyldimethylsilyl group, enabling the incorporation of a further synthetic handle.

One advantage of this approach is that either enantiomer of the intermediate boronate ester or the product allylsilane can be obtained simply by switching the groups on the carbamate and the boronate ester, thus obviating the need to use the (+)-sparteine surrogate.20 ent-19c was synthesized starting from ethyl diisopropyl carbamate 20 (Scheme 4). Deprotonation using sBuLi/(−)-sparteine followed by addition of phenyldimethylsilyl chloride gave organosilane 21. Subsequent lithiation using sBuLi/TMEDA followed by the addition of boronate ester 22a gave, after 1,2-metalate rearrangement, the intermediate boronate ester ent-18c in excellent yield. Olefination with vinyl lithium and methanolic iodine gave allylsilane ent-19c in 80% yield and 97:3 er.

The scope of the reaction was further exemplified in the synthesis of allylsilane 24, bearing the ubiquitous prenyl group, using the commercially available boronate ester 22b; excellent yields and er were observed throughout.

In summary, we have developed a simple method for the synthesis of tertiary allyl- or crotylsilanes in high er and dr using the lithiation—borylation reaction of alkyl carbamates with silaboronates. Using a related strategy, we have developed a unique reaction sequence that leads to quaternary allylsilanes in similarly high er.

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Supporting Information Available. Experimental procedures and full spectroscopic data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.