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Intramolecular radical hydrosilylation — the first radical 5-*endo-dig* cyclisation†

Stephan Amrein and Armido Studer*
Fachbereich Chemie der Universität Marburg, Hans-Meerwein-Strasse, 35032 Marburg, Germany.
E-mail: studer@mailer.uni-marburg.de; Fax: +49 6421 2825629; Tel: +49 6421 2825629

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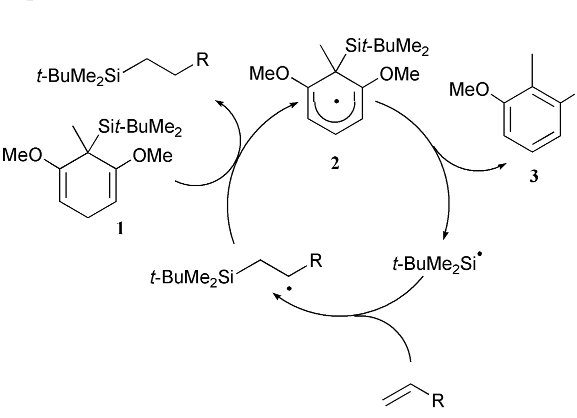
Intramolecular radical hydrosilylations using allyloxy- and propargyloxycyclohexadienylsilanes comprising 5-*endo-trig* as well as 5-*endo-dig* processes are presented.

Intramolecular hydrosilylation of allyloxy- or allenyloxysilanes using transition-metal catalysis is well established.[1] However, there are only scant reports in the literature on the intramolecular hydrosilylation of alkenyloxysilyl radicals. Roberts applied the concept of polarity reversal catalysis to transform alkenyloxysilanes into the corresponding cyclic alkoxysilanes.[2] Clive demonstrated that alkenyloxysilyl radicals can be generated from the corresponding vinyl radicals by 1,5-H-abstraction which undergo subsequent 5-*endo*-type radical cyclisation to afford after reduction cyclic alkoxysilanes.[3] Cyclic alkoxysilanes are very useful intermediates, since they can be readily converted to the corresponding diols by Tamao–Fleming oxidation.[4]

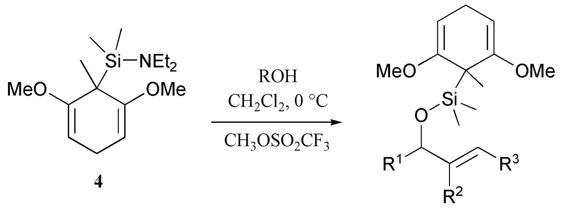
Recently, we presented the first results on the radical hydrosilylation using silylated cyclohexadienes of type **1**.[5] The bisvinylic methylene group acts as the hydrogen donor in these chain reactions.[6,7] Thus, H-transfer leads to a cyclohexadienyl radical **2**, which subsequently rearomatizes to provide the *tert*-butyldimethylsilyl radical and arene **3** (Scheme 1). Silyl radical addition onto the alkene leads to a β-silylalkyl radical, which upon reduction with **1** eventually affords the hydrosilylated alkene and the chain carrying radical **2**.

We conceived that our method can also be applied to intramolecular radical hydrosilylation reactions. To this end, the silylated cyclohexadiene has to be covalently bound to the olefin. As silylation reagent, we chose the amino silane **4**. Silylated cyclohexadiene **4** is readily prepared on a large scale and can be stored for months (see ESI†).

We first tested the silylation of allyl alcohol under different conditions. The aminosilane **4** was readily transformed to the corresponding chlorosilane upon treatment with acetyl chloride in CH_2Cl_2 at −78 °C.[8] However, it was difficult to isolate the chlorosilane. We therefore decided to remove the solvent at low temperature and to use the chlorosilane without further purification. Silylation of allyl alcohol with the crude chlorosilane in DMF using imidazole as a base at 0 °C afforded the silyl ether **5** in 37% yield. *N*-Methylation of the aminosilane with MeI in toluene at 80 °C[9] and subsequent addition of allyl alcohol gave the desired silyl ether **5** with a slightly better yield (41%). Methylation with methyl triflate at −5 °C in CH_2Cl_2 (30 min) and addition of allyl alcohol provided **5** in 45% yield. The best result was obtained upon addition of the methyl triflate to a solution of the allyl alcohol and the amino silane in CH_2Cl_2 at 0 °C. The silyl ether **5** was isolated in 70% yield. The silyl ethers **6** (53%), **7** (64%) and **8** (32%) were prepared in analogy (Scheme 2).



Scheme 1 Intermolecular radical hydrosilylation using Si-reagent **1**.

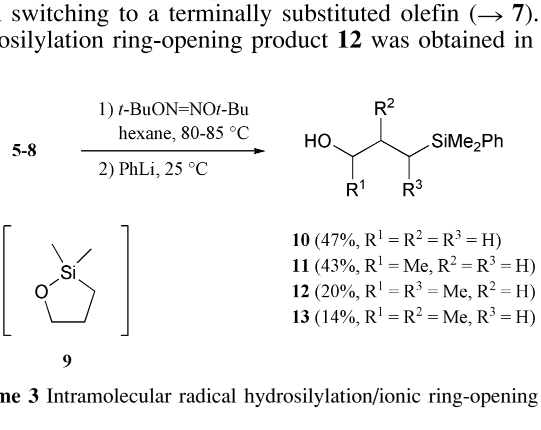


5 (70%, $R^1 = R^2 = R^3 = H$)
6 (53%, $R^1 = Me$, $R^2 = R^3 = H$)
7 (64%, $R^1 = R^3 = Me$, $R^2 = H$)
8 (32%, $R^1 = R^2 = Me$, $R^3 = H$)

Scheme 2 Preparation of the silyl ethers **5–8**.

Silyl radicals are known to undergo 5-*endo-trig* cyclisations.[2,3,10,11] As expected, the intramolecular hydrosilylation of silyl ether **5** in hexane using di-*tert*-butyl hyponitrite[12] as initiator (0.3 equiv.) in hexane at 80–85 °C (sealed tube, 0.25 M) afforded the desired 5-*endo* cyclisation product **9**. AIBN was not suitable as initiator in the intramolecular hydrosilylation. It turned out that alkoxysilane **9** is prone towards hydrolysis and is difficult to isolate. We therefore treated the crude reaction mixture with an excess of phenyllithium (PhLi) to provide alcohol **10** which was isolated in 47% overall yield (Scheme 3). All the following intramolecular hydrosilylations were conducted in analogy.

The secondary alcohol **11** was obtained in 43% yield starting from silyl ether **6**. A sharp decrease of the yield was observed upon switching to a terminally substituted olefin (→ **7**). The hydrosilylation ring-opening product **12** was obtained in 20%



10 (47%, $R^1 = R^2 = R^3 = H$)
11 (43%, $R^1 = Me$, $R^2 = R^3 = H$)
12 (20%, $R^1 = R^3 = Me$, $R^2 = H$)
13 (14%, $R^1 = R^2 = Me$, $R^3 = H$)

Scheme 3 Intramolecular radical hydrosilylation/ionic ring-opening reactions.

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† Electronic supplementary information (ESI) available: experimental data. See http://www.rsc.org/suppdata/cc/b2/b204879e/

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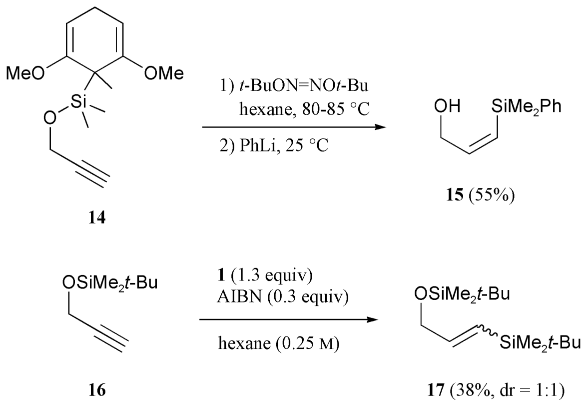
yield as a 2:1 mixture of diastereoisomers.‡ The silyl radical addition is probably rather slow for this cyclisation. The hydrosilylation was even worse with silyl ether **8** (→ **13**, 14% yield, dr = 1:1). We assume that the reduction of the hindered tertiary radical is not efficient with the silylated cyclohexadiene **8**. Surprisingly, no selectivity was observed for the reduction of the tertiary radical formed after the cyclisation of the silyl radical derived from **8** (1,2-induction).

Finally, we studied the intramolecular cyclisation using silylated propargyl alcohol **14**, which was prepared in 50% yield starting from propargyl alcohol. We were very pleased to observe that the intramolecular 5-*endo-dig* process could be accomplished (Scheme 4). Intramolecular hydrosilylation followed by ionic ring-opening provided alcohol **15** in 55% yield as a diastereoisomerically pure compound with (*Z*)-configuration. To the best of our knowledge this is the *first report* of a radical 5-*endo-dig* process. To exclude the possibility that product **15** was formed *via* an intermolecular process, we performed the intermolecular hydrosilylation of TBDMS-protected alcohol **16** using reagent **1** (AIBN (0.3 equiv.), hexane (0.25 M), 80–85 °C). For an intermolecular radical addition to an alkyl substituted alkyne low selectivity has to be expected.§ Indeed, the hydrosilylation of alkyne **16** provided vinyl silane **17** as a 1:1 mixture of diastereoisomers (38%). This clearly proves that the vinyl silane **15** must have been formed *via* an intramolecular radical reaction.



Scheme 4 First radical 5-*endo-dig* reaction.

In conclusion, we present a new method for the intramolecular radical hydrosilylation. Furthermore, we have discovered the first example of a radical 5-*endo-dig* cyclisation reaction.

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Notes and references

‡ The relative configuration of the major isomer was not assigned.

§ Alkyl substituted (non-conjugated) vinyl radicals are sp^2-hybridized and they invert with a very low barrier. The ratio of products formed depend on the equilibrium constant of the two interconverting vinyl radicals and on the rate constant of the reduction. In general low selectivities are obtained for the reduction of these σ-type vinyl radicals.[13]

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