INTRAMOLECULAR ANODIC OLEFIN COUPLING REACTIONS: THE USE OF ALLYLSILANES

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Abstract: The use of allylsilanes as directing groups in the intramolecular electrochemical coupling of electron rich olefins has been examined. The allylsilanes were shown to provide an effective means for controlling product selectivity, and led to the formation of five- and six-membered ring products in 59-84% isolated yields.

Recently, we reported that the intramolecular coupling of electron-rich olefins can be accomplished with the use of an anodic oxidation reaction.¹ These cyclizations were effectively initiated by the oxidation of alkyl and silyl enol ethers, and terminated with the use of styrenes, simple alkyl olefins, and enol ethers. Although the use of simple alkyl-substituted olefins held promise as a general means of carbon-carbon bond formation, these reactions often led to mixtures of products. This problem was particularly acute when a disubstituted olefin was employed as the terminating group. For example, the anodic oxidation of 1 at a platinum anode under constant current conditions led to the formation of three cyclized products in approximately equal yields.



Total yield = 35-60%

The formation of a product mixture in this case was not surprising, particularly when the reaction was viewed as proceeding through initial formation of a radical cation from the enol ether followed by cyclization to form either a secondary carbocation or a secondary radical that could be further oxidized to a secondary carbocation.² If this were the case, then the mixture of products would arise from the non-selective decomposition of the secondary carbocation. These considerations suggested that the electrochemical cyclizations could be channelled toward the formation of a single product with the use of an allylsilane as one of the olefin participants.³ However, the low oxidation potential of the allylsilane moiety,⁴ and the tendency for anodic allylsilane oxidations to afford allylic ether products raised concerns about the compatibility of the allylsilane group with the electrolysis conditions needed for carbon-carbon bond formation. Herein, we report

the first examples of allylsilanes being used to direct the regiochemical outcome of an anodic carbon-carbon bond forming reaction. The results of these studies are reported in Table 1.5

Table 1: Anodic Cyclizations using Allylsilanes^a



a.) Conditions: The oxidations were performed on degassed solutions of the substrate (ca. 0.04-0.01 M) in an undivided cell under constant current conditions (15-26 mA) using either a platinum or carbon anode and a platinum wire or carbon rod cathode. A 0.1 M solution of lithium perchlorate in one of the specified solvent systems was used as electrolyte. b.) The products were obtained as a mixture of cis and trans isomers. The ratio of the isomers varied from ca. 3:1 to 1.3:1. c.) Solvent A = 50% methanol/ tetrahydrofuran; Solvent B = 20% methanol/ methylene chloride. d.) Product was impure. e.) Reticulated Vitreous Carbon anode. f.) The product was impure. In addition a 7% yield of uncyclized material was obtained. g.) The yield is of a representative case. The range over four runs was 55-65%. h.) In this trial, 4d was isolated and then converted to 3d using acetic acid in methanol. The yield reported represents the total amount of 3d obtained.

Several of the examples in Table 1 deserve comment. The initial oxidation attempt (entry 1) utilized the electrochemical reaction conditions that had been the most successful in past cyclizations.¹ Hence, compound 2a was oxidized using constant current conditions, an undivided cell, a platinum anode, and a 1 *M* lithium perchlorate in 50% methanol/ tetrahydrofuran electrolyte solution. This oxidation led to the desired olefinic compound, 3a, in a 46% isolated yield. Along with 3a, a small amount of an ether product (4a) and a small amount of an impure vinylsilane product (5a) were obtained. The formation of the vinylsilane product was surprising, since it seemed unlikely that a vinylsilane would be formed by the elimination of a proton from the anticipated β -silyl carbocation (path a in Scheme 1). It seemed more likely that the vinylsilane would require that the radical cation cyclization led to the formation of a radical beta to the silicon atom, and that elimination occurred before the loss of a second electron to the anode surface. It was reasoned that if this mechanism

Scheme 1: Possible Mechanism for Vinylsilane Formation



operated to a large extent, then the cyclization reaction might benefit from the use of a carbon anode, an anode material known to foster two-electron oxidations.⁶ In practice (entry 2), the use of a reticulated vitreous carbon anode⁷ led to a dramatic increase in the cleanliness of the reaction and an 84% isolated yield of the desired product.

As evident from entries 4-7, the cyclizations could also be used to construct six-membered rings. These cyclizations were less efficient than those leading to the formation of five-membered rings and benefited from the use of solvent systems having lower concentrations of methanol. For example, the oxidation of 2c (entry 4) using constant current conditions, an undivided cell, a reticulated vitreous carbon anode, and a 1 *M* lithium perchlorate in 50% methanol/ tetrahydrofuran electrolyte solution led to only a 40% isolated yield of impure olefin 3c. The 300 MHz ¹H NMR of the crude product showed a large amount of unidentified polymethoxylated material. On the other hand, the oxidation of 2c using identical conditions except for a 0.4 *M* lithium perchlorate in 20 % methanol/ dichloromethane electrolyte solution (entry 5) led to the formation of a 59% isolated yield (range 55-65%) of olefin 3c along with a 10% yield of 4c. The yield of the oxidations showed no dependence upon electrolyte concentration. The switch to dichloromethane was made because dichloromethane had been reported to stabilize radical cations,⁸ and allowed for the use of lower methanol concentrations than did tetrahydrofuran led to severe fluctuations in current flow and drastic decreases in the yield of the cyclization products. On a final note, the use of gem methyl substituents did not lead to a significant increase in the yield of six-membered ring formation (entry 6).

The origin of the cyclized ether products (4) was examined. To this end, the oxidation of 2d was repeated using d⁴-methanol as the solvent. In this experiment, a 60% isolated yield of 3d was obtained along with a 10% yield of 4d. The ether products (4d) were analyzed after cleavage of the acetal with PPTS in acetone. Fifty-six percent of this material contained an -OCH₃ ether. This product clearly arose from intramolecular migration of the methoxy group that was initially part of the enol ether in 2d. The remaining 44% of the ether product contained an -OCD₃ group. This material was formed either from solvent trapping of the β -silyl carbocation, or from intramolecular migration of an -OCD₃ group from a mixed -OCH₃, -OCD₃ acetal formed during the oxidation reaction. At this time, neither mechanism can be ruled out.

Finally, it is important to note that the cyclized ether products (4) can readily be converted to the desired olefinic products by treatment with acid. For example, treatment of 4d with acetic acid in methanol led to the formation of 3d in a 74% isolated yield. Hence, product 3d could be obtained in a net 68% yield from the electrochemical oxidation of 2d (entry 7).

In summary, we have found that allylsilanes can be used to efficiently direct product formation in the intramolecular anodic olefin coupling reaction. *These cyclications represent the first examples of anodic carbon-carbon bond forming reactions that utilize allylsilane groups* for this purpose. The reactions have been shown to be useful for the construction of five- and six-membered rings. Further studies aimed at elucidating the mechanisms of the reactions and at determining the overall synthetic potential of the reactions are currently underway.

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