Allylsilanes as Carbon Nucleophiles in Intramolecular Pd(II)-Catalyzed 1,4-Addition to Conjugated Dienes

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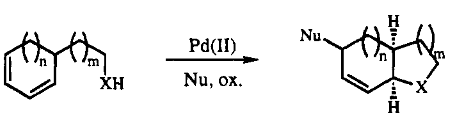
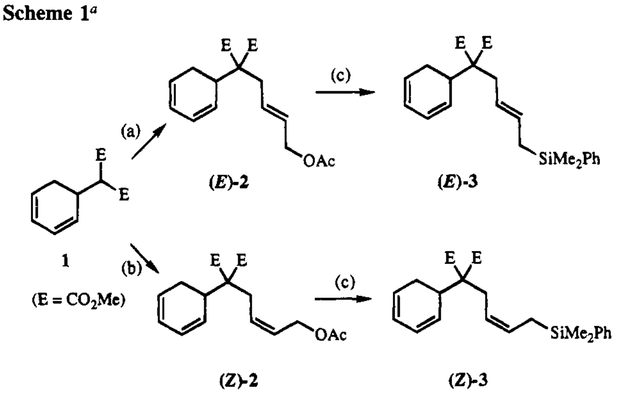
Nucleophilic additions to unsaturated hydrocarbons coordinated to transition metals are important organometallic processes in organic synthesis.[1] In this area, palladium(II) complexes have proven to be efficient due to their ability to coordinate olefins and dienes and induce nucleophilic attack.[1,2] A few years ago we discovered the Pd(II)-catalyzed 1,4-oxidation of conjugated dienes involving regio- and stereoselective addition of nucleophiles to the 1- and 4-positions of the 1,3-diene.[3] An intramolecular version of this Pd(II)-catalyzed 1,4-oxidation was developed recently and successfully applied to the construction of stereodefined heterocyclic systems (eq 1).[4] However, the reaction has so far been limited to heteroatom nucleophiles, and attempts to employ different types of stabilized carbon nucleophiles in the side chain have been unsuccessful.[5-7]



(1)

In our search to extend the reaction in eq 1 to C−C bond formation, we considered allylsilanes as possible carbon nucleophiles. We thought that the diene, activated by Pd(II), could be electrophilic enough to react in a Sakurai-type reaction with an allylsilane.[8-10] In this communication we report on a *Pd(II)-catalyzed intramolecular C−C bond formation by nucleophilic addition of an allylsilane to a coordinated diene*, leading to an overall 1,4-oxidation of the diene.

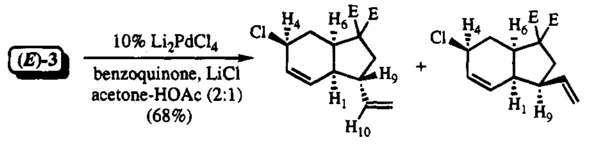
Scheme 1[a]



[a] (a) NaH (1.3 equiv), $Pd(OAc)_2$ (4%), PPh_3 (12%), (*E*)-$ClCH_2CH{=}CHCH_2OAc$[14a] (1.5 equiv), THF, r.t., 1.5 h, 82%. (b) NaH (1.3 equiv), (*Z*)-$BrCH_2CH{=}CHCH_2OAc$[14b] (1.4 equiv), THF, r.t., 1.5 h, 85%. (c) $PhMe_2SiLi$ (2 equiv), CuCN (1.4 equiv), THF, −60 °C, 4 h, 84% for (*E*)-**3**, 56% for (*Z*)-**3**.

Allylsilanes (*E*)- and (*Z*)-**3** were prepared from the corresponding allylic acetates by reaction with $PhMe_2SiLi$[11] in the presence of CuCN according to a known procedure (Scheme 1).[12,13] Both *E* and *Z* allylic acetates were synthesized from diene malonate **1**[4f] by reaction with (*E*)- and (*Z*)-4-halo-1-acetoxy-2-butene, respectively.[14]

Reaction of (*E*)-**3** with a catalytic amount of Li_2PdCl_4 (10%) in the presence of *p*-benzoquinone (1.5 equiv) and LiCl (2 equiv) in acetone−acetic acid (2:1) gave, after 16 h at room temperature, a mixture of two isomeric allylic chlorides **4** (α: β = 3:1)[15] in 68% isolated yield (eq 2,[13] Table 1, entry 1). The stereochemistry of both products was determined by NOE measurements, and it was found that the addition of carbon and Cl^- across the diene was completely stereoselective and only 1,4-*syn*-addition products were observed.[16] Under the same reaction conditions, (*Z*)-**3** reacted to give **4** in a highly stereoselective 1,4-*syn*-addition process (Table 1, entry 2). Interestingly, the ratio between the α and β isomers was opposite to that obtained from (*E*)-**3**, and now the β-isomer predominated (α: β = 1:3).



(2)

4 (α:β = 3:1)

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(1) (a) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987; pp 825−857. (b) Bäckvall, J. E. In *Advances in Metal-Organic Chemistry*; Liebeskind, L., Ed.; JAI Press: London, 1989; Vol. 1, pp 135−175. (c) Hegedus, L. S. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, U.K., 1991; Vol. 3, pp 551−583.

(2) For recent reviews on O, X^- nucleophiles, see: (a) References 1b,c. For recent reviews on N nucleophiles, see: (b) Hegedus, L. S. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1113−1126. (c) Larock, R. C.; Hightower, T. R. *J. Org. Chem.* **1993**, *58*, 5298−5300. (d) van Benthem, R. A. T. M.; Hiemstra, H.; Michels, J. J.; Speckamp, W. N. *J. Chem. Soc., Chem. Commun.* **1994**, 357−359.

(3) (a) Bäckvall, J. E.; Byström, S. E.; Nordberg, R. E. *J. Org. Chem.* **1984**, *49*, 4619−5631. (b) Bäckvall, J. E.; Nyström, J. E.; Nordberg, R. E. *J. Am. Chem. Soc.* **1985**, *107*, 3676−3786. (c) Reference 1b.

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(5) C−C Bond formation was recently achieved by insertion of the diene in an *in situ* generated vinylpalladium species: Bäckvall, J. E.; Nilsson, Y. I. M.; Andersson, P. G.; Gatti, P. G.; Wu, J. *Tetrahedron Lett.* **1994**, *35*, 5713−5716.

(6) The use of C-nucleophiles in the Pd(II)-promoted nucleophilic additions to olefins has only been described with stoichiometric amounts of palladium. For a recent review, see: Hegedus, L. S. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, U.K., 1991; Vol. 3, pp 571−583.

(7) Silylenol ethers react with olefins in the presence of stoichiometric Pd(II) in a rather general process: (a) Toyota, M.; Wada, T.; Nishikawa, Y.; Yanai, K.; Fukumoto, K. *Synlett* **1994**, 597−598. (b) Toyota, M.; Nishikawa, Y.; Motoki, K.; Yoshida, N.; Fukumoto, K. *Tetrahedron* **1993**, *48*, 11189−11204. (c) Larock, R. C.; Lee, N. *Tetrahedron Lett.* **1991**, *32*, 5911−5914. (d) See also ref 6.

(8) Hosomi, A.; Sakurai, H. *J. Am. Chem. Soc.* **1977**, *99*, 1673−1674 and references cited therein.

(9) Recently, a Pd(0)-catalyzed cyclization of an allylic carbonate with an allylsilane was described: Terakado, M.; Miyazawa, M.; Yamamoto, K. *Synlett* **1994**, 134−136.

(10) For some recent reviews on allylsilanes, see: (a) *The Chemistry of Organic Silicon Compounds*; Patai, S., Rappoport, Z., Eds.; Wiley: Chichester, U.K., 1989, Part 2. (b) Fleming, I.; Dunogues, J.; Smithers, R. *Org. React.* **1989**, *37*, 57−575. (c) Fleming, I., Ed. *Tetrahedron* **1988**, *44*, 3761−4292.

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(12) Majetich, G.; Defauw, J. *Tetrahedron* **1988**, *44*, 3833−3849.

(13) Abbreviations: brsm = based on recovered starting material; E = CO_2Me.

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(15) Descriptors α and β refer to the orientation of the vinyl substituent at C-9 toward the plane of the molecule.

(16) NOE data for **4**α: H_1−H_6, 11.5%; H_4−H_6, 6.8%; H_1−H_{10}, 7.9%. NOE data for **4**β: H_1−H_6, >5%; H_4−H_6, 6.5%; H_1−H_9, 9.0%.

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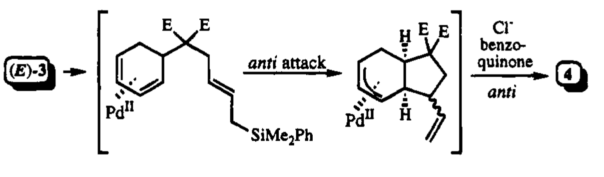
Table 1. Pd(II)-Catalyzed Carboannulation of ω-Dienyl Allylsilanes[a]

entry	silane	oxidant	acetone−HOAc	products (ratio)[b]	stereochem 1,4-addn[b,c]	yield (%)[d]
1	(*E*)-**3**	BQ[e]	2:1	**4** (α:β = 3:1)[f]	>98% *syn*	68
2	(*Z*)-**3**	BQ	2:1	**4** (α:β = 1:3)[f]	>98% *syn*	72
3	(*E*)-**7**	BQ	2:1	**10** (α:β = 1.4:1) + **11**	*syn*:*anti* 84:16	55
4	(*Z*)-**7**	BQ	1:1	**10** (α:β = 2.4:1) + **11**	*syn*:*anti* 74:26	66
5	(*E*)-**9**	CuCl$_2$	0:1	**12**[g,h]		50
6	(*Z*)-**9**	CuCl$_2$	1:1	**12**[i,j]		60

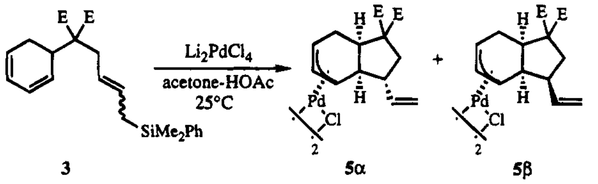
[a] Unless otherwise stated, the silane, Li$_2$PdCl$_4$ (10%), LiCl (2 equiv), and the oxidant (1.5 equiv of 1,4-benzoquinone or 2.5 equiv of CuCl$_2$) were stirred in acetone−HOAc (proportion) at room temperature under N$_2$ for 12−40 h. Dienes **3** were added slowly to the reaction mixture. [b] Ratio by ^{1}H NMR. [c] Refers to the addition across the diene system. In all cases the bridgehead protons were *cis* to each other. [d] Isolated yields. [e] BQ = 1,4-benzoquinone. [f] Small amounts of the Diels−Alder adduct (5−7%) were detected. [g] Acetate **13** was also isolated in 20% yield. [h] A 1.3:1 diastereomeric mixture. [i] 5 equiv of LiCl was used. [j] A 1:4 diastereomeric mixture (the major isomer was identical to the minor isomer from (*E*)-**9**).

The *syn* stereochemistry between the chloro group and C-9 in **4** is best explained by an external *anti* attack by the allylsilane on the coordinated diene to give an intermediate (π-allyl)-palladium complex followed by an external *anti* attack by chloride (eq 3). It is known that quinone-induced chloride attack on (π-allyl)palladium complexes occurs *anti*.[3b,4]



(3)

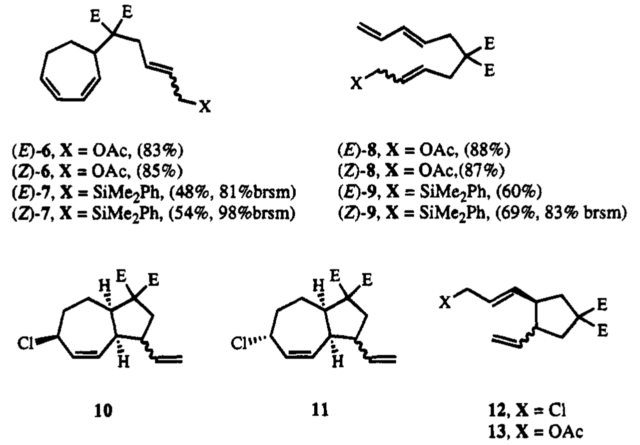
To obtain further support for the mechanism suggested in eq 3, the intermediate (π-allyl)palladium complexes from the dienyl silanes (*E*)- and (*Z*)-**3** were prepared. Reaction of (*E*)- and (*Z*)-**3** with 1 equiv of Li$_2$PdCl$_4$ in acetone−acetic acid (2:1) afforded (π-allyl) complexes **5α** and **5β** in ratios of 2.7:1 and 1:3, respectively (eq 4).[17,18] The ratios between the α- and β-vinyl isomers are in agreement with the product ratios obtained from (*E*)- and (*Z*)-**3** in the catalytic reaction.



(4)

	5α		5β
(*E*)-3	2.7	:	1
(*Z*)-3	1	:	3

In order to study the scope of this reaction, both *E* and *Z* isomers of allylsilanes **7** and **9** were prepared by following the same procedure as for **3**. Silanes **7** and **9** were cyclized under similar conditions to give the chlorides **10** and **12**, respectively (Figure 1).[13] Selected results are given in Table 1.



(*E*)-**6**, **X** = OAc, (83%)
(*Z*)-**6**, **X** = OAc, (85%)
(*E*)-**7**, **X** = SiMe$_2$Ph, (48%, 81%brsm)
(*Z*)-**7**, **X** = SiMe$_2$Ph, (54%, 98%brsm)

(*E*)-**8**, **X** = OAc, (88%)
(*Z*)-**8**, **X** = OAc,(87%)
(*E*)-**9**, **X** = SiMe$_2$Ph, (60%)
(*Z*)-**9**, **X** = SiMe$_2$Ph, (69%, 83% brsm)

10

11

12, X = Cl
13, X = OAc

Figure 1.

The best results concerning yield and selectivity were obtained with the cyclohexadiene derivatives **3** (Table 1, entries 1 and 2). In the reactions of the cycloheptadiene silanes **7** some *anti*-addition products **11** were observed along with **10**. Thus, (*E*)-**7** and (*Z*)-**7** afforded **10** and **11** in ratios of 84:16 and 74:26, respectively (Table 1, entries 3 and 4).[19]

For the acyclic substrates **9**, CuCl$_2$ was used as the oxidant in place of *p*-benzoquinone, since the latter gave large amounts of the Diels−Alder adduct with the diene (25−30%). With CuCl$_2$ as the oxidant, (*E*)- and (*Z*)-**9** afforded chlorides **12** in 50 and 60% yields, respectively (Table 1, entries 5 and 6). For (*E*)-**9**, pure HOAc gave a more efficient reaction, but in this case, acetate **13** was obtained as a side product (20%).

In summary, we have shown that allylsilanes can be used as carbon nucleophiles acting as "masked carbanions" in Pd(II)-catalyzed carboannulations to 1,3-dienes, in a process that leads to stereodefined 1,4-functionalization of the diene. To the best of our knowledge this is the first example of nucleophilic attack by an allylsilane on an olefin coordinated to a metal.

Acknowledgment. We thank Prof. H. H. Wasserman for fruitful discussions. Financial support from the Swedish Natural Science Research Council and from *Ministerio de Educación y Ciencia* (fellowship to A.M.C.) is gratefully acknowledged. We thank Johnson Matley for a loan of palladium chloride.

Supplementary Material Available: Text describing the synthesis and characterization of all new compounds (12 pages) available. This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(17) Complexes **5α** and **5β** were characterized by NMR. The *syn* relationship between Pd and the bridgehead protons was unambiguously established in **5β** by the use of 2,2′-bipyridine as a reporter ligand on Pd (Albinati, A.; Ammann, C. J.; Kunz, R. W.; Pregosin, P. S. *Organometallics* **1991**, *10*, 1800−1806). A NOE enhancement between the *ortho* proton in the bipyridine ligand and H$_1$ (3.4%) was observed.

(18) (a) The observed *trans* stereochemistry in the carbopalladation reaction to give **5** rules out a pathway involving transmetalation from the allylsilane to Li$_2$PdCl$_4$ with generation of a (π-allyl)palladium in the side chain, followed by *syn* insertion of the diene.[18b,c] The formation of **5α** and **5β** as the only observable products eliminates an additional alternative pathway for formation of **4** *via* chloropalladation of the diene and subsequent attack by the silane on the (π-allyl)palladium complex (*cf.* ref 9). (b) Simple allylsilanes react with Pd(II) complexes, forming the corresponding π-allyl palladium complex, by transfer of the allyl group: Kliegman, J. M. *J. Organomet. Chem.* **1971**, *29*, 73−77. Hayashi, T.; Konishi, M.; Kumada, M. *J. Chem. Soc., Chem. Commun.* **1983**, 736−737. Ogoshi, S.; Yoshida, W.; Ohe, K.; Murai, S. *Organometallics* **1993**, *12*, 578−579 and references therein. (c) Allyltrialkylsilanes and allyltrifluorosilanes react in Pd(0)-catalyzed cross-coupling reactions: Hatanaka, Y.; Gode, K.-i.; Hiyama, T. *Tetrahedron Lett.* **1994**, *35*, 1279−1282. Hatanaka, Y.; Ebina, Y.; Hiyama, T. *J. Am. Chem. Soc.* **1991**, *113*, 7075−7076.

(19) It was found that **10** slowly isomerizes to **11** in the presence of LiCl.