



Free radical addition to branched allylsilanes: stereoselective formation and elimination of β bromosilanes

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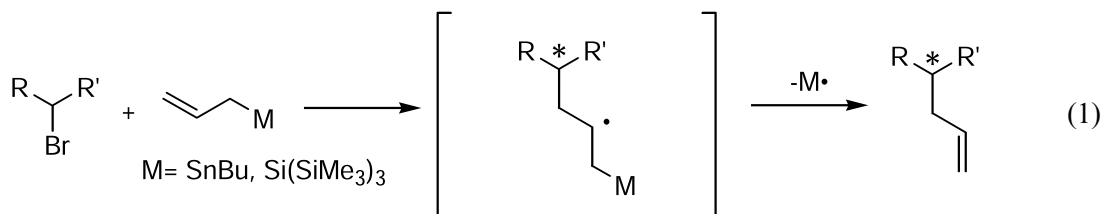
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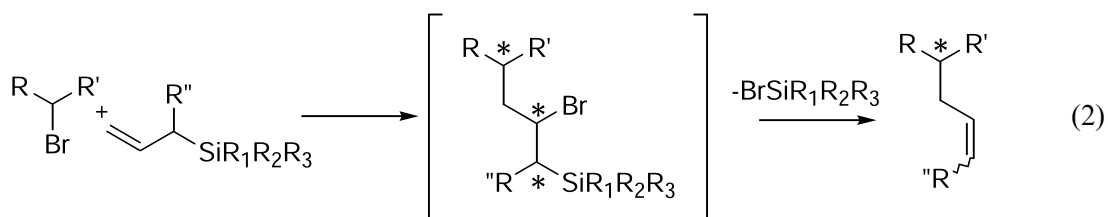
Abstract

Lewis acid-promoted free radical addition to 3-silyl-1-butenes occurs in good yield to give predominantly the *cis*-substituted alkene. The transfer reaction occurs by atom-transfer addition of the alkyl bromide precursor, an addition that occurs by Felkin–Anh control. Stereoselective *anti* elimination of the intermediate β -silylhalide gives the *cis* olefin. © 2000 Published by Elsevier Science Ltd.

Free radical reactions have received renewed interest because of recent demonstrations that control of the stereochemistry in these transformations is possible. Diastereoselective reactions involving substrate or chiral auxiliary-controlled processes are now well understood¹ and examples of enantioselective processes have also been reported.² The reaction of prostereogenic radicals with allylstannane radical traps has been a common transformation in which control of stereochemistry is at issue (Eqs. (1) and (2)). Trimethylallylsilanes and tris-trimethylsilylallylsilanes have also been investigated in radical reactions, some of which involve achiral Lewis acid-controlled transformations.³ Lewis acids can be used to control the facial bias in reactions of bidentate radicals and diastereoselectivity can be enhanced or even reversed by selection of an appropriate Lewis acid.⁴

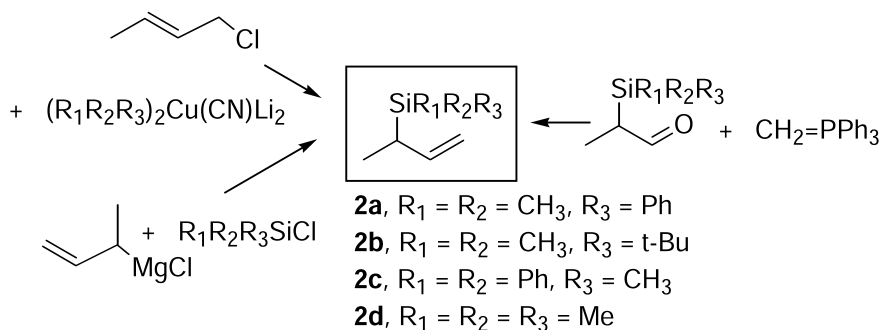


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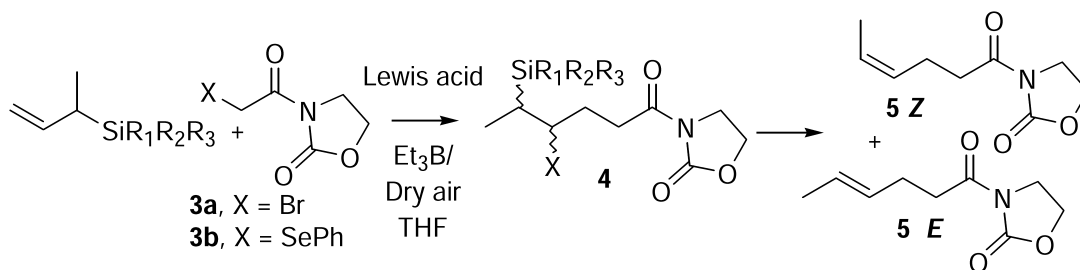
The atom transfer sequence with simple allylsilanes proceeds through an unstable β -bromosilane intermediate that then undergoes a non-radical elimination of bromosilane to give the alkene product. When $R' = H$, the resultant product is formally the same as in allyl transfer. A more interesting case for an atom transfer reaction is when R' is an alkyl group. Then, not only is a new stereogenic center created at the α -center, but also the alkene stereochemistry is at issue. In this report, we explore the diastereoselectivity of the alkene products formed in atom transfer reactions with branched allylsilanes.

Several methods for branched allylsilane synthesis were explored. The allyl Grignard method gave **2d** contaminated with 2–8% of the corresponding crotyl silane, an allylic transposition isomer, while the Wittig method provided only **2b**,⁵ therefore it was the preferred method for the preparation of this silane (Scheme 1). The higher order silylcuprate⁶ reacted in an S_N2' fashion with crotyl chloride to give **2a** and **2c** according to literature precedent.



Scheme 1.

The α bromoimide **3a** reacts with branched allylsilanes⁷ in a Lewis acid promoted transformation to give a mixture of alkenes, **5Z** and **5E** (Scheme 2).⁸ The reaction does not proceed without Lewis acid and the product distribution, yield, and reaction rate are highly solvent, temperature



Scheme 2.

and Lewis acid dependent, see Table 1. In general, the best yields and selectivities were observed for reactions carried out in THF with $\text{Yb}(\text{OTf})_3$ catalyst.⁹ The major product formed in every example studied was the *Z* alkene. The selectivities for formation of this less stable diastereomer were as high as 94:6.

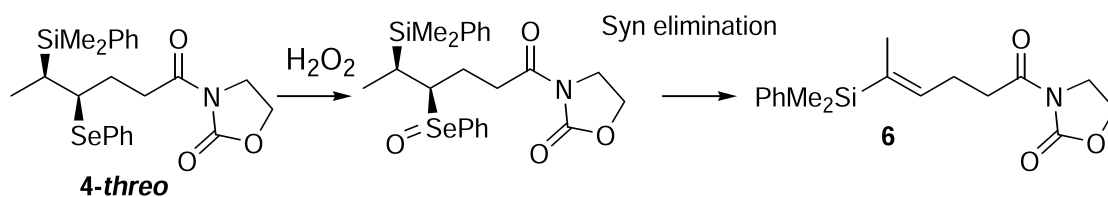
Table 1
Lewis acid-promoted atom transfer

entry	substrate	allylsilane	Lewis acid	Temperature	<i>Z</i> : <i>E</i> ratio	Yield(%)
1	3a	2a	$\text{Yb}(\text{OTf})_3$	0°C	65:35	82
2	3b	2a	$\text{Yb}(\text{OTf})_3$	0°C	92:8	45
3	3a	2a	$\text{Yb}(\text{OTf})_3$	-45°C	84 : 16	83
4	3a	2a	$\text{Yb}(\text{OTf})_3$	-78°C	91 : 9	81
5	3a	2a	$\text{Zn}(\text{OTf})_2$	-78°C	60 : 40	32
6	3a	2a	$\text{Sc}(\text{OTf})_3$	-78°C	56 : 44	21
7	3a	2b	$\text{Yb}(\text{OTf})_3$	-78°C	94 : 6	72
8	3a	2c	$\text{Yb}(\text{OTf})_3$	-78°C	94 : 6	75
9	3a	2d	$\text{Yb}(\text{OTf})_3$	-78°C	88 : 12	>95

The phenyl selenide **3b** gives products with higher selectivities than the bromide at room temperature does, but reaction of this substrate does not proceed at lower temperatures. Selectivity appears to be somewhat higher for bulkier silanes than for the smaller TMS derivative, but the allyl-TMS derivative, **2d**, is more reactive than the other silanes with nearly quantitative yields being obtained with short reaction times and small amounts of initiator.

Reaction of phenylselenide **3b** with silane **2a** provided an isolable intermediate **4**, that was a 9:1 mixture of two diastereomers.¹⁰ The *threo* and *erythro* isomers of **4** can be separated successfully by flash column chromatography on deactivated silica gel.¹¹ The major isomer was then subjected to oxidation by hydrogen peroxide at 0°C to give alkene **6** as the only isomer.

NOE difference experiments proved the configuration of the alkene **6** to be *E*. Assuming a *syn* elimination of selenol, the configuration of the major stereoisomer of **4** is thus *threo* (Scheme 3). A *threo* product suggests a Felkin–Anh transition state for the atom transfer reaction, consistent



Scheme 3.

with results obtained for analogous radical transformations.¹² Chromatography of *threo* **4** on silica gives only the *Z* stereoisomer of **5**, suggesting an *anti* elimination of X-SiR₃¹³ (Fig. 1).

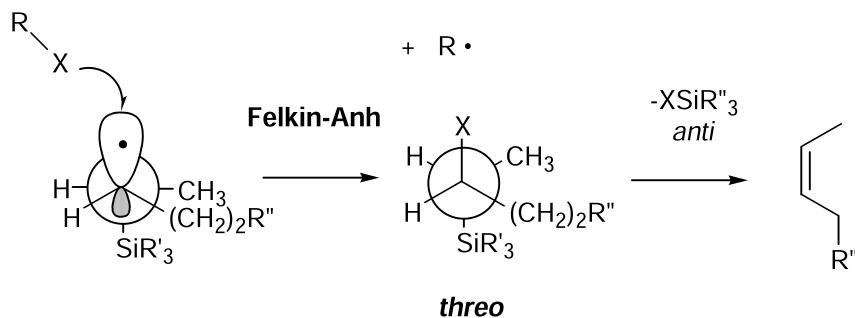


Figure 1. Stereochemistry of atom transfer and elimination

The use of branched allylsilanes expands the scope of diastereoselective atom transfer reactions. The transformation resembles the Peterson olefination but avoids the use of strongly basic conditions, providing *Z* alkenes under relatively mild reaction conditions. The scope and limitations of this reaction are currently under investigation.

Acknowledgements

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- The allylic (crotyl) isomer is formed in less than 2% by the use of the Wittig methodology.
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- In those cases where the starting allylsilane was contaminated with the allylic isomer, the crotyl silane reacted much more slowly than **2** did. Use of excess silane gave products containing insignificant amounts of the allylic isomer of **5**.
- The configuration of the product alkenes was determined by ¹H and ¹³C NMR and by accurate mass determination and independent synthesis (HRMS, calculated 183.0810; measured 183.0819). The *cis*- and *trans*-isomers were separated by chromatography on silver ion impregnated silica gel. The *cis*-isomer was later eluting. The vinylic vicinal proton–proton coupling constant for the *cis*-isomer was substantially less than that of the *trans*-isomer. The vinylic and allylic carbons displayed an upfield shift in the ¹³C spectrum from that of the *trans*-isomer.
- In a typical reaction, bromide **3a** (50 mg, 0.24 mmol) and Yb(OTf)₃ (164 mg, 0.26 mmol) were stirred in 12 mL of THF at rt for 1 h. The solution was cooled to –78°C and silane (1.2 mmol) was added via syringe. Dry air was blown on the surface of the solution continuously. BEt₃ (1.0 M, 0.24 mmol) was added 2 min later and the reaction stirred for 20 min. This was repeated until no starting bromide **3a** could be detected by GC. For the

- reactive silane **2d**, the reaction was complete in 5 min. The solution was quenched with 3 mL water and the mixture was then extracted with methylene chloride, and dried over MgSO₄. The products were purified by flash column chromatography on silica gel (85:15 hexanes:EtOAc) to give the products as a mixture of *cis:trans* alkenes.
- The two isomers can be distinguished by signals in the ¹H NMR due to the (-SiMe₂Ph) methyl protons at δ (CDCl₃) = major 0.29 (3H, s), 0.32 (3H, s) and minor 0.35 (3H, s), 0.42 (3H, s); (-CH₃) protons at major 1.10 (3H, d, *J* = 7.5 Hz) and minor 1.13 (3H, d, *J* = 7.4 Hz); (-CH(CH₃)SiMe₂Ph) methine proton at major 1.52 (1H, dq, *J*₁ = 2.4 Hz, *J*₂ = 7.5 Hz) and minor 1.48 (1H, dq, *J*₁ = 4.3 Hz, *J*₂ = 7.4 Hz); (-CH₂-CH(SePh)-) methylene protons at major 1.72–1.91 (2H, m) and minor 1.95–2.04 (1H, m), 2.13–2.22 (1H, m); (-CH₂CO-) methylene protons at major 3.00–3.15 (2H, m) and minor 2.71–2.79 (1H, m), 2.98–3.06 (1H, m); (-CHSePh) methine proton at major 3.6 (dt, *J*₁ = 11.6 Hz, *J*₂ = 2.6 Hz) and minor 3.3 (dt, *J*₁ = 4.3 Hz, *J*₂ = 7.2 Hz).
 - The phenylselenide product **4b** is converted to the alkene **5** on silica that has not been deactivated.
 - See, for example: Giese, B.; Damm, W.; Dickhaut, J.; Wetterich, F.; Sun, S.; Curran, D. P. *Tetrahedron Lett.* **1991**, 32, 6097.
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