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Radical Transfer Hydrosilylation/ Cyclization Using Silylated Cyclohexadienes

Stephan Amrein, Andreas Timmermann, and Armido Studer*

Fachbereich Chemie der Universität Marburg, Hans-Meerwein-Strasse, D-35032 Marburg

studer@mailer.uni-marburg.de

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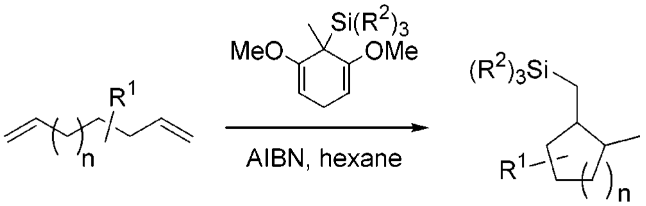
ABSTRACT



A new method for mild metal-free hydrosilylation is described. Silylated cyclohexadienes are used as radical transfer hydrosilylating reagents for various double and triple bonds. A trialkylsilane is transferred from a cyclohexadiene moiety to an alkene. The hydrosilylation can be combined with a C–C bond formation as shown for the preparation of silylated cycloalkanes from the corresponding dienes.

The hydrosilylation/cyclization reaction of dienes is a well-known process. These reactions are generally conducted using transition metals as catalysts. Cationic palladium complexes have been successfully used to catalyze these transformations.[1] Furthermore, neodynium[2] and more importantly yttrium[3] metallocene complexes catalyze these hydrosilylation/cyclization reactions.

From an ecological point of view, it would be highly desirable to conduct these reactions without using transition metals. However, there are only a few reports on *metal-free* hydrosilylation reactions. In general, radical hydrosilylation of alkenes cannot be conducted using trialkylsilanes. This is due to the rather strong Si−H bond in the trialkylsilanes.[4] The alkyl radical formed after initial silyl radical addition onto the alkene is not reduced with a trialkylsilane. Modified silanes, such as tris(trimethylsilyl)silane, have been successfully used in radical hydrosilylations.[5] In addition, Roberts presented some examples using the concept of polarity reversal catalysis.[6]

Recently, we introduced silylated cyclohexadienes as new tin-free radical reducing reagents.[7] Various typical radical reactions, such as dehalogenations, deselanations, deoxygenations, and intermolecular additions, were performed using these new reagents. The cyclohexadiene CH_2 moiety acts as the H-donor in these radical chain reactions. Reduction of radical R^2 with **1** affords cyclohexadienyl radical **2**. Rearomatization of **2** then provides the corresponding silyl radical, which is able to propagate the chain by reaction with the starting halide, xanthate, or phenylselanide R^2-X (Scheme 1). As byproduct, methylated resorcin diether **3** is formed. We conceived that the silylated cylohexadienes can also be used as radical hydrosilylating reagents: If the silyl radical formed in the rearomatization of **2** is allowed to react with an alkene, β-silyl radical **4** will be generated. Reduction of **4** with the cyclohexadiene **1** would then afford **2** and the

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[1] Widenhoefer, R. A.; DeCarli, M. A. *J. Am. Chem. Soc.* **1998**, *120*, 3805. Stengone, C. N.; Widenhoefer, R. A. *Tetrahedron Lett.* **1999**, *40*, 1451. Perch, N. S.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **1999**, *121*, 6960. Pei, T.; Widehoefer, R. A. *Org. Lett.* **2000**, *2*, 1469. Perch, N. S.; Pei, T.; Widenhoefer, R. A. *J. Org. Chem.* **2000**, *65*, 3836. Wang, X.; Chakrapani, H.; Stengone, C. N.; Widenhoefer, R. A. *J. Org. Chem.* **2001**, *66*, 1755.

[2] Onozawa, S.; Sakakura, T.; Tanaka, M. *Tetrahedron Lett.* **1994**, *35*, 8177.

[3] Molander, G. A. *Chemtracts* **1998**, *11*, 237 and references therein. Molander, G. A.; Dowdy, E. D. In *Topics in Organometallic Chemistry*; Kobayashi, S., Ed.; Springer-Verlag: New York, 1999; Vol. 2, pp 120−154.

[4] Chatgilialoglu, C. *Chem. Rev.* **1995**, *95*, 1229.

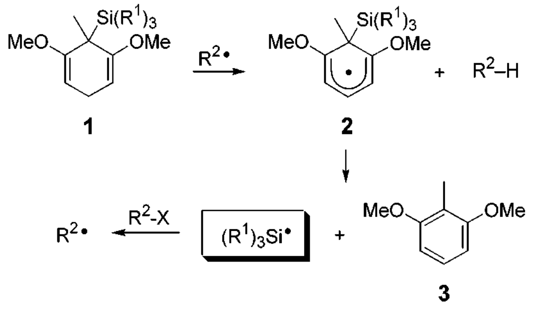
[5] Chatgilialoglu, C. *Acc. Chem. Res.* **1992**, *25*, 188.

[6] Roberts, B. P. *Chem. Soc. Rev.* **1999**, *28*, 25.

[7] Studer, A.; Amrein, S. *Angew. Chem., Int. Ed.* **2000**, *39*, 3080.

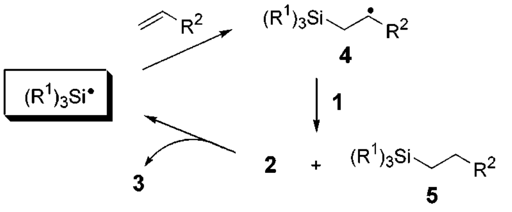
10.1021/ol016160c CCC: $20.00

Scheme 1. Silylated Cylohexadienes as Radical Reducing Reagents



hydrosilylation product **5**. Radical **2** will eventually fragment a silyl radical, thereby propagating the chain (Scheme 2).

Scheme 2. Silylated Cylohexadienes as Radical Hydrosilylating Reagents



This hydrosilylation of the alkene can formally be regarded as a *transfer-hydrosilylation*, since reagent **1** is transformed to the corresponding arene in a reverse hydrosilylation process. The driving force of this *transfer-hydrosilylation* is the resonance energy of the arene. Herein, we report the first applications of the silylated cyclohexadienes in metal-free hydrosilylation reactions.

The synthesis of cyclohexadiene **6** has previously been described.[7] The dimethylphenyl silyl derivative **7**, the triisopropyl compound **8**, and cyclohexadiene **9** were prepared in analogy (Figure 1).

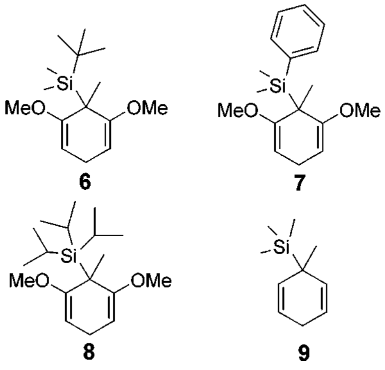
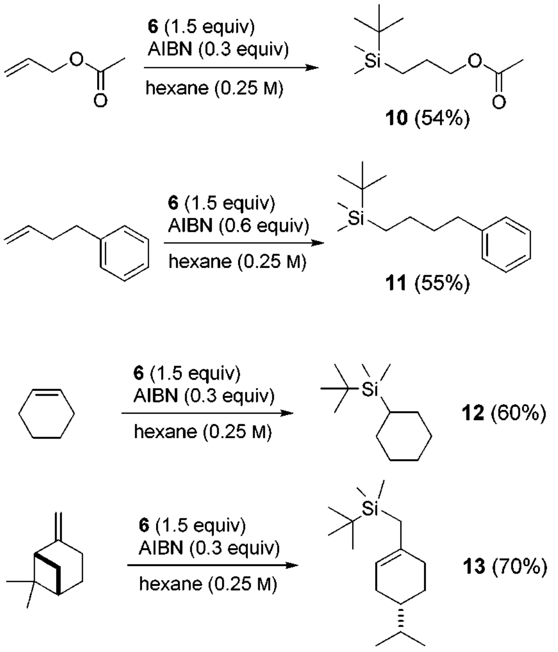


Figure 1. Silylated cyclohexadienes **6**−**9**.

Hydrosilylation of allyl acetate could easily be conducted with reagent **6** in hexane at 80−85 °C (sealed tube) using α,α′-azoisobutyronitrile (AIBN) as initiator. Best results were obtained with 1.5 equiv of the silylated cyclohexadiene and 0.3 equiv of AIBN. Under these conditions, the hydrosilylation product **10** was isolated in 54% yield (Scheme 3).

Scheme 3. Hydosilylation of Various Double Bonds with Reagent **6**



Hydrosilylation of 4-phenyl-1-butene worked equally well and **11** was isolated in 55% yield. Terminal substituted double bonds can also be hydrosilylated, as shown for the reaction of cyclohexene with **6** to form tetraalkylsilane **12** (60%). Hydrosilylation of *β*-pinene afforded the ring-opened cyclohexene derivative **13** in 70% yield. The initially formed *β*-silyl radical undergoes fast ring opening to form a tertiary radical, which is subsequently reduced with reagent **6** to provide compound **13**.

We next studied the hydrosilylation of various dienes which are easily prepared as described in the Supporting Informations. In these reactions the initially formed *β*-silyl radical undergoes a 5-*exo* radical cyclization to afford the corresponding primary radical, which after reduction provides a silylated cycloalkane. Treatment of diene **14** with reagent **6** provided the hydrosilylation/cyclization product **19** in 80% yield as a 4.3:1 (*cis*:*trans*) mixture of diastereoisomers (Table 1). The diastereoselectivity was determined by GC analysis. The relative configuration of the major isomer was assigned by comparison of the NMR data with literature values.[8] All other new compounds were assigned in analogy. The predominant formation of the *cis*-isomer is in agreement with the Beckwith−Houk model for 5-exo cyclization reactions.[9]

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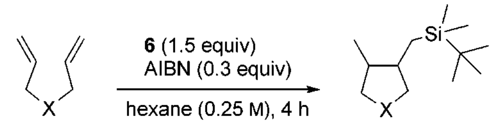
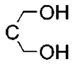
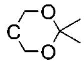
(8) Miura, K.; Oshima, K.; Utimoto, K. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 2348.

Table 1. Hydrosilylation/Cyclization of Various Dienes



14-18 **19-23**

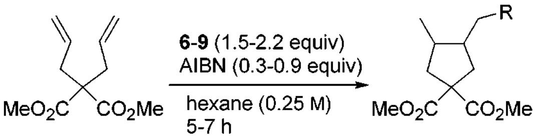
X	starting material	yield (%)	product	dr (*cis*:*trans*)
$C(CO_2Et)_2$	**14**	80	**19**	4.3 : 1
O	**15**	71	**20**	2.5 : 1
NTos	**16**[a]	76	**21**	2.0 : 1
	**17**[b]	62	**22**	2.3 : 1
	**18**	72	**23**	2.6 : 1

[a] Reaction took 7 h for completion. [b] 3 equiv of **6**, 0.6 equiv of AIBN.

Ether **15**, tosylamide **16**, and ketal **18** were readily transformed to the corresponding cycloalkanes **20**, **21**, and **23** in good yields with moderate selectivities. For tosylamide **16**, reaction took longer (7 vs 4 h). Under our standard conditions, hydrosilylation of diol **17** did not go to completion. However, with 3 equiv of Si reagent **6** and 0.6 equiv of initiator, high conversion was obtained and compound **22** was isolated in 62% yield (dr = 2.3:1).

Since the silyl group in the Si reagents can be readily varied (see Figure 1), basically *any* silyl group can be introduced via radical hydrosilylation using our approach. To demonstrate this fact, we studied the hydrosilylation of diene **24** using the Si reagents **6**−**9**. Hydrosilylation with reagent **6** under the standard conditions provided carbocycle **25** in 84% yield (Table 2). Hydrosilylation/cyclization with the bulkier dimethylphenylsilyl **7** and the triisopropylsilyl reagent **8** provided the corresponding products **26** (57%) and **27** (44%, not shown) in lower yields. However, upon using di-*tert*-butylperoxide as initiator at 140 °C in hexane (sealed tube), high yields can be obtained even with these bulky reagents, as shown for the hydrosilylation/cyclization with reagent **8** (82%, see Table 2). It turned out that the trimethylsilyl derivative **9** lacking the methoxy substituents is slightly less reactive.[10] The hydrosilylation could not be initiated using AIBN. However, with di-*tert*-butylperoxide as initiator smooth reaction occurred in hexane at 140 °C and the hydrosilylation/cyclization product **28** was isolated in 81% yield.

Table 2. Hydrosilylation/Cyclization of Diene **24** with Si Reagents **6**−**9**



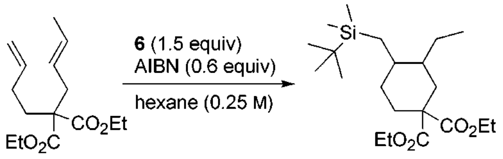
24 **25-28**

reagent	R	yield (%)	product	dr (*cis*:*trans*)
6	$SiMe_2t$-Bu	84	**25**	3.8 : 1
7	$SiMe_2Ph$	57	**26**	4.4 : 1
8[a]	$Si(i\text{-}Pr)_3$	82	**27**	2.6 : 1
9[a]	$SiMe_3$	81	**28**	3.1 : 1

[a] *t*-BuOO-*t*-Bu (0.5 equiv) was used as initiator at 140 °C.

We also studied hydrosilylation reactions comprising a 6-exo cyclization (Scheme 4). Reaction of diene **29** with reagent **6** afforded cyclohexane derivative **30** in 61% yield as 1:1 mixture of diastereoisomers.[11] As expected, the silyl radical added regioselectively at the unsubstituted terminal double bond of bisalkene **29**.

Scheme 4. Radical Hydrosilylation Comprising a 6-Exo Cyclization

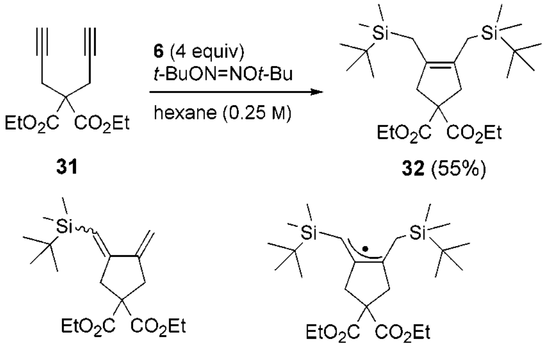


29

30
(61%, dr = 1:1)

Hydrosilylation of bisalkyne **31** under our standard conditions (Scheme 5) afforded double hydrosilylation product **32** in 11% yield along with unreacted starting material and mono silylation/cyclization compound **33**.[12] Under optimized conditions (4 equiv of **6**, *t*-BuON=NO*t*-Bu as initiator),[13] 55% of **32** was isolated. Reduction of the allyl radical **34** formed

Scheme 5. Hydrosilylation of Bisalkyne **31**



31

32 (55%)

33

34

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(9) Beckwith, A. L.; Schiesser, C. H. *Tetrahedron* **1985**, *41*, 3925. Spellmeyer, D. C.; Houk, K. N. *J. Org. Chem.* **1987**, *52*, 959.

(10) Amrein, S. Unpublished results.

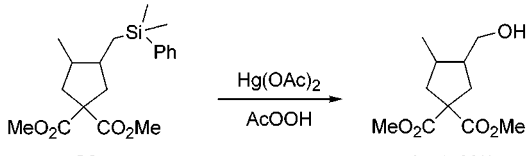
(11) About 5% unreacted starting material remained.

(12) Ojima, I.; Zhu, J.; Vidal, E. S.; Kass, D. F. *J. Am. Chem. Soc.* **1998**, *120*, 6690.

after silyl radical addition to diene **33** occurred regioselectively at the less hindered site (secondary vs tertiary radical).

The hydrosilylation products, if appropriately substituted at silicon, can be readily oxidized to the corresponding alcohols using the well-known Tamao−Fleming oxidation protocol.[14] This certainly expands the utility of our new method. For instance, bisester **26** (*cis*:*trans* = 4:1) was transformed to alcohol **35** in 73% yield (*cis*:*trans* = 4:1, Scheme 6).[15]

Scheme 6. Tamao−Fleming Oxidation



26 **35** (73%)

In conclusion, we report a new method for radical hydrosilylation using silylated cyclohexadienes as *metal-free transfer-hydrosilylating* reagents. Double as well as triple bonds can readily be hydrosilylated with the new method. 1,5- and 1,6-dienes undergo the hydrosilylation/cyclization reaction to afford silylated cycloalkanes. To the best of our knowledge, this is the first report of a transfer-hydrosilylation reaction.

Acknowledgment. We thank the Swiss Science National Foundation (2100-055280.98/1) for funding our work. The work described herein is part of the planned dissertation of S.A.

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

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(13) Mendenhall, G. D. *Tetrahedron Lett.* **1983**, *24*, 451.

(14) Jones, G. R.; Landais, Y. *Tetrahedron* **1996**, *52*, 7599.

(15) The same oxidation has already been reported: Widenhoefer, R. A.; Stengone, C. N. *J. Org. Chem.* **1999**, *64*, 8681.