# Intramolecular Anodic Olefin Coupling Reactions: The Use of Allyl- and Vinylsilanes in the Construction of Quaternary Carbons

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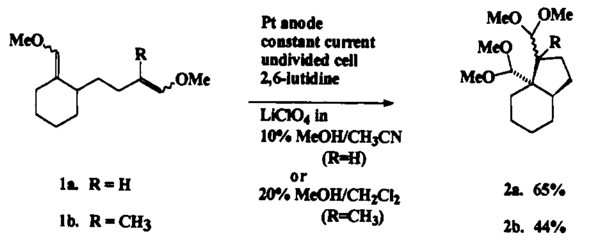
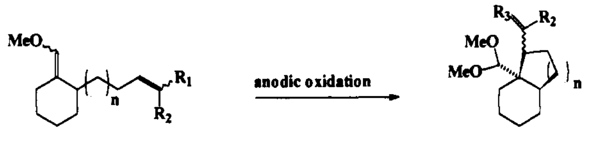
*Summary:* Intramolecular anodic olefin coupling reactions involving the use of either an allylsilane as one of the olefin participants or a vinylsilane as part of a temporary silicon tether have been shown to be compatible with the formation of quaternary carbons.

Recently, we reported that the intramolecular anodic coupling of enol ethers could lead to the formation of fused bicyclic ring skeletons and the generation of quaternary carbons (Scheme I).[1] These cyclizations led to carbon-carbon bond formation even when forming the bond meant the generation of two vicinal quaternary centers! In addition, these reactions led to compounds that had exclusively cis stereochemistry about the ring junction. The success of these reactions led us to wonder if electrochemically initiated oxidative cyclization reactions could provide a useful method for synthesizing quaternary carbons in a stereoselective fashion.[2] Initially, the generality of such a process was not clear since anodic olefin coupling reactions involving bis enol ether substrates were the most facile electrochemical cyclizations that we had studied. For example, the coupling of enol ethers to form five- and six-membered ring products could be carried out in pure methanol, whereas the majority of intramolecular anodic olefin coupling reactions required the use of cosolvents such as tetrahydrofuran, acetonitrile, or dichloromethane.[3] Without the cosolvents these reactions led to solvent trapping of the radical cation before cyclization and poor mass balances. Would the use of a less facile olefin coupling reaction still allow for the generation of quaternary carbons? We report here that anodic olefin coupling reactions involving allyl- and vinylsilanes can lead to good yields of quaternary carbons with control of relative stereochemistry. In addition, *we report the first example of an electrochemical reaction that makes use of a temporary silicon tether.*[4]

### Scheme I



### Scheme II[a]



3a. n=1, $R_1$=$CH_2$TMS, $R_2$=H

3b. n=1, $R_1$=$CH_2$TMS, $R_2$=$CH_3$

3c. n=2, $R_1$=$CH_2$TMS, $R_2$=H

3d. n=2, $R_1$=OMe, $R_2$=H

4a. n=1, $R_3$=$CH_2$, $R_2$=H 74%

4b. n=1, $R_3$=$CH_2$, $R_2$=$CH_3$ 62%

4c. –

4d. n=2, $R_3$=OMe,OMe, $R_2$=H 70%

[a] Conditions. For **3a**: reticulated vitreous carbon (RVC) anode, platinum wire cathode, constant current conditions in an undivided cell, a 0.4 N $LiClO_4$ in 20% $MeOH/CH_2Cl_2$ electrolyte solution, $K_2CO_3$, 2.1 F/mol. For **3b**: RVC anode, carbon rod cathode, constant current conditions in undivided cell, a 0.5 N $LiClO_4$ in 50% MeOH/THF electrolyte solution, $K_2CO_3$, 0 °C, 2 F/mol. For **3d**: platinum gauze anode, carbon rod cathode, constant current conditions in undivided cell, a 0.5 N $LiClO_4$ in 10% $MeOH/CH_3CN$ electrolyte solution, 2,6-lutidine, 2 F/mol.

The utility of intramolecular anodic olefin coupling reactions involving allylsilane participants for making quaternary carbons was examined by synthesizing and oxidizing substrates **3a-c** (Scheme II).[5] Compound **3a** was oxidized using constant current conditions, a reticulated vitreous carbon anode, a 0.4 N lithium perchlorate in 20% methanol/dichloromethane electrolyte solution, and an undivided cell.[6] Potassium carbonate was used as a proton scavenger, and a carbon rod was used as the auxiliary electrode. After 2.1 F/mol of charge had been passed, a 74% isolated yield of product **4a** was obtained. In a similar reaction, substrate **3b** was oxidized using a 0.5 N lithium perchlorate in 50% methanol/tetrahydrofuran electrolyte solution at 0 °C in order to form a 62% isolated yield of product **4b**. In this case, a 7% yield of recovered starting

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[1] Moeller, K. D.; Tinao, L. V. *J. Am. Chem. Soc.* **1992**, *114*, 1033.

[2] For recent examples of quaternary carbon synthesis see: (a) Canet J.-L.; Fadel, A.; Salaün, J. *J. Org. Chem.* **1992**, *57*, 3463. (b) Pearson, A. J.; Khetani, V. D. *J. Am. Chem. Soc.* **1989**, *111*, 6778. (c) Romo, D.; Meyers, A. I. *Tetrahedron* **1991**, *47*, 9503. (d) Fuji, K.; Node, M.; Nagasawa, H.; Naniwa, Y.; Taga, T.; Machida, K.; Snatzke, G. *J. Am. Chem. Soc.* **1989**, *111*, 7921 as well as references cited therein.

[3] (a) Moeller, K. D.; Marzabadi, M. R.; Chiang, M. Y.; New, D. G.; Keith, S. *J. Am. Chem. Soc.* **1990**, *112*, 6123. (b) Moeller, K. D.; Hudson, C. M. *Tetrahedron Lett.* **1991**, *32*, 2307. (c) Hudson, C. M.; Marzabadi, M. R.; Moeller, K. D.; New, D. G. *J. Am. Chem. Soc.* **1991**, *113*, 7372.

[4] For previous examples of temporary silicon tethers see: (a) Nishiyama, H.; Kitajima, T.; Matsumoto, M.; Itoh, K. *J. Org. Chem.* **1984**, *49*, 2298. (b) Tamao, K.; Maeda, K.; Yamaguchi, T.; Ito, Y. *J. Am. Chem. Soc.* **1989**, *111*, 4984. (c) Koreeda, M.; Hamann, L. G. *J. Am. Chem. Soc.* **1990**, *112*, 8175. (d) Shea, K. J.; Zandi, K. S.; Staab, A. J.; Carr, R. *Tetrahedron Lett.* **1990**, *31*, 5885. (e) Shea, K. J.; Staab, A. J.; Zandi, K. S. *Tetrahedron Lett.* **1991**, *32*, 2715. (f) Stork, G. 32nd National Organic Symposium, Minneapolis, June 1991. (g) Stork, G.; Suh, H. S.; Kim, G. *J. Am. Chem. Soc.* **1991**, *113*, 7054. (h) Myers, A. G.; Gin, D. Y.; Widdowson, K. L. *J. Am. Chem. Soc.* **1991**, *113*, 9661. (i) Gillard, J. W.; Fortin, W.; Grimm, E. L.; Maillard, M.; Tjepkama, M.; Bernstein, M. A.; Glaser, R. *Tetrahedron Lett.* **1991**, *32*, 1145. (j) Xi, Z.; Agback, P.; Plavec, J.; Sandstrom, A.; Chattopadhyaya, J. *Tetrahedron* **1992**, *48*, 349. (k) Stork, G.; Kim, G. *J. Am. Chem. Soc.* **1992**, *114*, 1087. (l) Stork, G.; Chan, T. Y.; Breault, G. A. *J. Am. Chem. Soc.* **1992**, *114*, 7578. (m) Craig, D.; Reader, J. C. *Tetrahedron Lett.* **1992**, *33*, 4073. (n) Journet, M.; Malacria, M. *J. Org. Chem.* **1992**, *57*, 3085. (o) Sieburth, S. McN.; Fensterbank, L. *J. Org. Chem.* **1992**, *57*, 5279.

[5] All new compounds were characterized by $^1$H NMR, $^{13}$C NMR, IR, and mass spectrometry. The syntheses of the substrates will be described in detail at a later date.

[6] Preparative electrolyses were conducted using a Model 630 coulometer, a Model 410 potentiostatic controller, and a Model 420A power supply purchased from The Electrosynthesis Company, Inc. Reticulated vitreous carbon, carbon rods, and platinum electrodes were also purchased from the Electrosynthesis Company, Inc. The scale of the reactions reported in this manuscript ranges from the use of *ca.* 100 mg to the use of 500 mg (0.5–1.7 mmol) of substrate.

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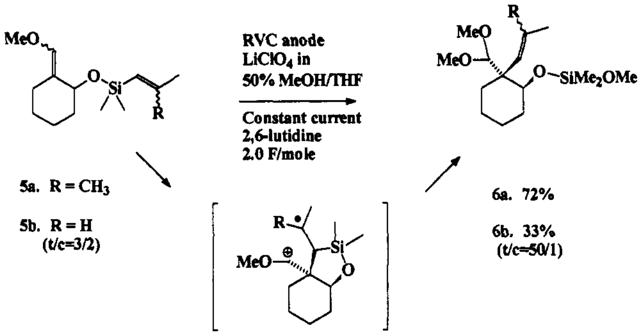
material was obtained.[7] In both cases, the reaction led to exclusively cis-fused products and generation of the quaternary carbon with control of relative stereochemistry. The ring juncture stereochemistry was assigned by analogy to compounds **2a** and **2b**. A mixture of isomers (1:1 for **4a** and 2:1 for **4b**) was obtained at the stereogenic center on the newly formed ring.

Unlike the cyclizations that formed five-membered rings, the use of an allylsilane to form a six-membered ring proved to be incompatible with the generation of a quaternary carbon. In all cases, the oxidation of **3c** failed to generate the desired bicyclic product. This reaction served to further highlight the differences between allylsilane and enol ether terminating groups in the intramolecular anodic olefin coupling reaction. For comparison, the oxidation of bis enol ether substrate **3d** led to the formation of both a six-membered ring and a quaternary carbon in a 70% isolated yield (a 2.3:1 ratio of stereoisomers was obtained). As in earlier experiments, the enol ether group proved to be a more effective terminating group than did the allylsilane.

The success of these reactions for forming quaternary carbons combined with recent successes involving the use of temporary silicon tethers for controlling the reactions of reactive intermediates[4] suggested the use of a temporary silicon tether in an anodic olefin coupling reaction. If such a reaction was successful, then it would seem possible to use anodic olefin coupling reactions to control the stereochemistry of quaternary carbons that were not part of a bicyclic ring skeleton. But would a temporary silicon tether survive the electrolysis reaction?

In order to test this idea, substrates **5a** and **5b** were synthesized using the chemistry developed by Stork.[8] The oxidation of **5a** was accomplished using constant current conditions, a reticulated vitreous carbon anode, a 0.4 N lithium perchlorate in 50% methanol/tetrahydrofuran electrolyte solution, and 2,6-lutidine as a proton scavenger. After 2.0 F/mol of charge had been passed, *a 72% isolated yield of* **6a** *was obtained as a single isomer.* The stereochemistry of **6a** was assigned by treatment of **6a** with 0.5 N HCl in water and methanol at room temperature. These conditions led not only to cleavage of the acetal and the silyl ether, but also to a scrambling of the alcohol stereochemistry. The stereochemistry of both diastereomeric alcohol aldehydes was assigned using NOE difference spectroscopy. Compound **6a** was then converted to a single alcohol aldehyde stereoisomer using a mixture of 1.5 mL of concd HCl, 1.5 mL of water, and 47 mL of methanol at 0 °C. This aldehyde alcohol was compared to the previously assigned diastereomers. The comparison clearly indicated that **6a** was assigned correctly as illustrated in Scheme III.[9]

**Scheme III**



This result was exciting not only because it demonstrated the potential for electrochemistry as a tool for synthesizing quaternary centers with control of stereochemistry, but also because it demonstrated the ability of electrochemistry to initiate oxidative cyclizations with *very* acid-sensitive substrates. Substrate **5a** decomposed rapidly to the corresponding, $\alpha,\beta$-unsaturated aldehyde, even on contact with triethylamine-treated silica gel.

These reactions led to the formation of a quaternary carbon even when a relatively unreactive disubstituted olefin was utilized as the nucleophile, although the yield was lower. For example, the anodic oxidation of **5b** led to a 33% isolated yield of **6b**. As in the earlier case, only a single stereoisomer at the quaternary center was obtained. A 50:1 ratio of trans/cis olefin isomers was obtained (the starting material was a 3:2 ratio of trans/cis olefin isomers).

In conclusion, both allylsilanes and vinylsilanes can be used in intramolecular anodic olefin coupling reactions in order to construct quaternary carbons. The use of a silicon tether was found to be compatible with the electrolysis conditions. These reactions led to the formation of the quaternary carbon with control over relative stereochemistry. The generality of using silicon tethers in anodic olefin coupling reactions and the application of these reactions to synthesis are currently being explored.

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**Supplementary Material Available:** Characterization data for **3a**, **3b**, **3d**, **4a**, **4b**, **4d**, **5a**, **5b**, **6a**, and **6b** and a general anodic oxidation procedure (for **5a**) (6 pages). This material is contained in 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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[7] The change in the reaction conditions for these two cases reflects the reaction conditions developed for earlier cyclizations using di- and trisubstituted allylsilanes (ref 3c).

[8] Stork, G.; Keitz, P. F. *Tetrahedron Lett.* **1989**, *30*, 6981.

[9] The alcohol aldehyde isomer derived from **6a** without isomerization showed an NOE enhancement of <0.05% between the vinyl proton and the proton $\alpha$ to the hydroxyl group. The NOE enhancement between these two protons in the second isomer (derived from scrambling of the alcohol stereochemistry) was 1.01%.