

# Intramolecular Additions of Alcohols and Carboxylic Acids to Inert Olefins Catalyzed by Silver(I) Triflate

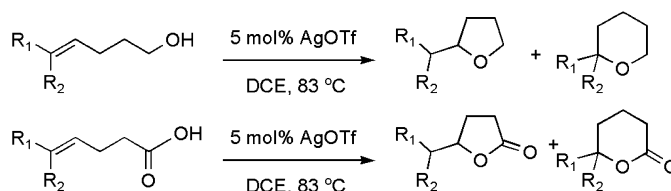
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## ABSTRACT



Intramolecular additions of hydroxyl or carboxyl groups to inert olefins catalyzed by simple silver(I) triflate are described. Good to excellent yields can be obtained for a range of substrates under relatively mild conditions. This reaction represents one of the simplest methods to construct cyclic ethers or lactones.

Silver-catalyzed reactions have recently begun to emerge as important methods for organic synthesis.<sup>1</sup> Silver(I) salts have been used as Lewis acids to catalyze a variety of transformations<sup>2–9</sup> and also exhibit interesting activity in catalyzing

oxidation reactions.<sup>10</sup> Silver(I) is known to interact with unsaturated hydrocarbons,<sup>11</sup> while the use of silver(I) salts to activate such substrates has been primarily limited to allenes<sup>12</sup> and alkynes<sup>13</sup> so far. We have discovered that

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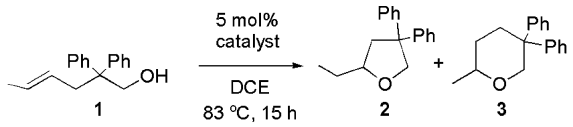
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silver(I) triflate is an excellent catalyst for intramolecular hydroalkoxylation and hydroacyloxylation of inert olefins. The hydroalkoxylation of olefins has traditionally been mediated by stoichiometric amounts of toxic metal ions, followed by reduction.<sup>14</sup> Catalytic processes for such transformations are limited, particularly for unactivated olefins.<sup>15</sup> While palladium has been used to catalyze addition of different nucleophiles to olefins, subsequent  $\beta$ -hydride elimination reactions often occur to give the unsaturated products.<sup>16</sup> Recently, platinum,<sup>17</sup> gold,<sup>18</sup> tin,<sup>19</sup> ruthenium,<sup>20</sup> and iridium<sup>21</sup> have been shown to act as good catalysts for intramolecular and intermolecular hydroalkoxylation of unactivated olefins. These metals are either toxic or relatively expensive. We report here a simple and economic method for mediating such a transformation.

The cyclization reaction of 2,2-diphenyl-4-hexene-1-ol **1** to afford the cyclic ethers **2** or **3** was used in our initial screening of potential catalysts. We discovered that 5 mol % of silver(I) triflate efficiently catalyzes this reaction. The products were obtained in excellent yield (>95%) after 15 h at 83 °C in 1,2-dichloroethane (Table 1). The use of other

**Table 1.** Efficiency of Intramolecular Hydroalkoxylation of Olefins Mediated by Selected Lewis Acids



entry	catalyst	yield <sup>a</sup> (%)
1	CF <sub>3</sub> CO <sub>2</sub> Ag	0
2	C <sub>6</sub> H <sub>5</sub> CO <sub>2</sub> Ag	0
3	AgOTf	0
4	AgNO <sub>3</sub>	0
5	AgOTf	>95 (10:1)
6	AgOTf/5.5 mol % of Ph <sub>3</sub> P	<10
7	AgOTf/5.5 mol % of (C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub> P	90 (10:1)
8	Zn(OTf) <sub>2</sub>	0
9	Sc(OTf) <sub>3</sub>	50

<sup>a</sup> Yield based on <sup>1</sup>H NMR using an internal standard.

silver salts failed to yield the desired products as revealed by <sup>1</sup>H NMR (Table 1, entries 1–4). The reaction also occurred in the presence of an electron-deficient ligand (Table 1, entry 7), whereas less than 10% conversion was

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obtained when triphenylphosphine was used (Table 1, entry 6). No product was observed with Zn(OTf)<sub>2</sub> in a control experiment. With Sc(OTf)<sub>3</sub> as the Lewis acid, a 50% product yield was obtained.

Further investigation into the scope of this reaction indicated that good to excellent yields can be obtained with a range of substrates, as shown in Table 2. The reaction gives

**Table 2.** Silver(I)-Catalyzed Intramolecular Addition of Hydroxyl Groups to Olefins<sup>a</sup>

entry	substrate	product	yield <sup>b</sup>
1			96% <sup>c</sup>
2			95% <sup>c</sup>
3			89% (10 : 1) <sup>d</sup>
4			95%
5			86% (2.7 : 1) <sup>d,f</sup>
6			88%
7			72%
8	R = H	R = H	89%
9	R = TIPS	R = TIPS	52% <sup>e</sup>
10	R = Ac	R = Ac	98%
11	R = Bz	R = Bz	94%
12			71% <sup>f</sup>
13			84%
14			87%

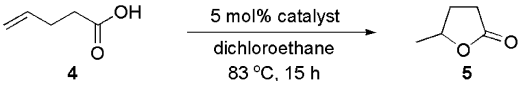
<sup>a</sup> Reactions were conducted with 1–2 mmol of substrate and 5 mol % of AgOTf in 4–6 mL of dichloroethane at 83 °C for 15 h. <sup>b</sup> Isolated yields are reported here. <sup>c</sup> <sup>1</sup>H NMR yields based on an internal standard. <sup>d</sup> Ratio based on isolated yields. <sup>e</sup> When 5 mol % of HOTf was used as catalyst, the isolated yield was <10%. <sup>f</sup> Reaction completed in 36 h.

preferentially the Markovnikov ethers as expected. Similar regioselectivity has been observed for the platinum-based system.<sup>17</sup> The reaction of terminal  $\gamma$ -hydroxyl alkenes leads exclusively to the formation of the 5-*exo* cyclization products

in good to excellent yields (Table 2, entries 1, 4, and 5). The use of a terminal monosubstituted olefin gave a mixture of the 5-*exo* and 6-*endo* cyclic products with the 5-*exo* product significantly favored (Table 2, entry 3). However, the 6-*endo* cyclic ethers were found to be the sole products for terminal di-substituted alkenes (Table 2, entries 2 and 13) and a  $\gamma$ -hydroxyl alkene with a phenyl substitution at the terminus (Table 2, entry 14). This reaction is general for alkenes bearing various substitutions at the  $\alpha$ ,  $\beta$  and  $\gamma$ -carbon atoms and tolerates different functional groups. The silver(I) triflate-catalyzed hydroalkoxylation is also applicable to the synthesis of fused- and spirobicyclic ethers in good yields (Table 2, entries 6 and 12).

Expanding our investigation to carboxylic acids, we again found that silver(I) triflate was the optimal catalyst while other silver or triflate salts failed to catalyze the reaction, with the exception of scandium(III) triflate, though at lower yields than silver triflate (Table 3). Similarly, the efficiency

**Table 3.** Efficiency of Intramolecular Additions of Carboxylic Acids to Olefins<sup>a</sup>



entry	catalyst	yield <sup>a</sup> (%)
1	CF <sub>3</sub> CO <sub>2</sub> Ag	0
2	C <sub>6</sub> H <sub>5</sub> CO <sub>2</sub> Ag	0
3	AgOTs	0
4	AgF	0
5	AgNO <sub>3</sub>	0
6	AgOTf	>95
7	Zn(OTf) <sub>2</sub>	0
8	Sc(OTf) <sub>3</sub>	70

<sup>a</sup> Yield based on <sup>1</sup>H NMR using an internal standard.

and regioselectivity of hydroacyloxylation is also sensitive to terminal olefinic substitution (Table 4). Testing our reaction conditions on hex-5-enoic acid resulted in the predominant formation of the six-membered ring (Table 4, entry 9), along with small amounts of the five-membered ring. The formation of the five-membered ring presumably comes from olefin migration catalyzed by silver(I); similar chemistry has been observed recently with gold(I) as well.<sup>18</sup> The strictly *cis* relation of the substitutions on the two bridgehead carbons can be always seen in the formation of the fused ring systems for substrates containing either an alcohol (Table 2, entry 12) or a carboxylic acid (Table 4, entry 8) as the nucleophiles.

Our proposed mechanism for the silver(I) triflate-mediated hydroalkoxylation or hydroacyloxylation is shown in Scheme 1. The silver(I) ion binds and activates the double bond, which is then attacked by the oxygen-nucleophile on the opposite face. This affords an intermediate with the newly formed carbon–oxygen bond positioned *trans* to the silver–carbon bond. Subsequent proton-transfer results in the

**Table 4.** Silver(I)-Catalyzed Intramolecular Addition of Carboxylic Acids to Olefins<sup>a</sup>

entry	substrate	product	yield <sup>b</sup>
1			74%
2			88%
3			96%
4			93% (3.2 : 1) <sup>c</sup>
5			85%
6			94% (1.7 : 1) <sup>c,d</sup>
7			75%
8			89% <sup>d</sup>
9			91% (1 : 10) <sup>c</sup>

<sup>a</sup> Reactions were conducted under the conditions described in Table 2.

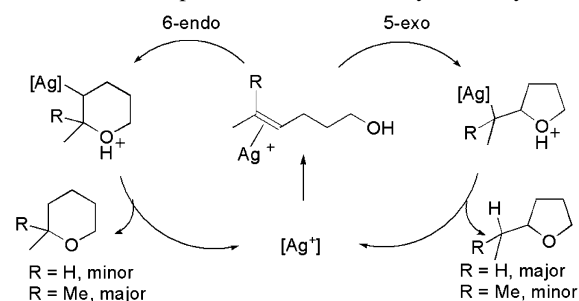
<sup>b</sup> The isolated yields are reported here. <sup>c</sup> Ratio based on isolated yield.

<sup>d</sup> Reaction completed in 36 h.

formation of the product and regeneration of the silver(I) catalyst.

We monitored the intramolecular silver(I)-catalyzed hydroalkoxylation of olefin **1** with <sup>1</sup>H NMR spectroscopy.<sup>22</sup>

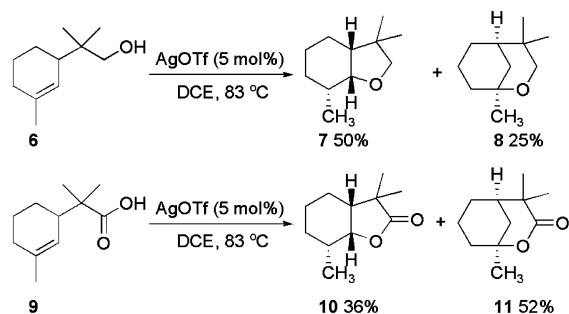
**Scheme 1.** Proposed Mechanism for Hydroalkoxylation



Addition of silver(I) triflate to an equimolar solution of olefin **1** in methylene chloride- $d_2$  results in significant lower field shifts of the alkene proton signals in the  $^1\text{H}$  NMR spectrum at room temperature. The similar signal shifts were also observed at room temperature in 1,2-dichloroethane- $d_4$  while further shifts occur upon heating to 80 °C. The reaction was followed by  $^1\text{H}$  NMR at 80 °C. A smooth formation of the desired product and a steady decrease of the olefin signals were observed. These results indicate that the silver(I) ion interacts with the olefin to form a  $\pi$ -complex<sup>11</sup> during the course of the reaction. Potential release of triflic acid via metathesis of the silver(I) ion with the OH bond of the substrate is not likely the mechanism. In fact,  $\text{Zn}(\text{OTf})_2$  and  $\text{Sc}(\text{OTf})_3$  can interact with alcohols more strongly than silver(I). Yet,  $\text{Zn}(\text{OTf})_2$  is inactive and  $\text{Sc}(\text{OTf})_3$  gives a lower conversion than silver(I) triflate (Table 1). The activity of the silver(I) ion can be tuned with ligands (entries 6 and 7, Table 1) and the fact that some acid-sensitive groups can be tolerated (entries 7 and 9, Table 2) further support this notion. In fact, 5% HOTf was used as a control for a TIPS protected substrate (entry 9, Table 2) and less than 10% of the desired product (with TIPS on) was isolated under the same reaction conditions.

Two additional substrates (**6** and **9** in Scheme 2) were prepared to probe the stereoselectivity of the silver(I)-catalyzed reaction. Products **7** and **8** were isolated in a 2:1 ratio under the standard reaction conditions with substrate **6**. Similarly, reaction with **9** was carried out to give **10** (36%) and **11** (52%). The substituents on the bridgehead carbons of products **7** and **10** have a strictly cis geometry to the neighboring methyl groups.<sup>23</sup> This observation indicates that the nucleophile attacks the face of the double-bond opposite

**Scheme 2.** Investigation of Stereochemistry



to which silver is bound in the intermediate state, supporting our proposed mechanism.

In summary, we present here the silver(I)-catalyzed intramolecular addition of hydroxyl or carboxyl groups to unactivated olefins to form cyclic ethers or lactones, respectively. The use of silver is economic as compared to stoichiometric amounts of toxic metal ions or catalytic amounts of expensive transition metal ions employed previously. This procedure may also be expanded to other types of additions to simple olefins.

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**Supporting Information Available:** Experimental details and Figure S1–S13. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(22) For details, see Figures S1–S13 in the Supporting Information.

(23) The assignment of the stereochemistry of compound **7** is based on the 2D NMR experiments (for details, see the Supporting Information). Similarly, we determine the stereochemistry of compound **10** by comparison with compound **7**. And also see: Doyle, M. P.; Kalinin, A. V.; Ene, D. G. *J. Am. Chem. Soc.* **1996**, *118*, 8837–8846.