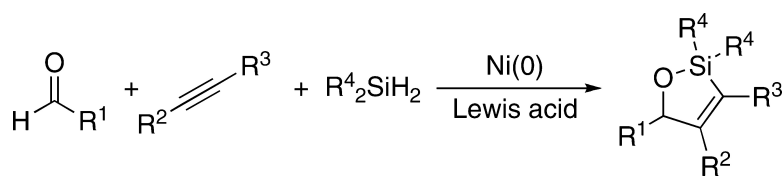


Dehydrogenative Cyclocondensation of Aldehydes, Alkynes, and Dialkylsilanes

Ryan D. Baxter, and John Montgomery

J. Am. Chem. Soc., **2008**, 130 (30), 9662-9663 • DOI: 10.1021/ja803774s • Publication Date (Web): 04 July 2008

Downloaded from <http://pubs.acs.org> on February 8, 2009



More About This Article

Additional resources and features associated with this article are available within the HTML version:

- Supporting Information
- Links to the 3 articles that cite this article, as of the time of this article download
- Access to high resolution figures
- Links to articles and content related to this article
- Copyright permission to reproduce figures and/or text from this article

[View the Full Text HTML](#)



Dehydrogenative Cyclocondensation of Aldehydes, Alkynes, and Dialkylsilanes

Ryan D. Baxter and John Montgomery*

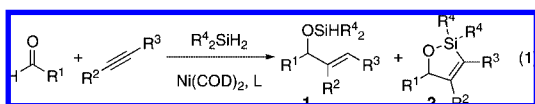
Department of Chemistry, University of Michigan, 930 North University Avenue, Ann Arbor, Michigan 48109-1055

Received May 20, 2008; E-mail: jmontg@umich.edu

Oxasilacyclopentenes and oxasilacyclopentanes are useful synthetic intermediates in a broad variety of organic transformations including oxidations, cross-couplings, and cycloadditions.¹ They are typically prepared by either intramolecular hydrosilylations² or silylformylations,³ ring-closing metathesis reactions,⁴ or cycloadditions of silylene synthetic equivalents.^{1a,5} The latter of these strategies has the advantage of utilizing two simple π -components in a multicomponent cycloaddition that involves silylene transfer from a silylene synthetic equivalent. While impressive advances have been made in a number of reactions involving a variety of silylene synthetic equivalents, the use of silacyclopropanes has emerged as the most general protocol.^{5a-c} However, the impressive scope of reactions and utility of the five-membered silacyclic products is somewhat offset by the requirement for prior synthesis and bulb-to-bulb distillation of the silacyclopropane starting material.

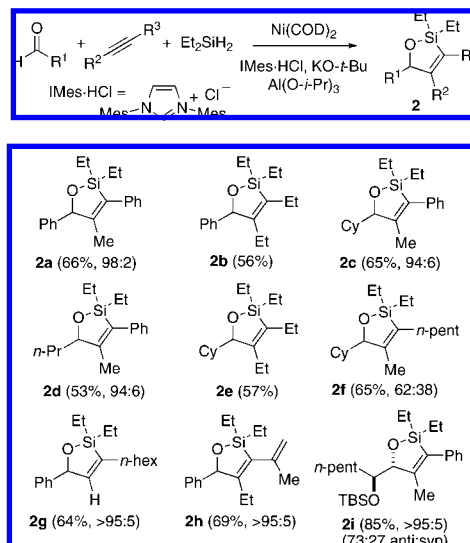
The dehydrogenative cyclocondensation of dialkylsilanes with two π -components would provide an attractive strategy for preparation of silacyclic compounds while having the advantage of employing a simple, stable, commercially available silylene synthetic equivalent. Whereas fundamental advances have been made in the dehydrogenation of dialkylsilanes with transition metals to generate metal silylene complexes,⁶ the catalytic incorporation of the silylene unit derived from a dialkylsilane into an organic product has not been demonstrated.⁷ Herein we describe an unexpected catalytic process that establishes the viability of dehydrogenative cyclocondensations of dialkylsilanes, and that provides a novel entry to oxasilacyclopentenes in a one-step process from commercial reagents.

In the course of studying nickel-catalyzed reductive coupling reactions of aldehydes, alkynes, and dialkylsilanes,⁸ we found, in some instances, that the expected silylated allylic alcohol **1** was accompanied by the unexpected formation of silacycle **2** in addition to other minor products derived from hydrosilylation of the aldehyde and/or alkyne (eq 1). Compound **1** was not converted to **2** under



the conditions of catalysis. The dehydrogenative three-component entry to compound **2** was of particular interest to us considering the potential impact of developing dialkylsilanes as silylene synthetic equivalents in multicomponent cycloadditions. Extensive variation of ligand structure, stoichiometry, order of addition, Lewis acidic additives, and silane structure illustrated that near-optimal yields for production of compound **2** could be achieved with the aldehyde as the limiting reagent and only a slight excess of the alkyne and silane (1.1 equiv each, added by syringe drive). Al(O-*i*-Pr)₃ and Et₂SiH₂ were the optimum Lewis acid and silane components of those examined. Using these optimized conditions, the scope and generality of the dehydrogenative cyclocondensation of aldehydes, alkynes, and Et₂SiH₂ was explored (Table 1).

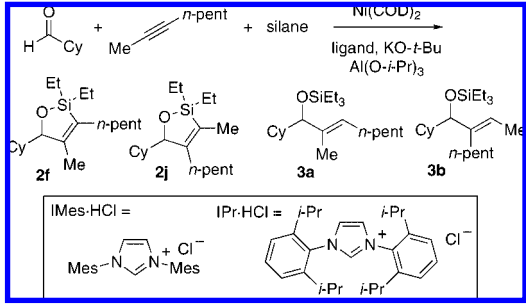
Table 1. Dehydrogenative Cyclocondensations^a



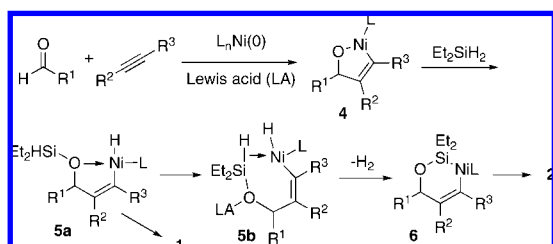
^a Reaction conditions: Ni(COD)₂, IMes·HCl, KO-*t*-Bu (10 mol % each), Al(O-*i*-Pr)₃ (1.5 equiv), aldehyde (1.0 equiv), alkyne and Et₂SiH₂ (1.1 equiv each), THF/toluene, rt. Isolated chemical yield and regioselectivity of alkyne insertion are provided in parentheses.

Couplings of benzaldehyde with phenyl propyne and with 3-hexyne proceeded with moderate efficiency (products **2a** and **2b**), and cyclohexyl carboxyaldehyde and butyraldehyde were also excellent participants with various alkynes (products **2c**–**2f**). Whereas couplings with phenyl propyne were uniformly highly regioselective (products **2a**, **2c**, and **2d**), a coupling with 2-octyne proceeded with poor selectivity (product **2f**). Additionally, couplings of a terminal alkyne (product **2g**), a conjugated enyne (product **2h**), and an α -silyloxy aldehyde (product **2i**) were efficient, with each of these examples proceeding with excellent regiocontrol of the alkyne insertion.

Although the net dehydrogenative cyclocondensation exhibits some similarity to the copper-catalyzed addition of silacyclopropenes to aldehydes, as reported by Woerpel,^{5a} the scope and regioselectivity of the two procedures are markedly different. For example, couplings of butyraldehyde and phenyl propyne are highly regioselective in both procedures. Notably, the nickel-catalyzed procedure affords compound **2d** (Table 1), whereas the copper-catalyzed silacyclopropene procedure produces the opposite regioisomer with >95:5 selectivity. In addition to this regioselectivity comparison, several lines of reasoning suggest that the nickel-catalyzed process proceeds by a different mechanism than that operative in true silylene transfer reactions. First, the silacyclopropenes used in silylene addition reactions by Woerpel are unreactive with aldehydes upon exposure to the nickel catalyst and Lewis acid employed in the coupling procedure developed herein. Additionally, omitting the aldehyde component in the nickel-catalyzed

Table 2. Regioselectivity of Aldehyde, Alkyne, Silane Couplings


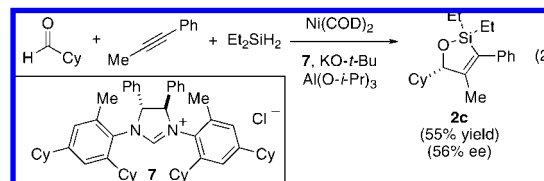
entry	silane	ligand	products (ratio)	% yield
1	Et ₂ SiH ₂	IMes	2f:2j (62:38)	65
2	Et ₃ SiH	IMes	3a:3b (63:37)	76
3	Et ₂ SiH ₂	IPr	2f:2j (12:88)	38
4	Et ₃ SiH	IPr	3a:3b (10:90)	58

Scheme 1. Proposed Mechanism

process involving dialkylsilanes leads to simple hydrosilylation of the alkyne, with no evidence for formation of silylene-derived products being obtained. Finally, aldehyde/alkyne/dialkylsilane oxidative cycloadditions proceed with essentially identical regioselectivity as aldehyde/alkyne/trialkylsilane couplings⁹ across a range of ligand structures. These very close parallels suggest involvement of a common intermediate in these two nickel-catalyzed reactions, and the latter of these pathways involving trialkylsilanes cannot involve a silylene species. To illustrate this issue, the regioselectivity of the nickel-catalyzed couplings of cyclohexyl carboxaldehyde and 2-octyne with diethylsilane and triethylsilane, using both IMes and IPr as ligand, was examined. The solvent composition, Lewis acid concentration, and all other variables were identical in these comparative experiments. In couplings involving the IMes/Ni(0) catalyst system, couplings with diethylsilane proceeded with 62:38 regioselectivity (Table 2, entry 1), whereas couplings with triethylsilane proceeded with 63:37 regioselectivity (Table 2, entry 2). Similarly, couplings with the IPr/Ni(0) catalyst system proceeded with the reversed regioselectivity both in couplings of diethylsilane (12:88 ratio, Table 2, entry 3) and triethylsilane (10:90 ratio, Table 2, entry 4).

While the involvement of metal silylenes is a distinct possibility,¹⁰ a mechanistic framework that involves a common intermediate in the formation of both products **1** and **2** seems more likely based upon the above considerations. A possible mechanism involves the common production of metallacycle **4**, derived from the oxidative cyclization of an aldehyde/alkyne complex of Ni(0) (Scheme 1).⁹ σ -Bond metathesis of the Ni–O and Si–H bonds would afford intermediate **5a**, leading to product **1** (or analogous structures **3**), as previously proposed. Alternatively, σ -bond metathesis of the Si–H and Ni–H bonds of **5a** would extrude H₂ and form intermediate **6**,¹¹ which would produce the observed silacycle **2** upon reductive elimination. The role of the Lewis acid is unclear, although disruption of a Ni–O interaction in intermediate **5a** via Lewis acid coordination to oxygen, as depicted in **5b**, may facilitate H₂ extrusion.

Given the potential of mechanistic similarities in the production of compounds **2** and **3**, chiral ligand **7**, which was recently developed for use in asymmetric couplings of aldehydes, alkynes, and trialkylsilanes,^{9d} was examined in the asymmetric preparation of **2c**. This preliminary experiment proceeded in 56% ee and 55% isolated yield, which represents the first asymmetric cycloaddition involving formal silylene transfer (eq 2).



In summary, the use of a dialkylsilane as a silylene synthetic equivalent in a catalytic multicomponent cyclocondensation has been demonstrated for the first time. Synthetically useful silacycles are prepared by the procedure, and a mechanism involving nickel metallacycles derived from oxidative cyclization of Ni(0) with an aldehyde and alkyne is proposed. Additionally, the first example of the asymmetric formation of a silacyclic product via three-component cycloaddition is provided. Further elaboration of this conceptual framework in other classes of reactions is in progress.

Acknowledgment. The authors wish to acknowledge receipt of NSF grant CHE-0718250 in support of this work. R.D.B. acknowledges receipt of a U.S. DOE GAANN Fellowship (P200A060119). Scott Bader is thanked for helpful suggestions.

Supporting Information Available: Full experimental details and copies of NMR spectral data (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

References

- (1) (a) Franz, A. K.; Woerpel, K. A. *Acc. Chem. Res.* **2000**, *33*, 813. (b) Denmark, S. E.; Pan, W. *Org. Lett.* **2001**, *3*, 61. (c) Halvorsen, G. T.; Roush, W. R. *Org. Lett.* **2007**, *9*, 2243.
- (2) (a) Maifeld, S. V.; Lee, D. *Org. Lett.* **2005**, *7*, 4995. (b) Denmark, S. E.; Pan, W. *Org. Lett.* **2002**, *4*, 4163. (c) Bergens, S. H.; Noheda, P.; Whelan, J.; Bosnich, B. *J. Am. Chem. Soc.* **1992**, *114*, 2121. (d) Bergens, S. H.; Noheda, P.; Whelan, J.; Bosnich, B. *J. Am. Chem. Soc.* **1992**, *114*, 2128.
- (3) (a) Leighton, J. L.; Chapman, E. *J. Am. Chem. Soc.* **1997**, *119*, 12416. (b) O'Malley, S. J.; Leighton, J. L. *Angew. Chem., Int. Ed.* **2001**, *40*, 2915.
- (4) Denmark, S. E.; Yang, S.-M. *Org. Lett.* **2001**, *3*, 1749.
- (5) (a) Clark, T. B.; Woerpel, K. A. *J. Am. Chem. Soc.* **2004**, *126*, 9522. (b) Driver, T. G.; Woerpel, K. A. *J. Am. Chem. Soc.* **2004**, *126*, 9993. (c) Franz, A. K.; Woerpel, K. A. *J. Am. Chem. Soc.* **1999**, *121*, 949. (d) Okinoshima, H.; Yamamoto, K.; Kumada, M. *J. Am. Chem. Soc.* **1972**, *94*, 9263. (e) Tamao, K.; Kobayashi, K.; Ito, Y. *Synlett* **1992**, 539. (f) Ohmura, T.; Masuda, K.; Sugimoto, M. *J. Am. Chem. Soc.* **2008**, *130*, 1526.
- (6) (a) Mork, B. V.; Tilley, T. D. *J. Am. Chem. Soc.* **2001**, *123*, 9702. (b) Waterman, R.; Hayes, P. G.; Tilley, T. D. *Acc. Chem. Res.* **2007**, *40*, 712. (c) Also see: Litz, K. E.; Henderson, K.; Gourley, R. W.; Holl, M. M. B. *Organometallics* **1995**, *14*, 5008.
- (7) Alkene hydrosilylation involving Si–H bond insertion of a monoalkylsilane-derived silylene intermediate has been proposed. Glaser, P. B.; Tilley, T. D. *J. Am. Chem. Soc.* **2003**, *125*, 13640.
- (8) For reviews of aldehyde/alkyne reductive couplings, see: (a) Montgomery, J. *Angew. Chem., Int. Ed.* **2004**, *43*, 3890. (b) Montgomery, J.; Sormunen, G. *J. Top. Curr. Chem.* **2007**, *279*, 1. (c) Iida, H.; Krichshe, M. *J. Top. Curr. Chem.* **2007**, *279*, 77. (d) Moslin, R. M.; Miller-Moslin, K.; Jamison, T. F. *Chem. Commun.* **2007**, 4441.
- (9) (a) Tang, X.-Q.; Montgomery, J. *J. Am. Chem. Soc.* **1999**, *121*, 6098. (b) Tang, X.-Q.; Montgomery, J. *J. Am. Chem. Soc.* **2000**, *122*, 6950. (c) Mahandru, G. M.; Liu, G.; Montgomery, J. *J. Am. Chem. Soc.* **2004**, *126*, 3698. (d) Chaulagain, M. R.; Sormunen, G. J.; Montgomery, J. *J. Am. Chem. Soc.* **2007**, *129*, 9568. (e) For recent isolation of an aldehyde/alkyne-derived nickel metallacycle, see: Ogoshi, S.; Arai, T.; Ohashi, M.; Kurosawa, H. *Chem. Commun.* **2008**, 1347.
- (10) For involvement of Pd catalysis in three-component couplings involving silylene transfer, see: (a) Nevarez, Z.; Woerpel, K. A. *Org. Lett.* **2007**, *9*, 3773. (b) Palmer, W. S.; Woerpel, K. A. *Organometallics* **2001**, *20*, 3691.
- (11) As verification of the production of H₂ under the conditions of catalysis, the characteristic signal for H₂ at δ 4.5 in toluene-*d*₈ was observed in a sealed tube ¹H NMR experiment.

JA803774S