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Cationic Carbohydroxylation of Alkenes and Alkynes Using the Cation Pool Method

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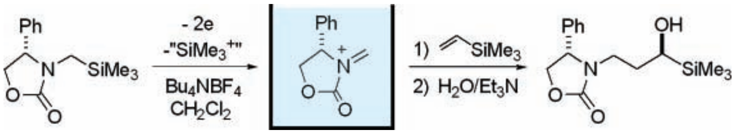
ABSTRACT

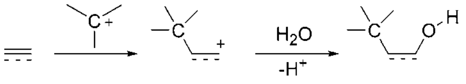


The reactions of an *N*-acyliminium ion pool with alkenes and alkynes gave γ-amino alcohols and β-amino carbonyl compounds, respectively, after treatment with H_2O/Et_3N. The present reaction serves as an efficient method for cationic carbohydroxylation of alkenes and alkynes. When vinyltrimethylsilane was used as an alkene, the reaction was highly diastereoselective and served as an access to an enantiomerically pure α-silyl-γ-amino alcohol.

Carbo-oxylation (carbohydroxylation and carboalkoxylation), where an organic group and an oxy (hydroxyl or alkoxy) group add across a carbon−carbon double bond or triple bond, is an important transformation in organic synthesis. Several methods involving radical,[1] photochemical,[2] and transition metal catalyzed[3] reactions have been developed to do so. 1,3-Dipolar cycloaddition of nitrile oxides[4] and nitrones[5] followed by the cleavage of the N−O bond of the cycloadducts also serves as good and efficient methods for carbohydroxylation.

The addition of a carbocation to a carbon−carbon multiple bond, followed by the quenching of the resulting carbocation by water, also serves as a good and efficient method for carbohydroxylation (Scheme 1). However, only a few papers on cationic carbohydroxylation have appeared in the literature[6,7] Stimulated by the straightforwardness of this approach, we have investigated cationic carbohydroxylation using the "cation pool" method[8] that we have recently developed and report here our findings.

Scheme 1. Cationic Carbohydroxylation



In the "cation pool" method, carbocations are generated by low-temperature electrochemical oxidation and accumu-

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[1] Wetter, C.; Jantos, K.; Woithe, K.; Studer, A. *Org. Lett.* **2003**, *5*, 2899.

[2] Bach, T. *Tetrahedron Lett.* **1994**, *35*, 1855.

[3] (a) Nakamura, H.; Sekido, M.; Ito, M.; Yamamoto, Y. *J. Am. Chem. Soc.* **1998**, *120*, 6838. (b) Monteiro, N.; Balme, G. *Synlett* **1998**, 746. (c) Fürstner, A.; Szillat, H.; Stelzer, F. *J. Am. Chem. Soc.* **2000**, *122*, 6785. (d) Nakamura, I.; Bajracharya, G. B.; Mizushima, Y.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2002**, *41*, 4328.

[4] (a) Kozikowski, A. P.; Chen, Y.-Y.; Wang, B. C.; Xu, Z.-B. *Tetrahedron* **1984**, *40*, 2345. (b) Kanemasa, S.; Nishiuchi, M.; Kamimura, A.; Hori, K. *J. Am. Chem. Soc.* **1994**, *116*, 2324. (c) Bode, J. W.; Carreira, E. M. *J. Am. Chem. Soc.* **2001**, *123*, 3611 and references therein.

[5] For example, see: (a) Goti, A.; Cacciarini, M.; Cardona, F.; Cordero, F. M.; Brandi, A. *Org. Lett.* **2001**, *3*, 1367. (b) Brandi, A.; Cicchi, S.; Paschetta, V.; Pardo, D. G.; Cossy, J. *Tetrahedron Lett.* **2002**, *43*, 9357 and references therein.

[6] (a) Bott, K. *Tetrahedron Lett.* **1970**, 4301. (b) Bott, K. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 171. For examples of intramolecular carbohydroxylation using acyliminium ions, see: Royer, J.; Bonin, M.; Micouin, L. *Chem. Rev.* **2004**, *104*, 2311.

[7] In cationic polymerization, an active polymer end is usually trapped by the reaction with an alcohol. Therefore, the last step of cationic polymerization is carboalkoxylation, although transfer reactions also take place before quenching. For example, see: *Cationic Polymerization Fundamentals and Applications*; Faust, R., Schaffer, T. D., Eds.; American Chemical Society: Washington, DC, 1997.

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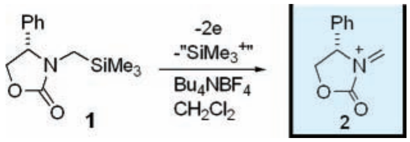
lated in the absence of nucleophiles. The “cation pool” method has been successfully applied to the generation and reactions of *N*-acyliminium ions and alkoxycarbenium ions. We envisioned that the reaction of a “cation pool” with an alkene or alkyne followed by the trapping of the resulting carbocation by water would lead to the formation of the corresponding carbohydroxylation product. The concept works.

We chose to study the *N*-acyliminium ion **2** generated from **1** as shown in Scheme 2 because of the following reasons: the carbonyl group is expected to interact strongly with the carbocation generated by the addition to an alkene or alkyne (vide infra) and stabilize it; without such stabilization, the second carbocation would decompose before the workup with water. It is also important to note that the 4-phenyl-2-oxazolidinone[9] group is easily removed after the carbohydroxylation. Another important feature of **2** is the possibility of asymmetric induction.[9]

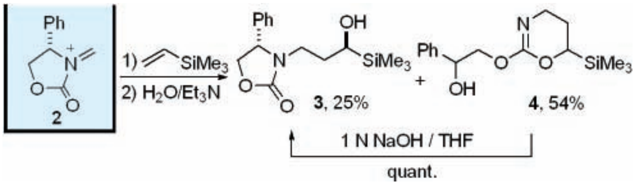
Scheme 2. Formation of *N*-Acyliminium Ion Pool **2**



Thus, *N*-acyliminium ion **2** was generated by the anodic oxidation of silyl-substituted carbamate **1** having a silyl group as an electroauxiliary,[10] which was synthesized from (*S*)-4-phenyl-2-oxazolidinone in Bu_4NBF_4/CH_2Cl_2 and accumulated as a solution in the absence of a nucleophile.

We first examined the reaction with vinyltrimethylsilane. The reaction took place smoothly at −50 to −25 °C to give compounds **3** and **4** in 25% and 54% yields, respectively, after treatment with H_2O/Et_3N (Scheme 3). Both **3** and **4** were single stereoisomers. Compound **4** was easily converted into **3**, as a single stereoisomer in quantitative yield, by the treatment with 1 N NaOH in THF at room temperature for 72 h. The stereochemistry was the same as that of the compound obtained directly from **2** and vinyltrimethylsilane. The stereochemistry of **3** was determined by X-ray analysis. As shown in Figure 1, the configuration of the carbon bearing the hydroxyl group was found to be *S*.

Scheme 3. Reaction of **2** with Vinyltrimethylsilane



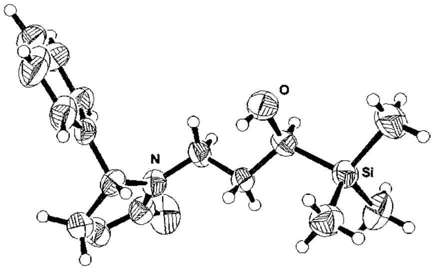
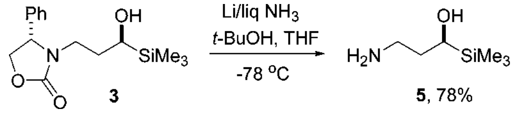


Figure 1. X-ray structure of **3**.

Therefore, the present reaction is expected to serve as an efficient method for the preparation of enantiomerically pure amino alcohols,[11] which are useful intermediates for the synthesis of various biologically interesting molecules. In fact, **3** was converted into free amino alcohol **5** as shown in eq 1.[10] Compound **5** is of potential interest from the viewpoint of its coordination ability to metals because the hydroxyl group is activated by the interaction of the oxygen p orbital with the C−Si σ orbital.[12]



(1)

The reaction of **2** with an alkyl-substituted olefin also proceeded smoothly, but products **6** and **7** were obtained as a mixture of diastereomers (eq 2). The reactions with *trans* and *cis* stilbenes gave carbohydroxylated compound **8** as a mixture of diastereomers (eqs 3 and 4). The reaction with vinyl acetate gave the corresponding aldehyde **9** presumably via the initial carbohydroxylation product (eq 5).

Although the detailed mechanism of the present reaction has not yet been established, the following speculation is reasonable (Scheme 4).

The initial reaction of **2** with an alkene presumably gives cycloadduct **10**,[13] a stabilized form of carbocation **11** (vide

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(8) (a) Yoshida, J.; Suga, S.; Suzuki, S.; Kinomura, N.; Yamamoto, A.; Fujiwara, K. *J. Am. Chem. Soc.* **1999**, *121*, 9546. (b) Suga, S.; Suzuki, S.; Yamamoto, A.; Yoshida, J. *J. Am. Chem. Soc.* **2000**, *122*, 10244. (c) Suga, S.; Okajima, M.; Yoshida, J. *Tetrahedron Lett.* **2001**, *42*, 2173. (d) Suga, S.; Suzuki, S.; Yoshida, J. *J. Am. Chem. Soc.* **2002**, *124*, 30. (e) Yoshida, J.; Suga, S. *Chem. Eur. J.* **2002**, *8*, 2650. (f) Suga, S.; Watanabe, M.; Yoshida, J. *J. Am. Chem. Soc.* **2002**, *124*, 14824. (g) Suga, S.; Nagaki, A.; Yoshida, J. *Chem. Commun.* **2003**, 354.

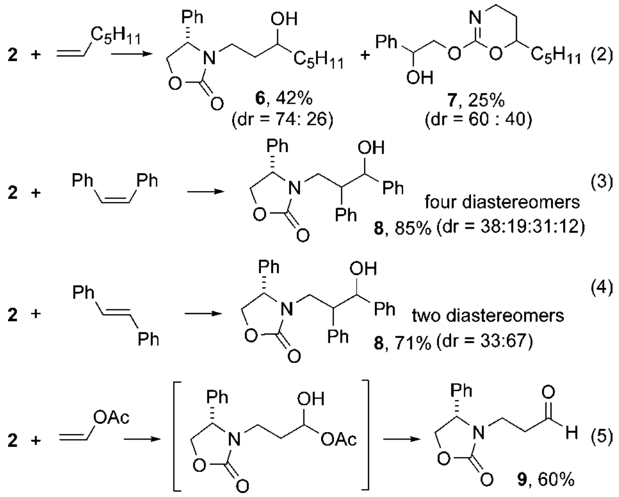
(9) (a) Leroux, M.-L.; Gall, T. L.; Mioskowski, C.; *Tetrahedron: Asymmetry* **2001**, *12*, 1817. (b) Marcantoni, E.; Mecozzi, T.; Petrini, M. *J. Org. Chem.* **2002**, *67*, 2989.

(10) Yoshida, J.; Nishiwaki, K. *J. Chem. Soc., Dalton Trans.* **1998**, 2589.

(11) For example, see: (a) Yamamoto, Y.; Komatsu, T.; Maruyama, K. *J. Chem. Soc., Chem. Commun.* **1985**, 814. (b) Barluenga, J.; Férnández-Marí, F.; Viado, A. L.; Aguilar, E.; Olano, B. *J. Org. Chem.* **1996**, *61*, 5659. (c) Toujas, J.-L.; Toupet, L.; Vaultier, M. *Tetrahedron* **2000**, *56*, 2665. (d) Kochi, T.; Tang, T. P.; Ellman, J. A. *J. Am. Chem. Soc.* **2002**, *124*, 6518. (e) Córdova, A. *Synlett* **2003**, 1651 and references therein.

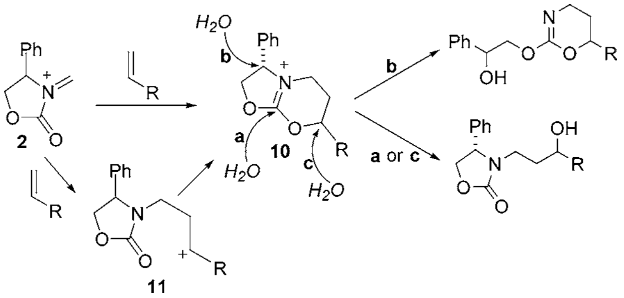
(12) (a) Yoshida, J.; Maekawa, T.; Murata, T.; Matsunaga, S.; Isoe, S. *J. Am. Chem. Soc.* **1990**, *112*, 1962. See also ref 9.

(13) Suga, S.; Nagaki, A.; Tsutsui, Y.; Yoshida, J. *Org. Lett.* **2003**, *5*, 945.



supra). In the case of vinyltrimethylsilane, a concerted [4 + 2] cycloaddition mechanism seems to be predominant,[13] and the stereochemistry of the final product should be determined in this step. In the case of alkyl- and aryl-substituted alkenes, however, a stepwise mechanism involving a intermediate **11** may also play a role, and this leads to lower diastereoselectivity. In the workup process, water attacks the carbon bearing two oxygen atoms to give carbohydroxylation products such as **3** (path a). Water may also attack the benzylic carbon to give byproducts such as **4** (path b). Another possibility to be considered is the attack of the carbon bearing R (path c). Clearly more data must be accumulated before accurate mechanistic conclusions can be drawn.

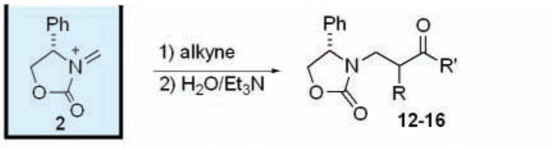
Scheme 4. Mechanism of Cationic Carbohydroxylation Using **2**



Alkynes were also quite effective for the reaction with *N*-acyliminium ion **2**, and the corresponding ketones **12**−**16** were formed in good yields as shown in Table 1. In the case of disubstituted alkynes, a mixture of two diastereomers was obtained.

Removal of the oxazolidinone group was accomplished as demonstrated by the following example (Scheme 5). Protection of the carbonyl group of **16** as an acetal followed by the reduction with Li/liq NH_3 gave **18**. Because compound **18**, which has a free amino group, was quite unstable, the amino group was immediately protected as a carbamate to obtain **19**. The removal of the acetal gave **20**.

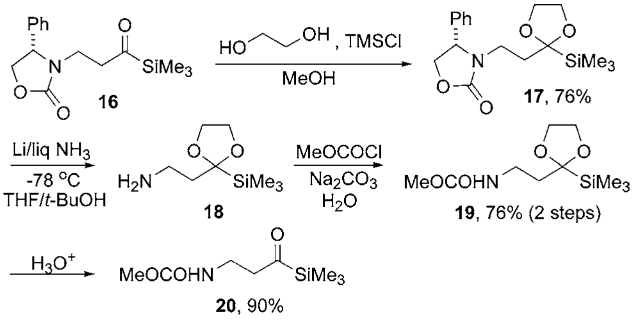
Table 1. Reaction of *N*-Acyliminium Ion **2** and Alkynes[a]



alkyne	product	yield (%)[b]
$\equiv$–C_6H_{13}	**12** (R = H, R′ = C_6H_{13})	47
$\equiv$–Ph	**13** (R = H, R′ = Ph)	63
CH_3–$\equiv$–Ph	**14** (R = CH_3, R′ = Ph)	58 (dr = 83:17)[c]
Ph–$\equiv$–Ph	**15** (R = Ph, R′ = Ph)	81 (dr = 68:32)[c]
$\equiv$–$SiMe_3$	**16** (R = H, R′ = $SiMe_3$)	70

[a] The reactions were carried out with **2** (prepared from 0.40 mmol of **1**) and an alkyne (0.36 mmol) at −25 °C for 15 min. Then 7% H_2O/Et_3N (0.4 mL) was added to the reaction mixture at the same temperature. [b] Isolated yields. [c] Diastereomer ratio was determined by NMR.

Scheme 5. Removal of the Oxazolidinone Group from **11**



The present findings offer an example of cationic carbohydroxylation of carbon−carbon multiple bonds using the “cation pool” method. It is also noteworthy that the reaction serves as a straightforward access to optically active α-silyl-γ-amino alcohols from vinylsilane. Further work aimed at revealing scope and limitations of the present reaction and its applications to synthesis is currently in progress.

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Supporting Information Available: Experimental procedures and analytical and spectroscopic data of compounds and CIF files for the X-ray structural analysis of **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

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