Communication
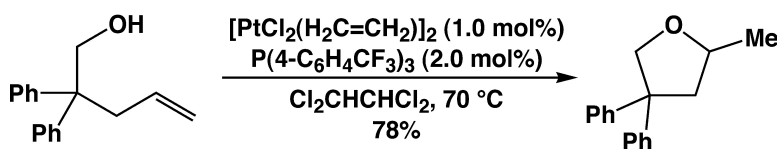
Platinum-Catalyzed Intramolecular Hydroalkoxylation of - and -Hydroxy Olefins to Form Cyclic Ethers

Hua Qian, Xiaoqing Han, and Ross A. Widenhoefer

More About This Article

Additional resources and features associated with this article are available within the HTML version:

- Supporting Information
- Links to the 12 articles that cite this article, as of the time of this article download
- Access to high resolution figures
- Links to articles and content related to this article
- Copyright permission to reproduce figures and/or text from this article

View the Full Text HTML

Platinum-Catalyzed Intramolecular Hydroalkoxylation of γ- and δ-Hydroxy Olefins to Form Cyclic Ethers

Hua Qian, Xiaoqing Han, and Ross A. Widenhoefer*

P. M. Gross Chemical Laboratory, Duke University, Durham, North Carolina 27708-0346
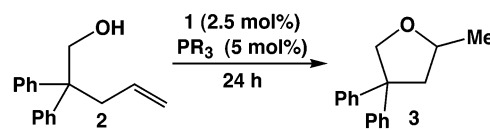
Received April 17, 2004; E-mail: rwidenho@chem.duke.edu

The prevalence of saturated oxygen heterocycles in both naturally occurring and biologically active molecules[1] including the acetogenins and polyether antibiotics has fueled interest in the development of new and efficient methods for the synthesis of cyclic ethers.[2] A particularly attractive approach to the synthesis of cyclic ethers is via the intramolecular addition of the O−H bond of an alcohol across the C≡C bond of a pendant olefin. Although olefin hydroalkoxylation is catalyzed by Brønsted acids, such approaches are of limited synthetic utility.[2,3] Rather, selective olefin hydroalkoxylation typically requires employment of a stoichiometric amount of an often toxic electrophile followed by reduction with an activated metal or metal hydride reagent in a separate step.[2,4] Transition metal catalysis represents a potential means to achieve selective olefin hydroalkoxylation under mild conditions. However, efficient catalytic hydroalkoxylation has been achieved only in the cases of C≡C[5] and activated C=C bonds such as allenes,[6] 1,3-dienes,[7] and Michael acceptors.[8−11] Here we report a mild and efficient platinum-catalyzed protocol for the intramolecular hydroalkoxylation of unactivated γ- and δ-hydroxy olefins.

Simple platinum(II) complexes including [PtCl₂(H₂C=CH₂)]₂ (**1**) catalyze the hydroalkylation,[12] hydroarylation,[13] and hydroamination[14] of unactivated olefins. On the basis of these examples, we considered that **1** might also catalyze the hydroalkoxylation of unactivated olefins. Unfortunately, the procedures optimized for C−C[12,13] and C−N[14] bond formation proved largely ineffective for the conversion of 2,2-diphenyl-4-penten-1-ol (**2**) to 2-methyl-4,4-diphenyltetrahydrofuran (**3**) (Table 1, entries 1 and 2).[15] Therefore, the efficiency of the platinum-catalyzed conversion of **2** to **3** was optimized as a function of solvent and phosphine (Table 1). From these experiments, an effective protocol was identified; reaction of **2** with a catalytic mixture of **1** (2.5 mol %) and P(4-C₆H₄CF₃)₃ (5 mol %) in Cl₂CHCHCl₂ at 70 °C for 24 h led to the isolation of **3** in 82% yield as a single regioisomer (Table 1, entry 9).[16] Effective conversion of **2** to **3** was also realized with 1% catalyst loading (Table 1, entry 10).

Platinum-catalyzed hydroalkoxylation of γ-hydroxy olefins tolerated substitution at the α, β, and γ-carbon atoms and at the internal and cis and trans terminal olefinic positions (Table 2, entries 1−15). Platinum-catalyzed hydroalkoxylation tolerated a number of functional groups including pivaloate and acetate esters, amides, silyl and benzyl ethers, and pendant hydroxyl and olefinic groups (Table 2, entries 3−9). The efficiency and regioselectivity of hydroalkoxylation was sensitive to terminal olefinic substitution. For example, whereas 5-methyl-2,2-diphenyl-4-hexen-1-ol underwent 6-*endo* cyclization in high yield, (*Z*)-2,2-diphenyl-4-hepten-1-ol underwent 5-*exo* cyclization in moderate yield (Table 2, entries 10 and 11).[15] In comparison, Pt-catalyzed cyclization of (*E*)-2,2-diphenyl-4-hexen-1-ol led to the isolation of a 3.6:1 mixture of five- and six-membered heterocycles in 63% combined yield (Table 2, entry 12). Platinum-catalyzed hydroalkoxylation was also applicable to the

Table 1. Effect of Solvent and Phosphine on the Platinum-Catalyzed Hydroalkoxylation of **2** Catalyzed by [PtCl₂(H₂C=CH₂)]₂ (**1**)

entry	PR₃	temp (°C)	solvent	yield (%)
1	none	80	dioxane	12[a,b]
2	PPh₃	80	dioxane	42[a,c]
3	PPh₃	80	CCl₄	12[a]
4	PPh₃	80	C₂H₄Cl₂	32[a]
5	PPh₃	80	C₂H₂Cl₄	65[a]
6	PPh₃	70	C₂H₂Cl₄	70[a]
7	P(4-C₆H₄OMe)₃	70	C₂H₂Cl₄	60[d]
8	P(4-C₆H₄Cl)₃	70	C₂H₂Cl₄	68[d]
9	P(4-C₆H₄CF₃)₃	70	C₂H₂Cl₄	82[d]
10	P(4-C₆H₄CF₃)₃	70	C₂H₂Cl₄	78[d,e]
11	P[3,5-C₆H₃(CF₃)₂]₃	70	C₂H₂Cl₄	49[d]
12	P(OCH₃)₃	70	C₂H₂Cl₄	45[d]
13	P(2-furyl)₃	70	C₂H₂Cl₄	76[d]

[a] GC yield versus internal standard. [b] 10 mol % of **1** employed. [c] 5 mol % of **1** and 10 mol % PPh₃ employed. [d] Isolated yield of ≥95% pure material. [e] 1 mol % of **1** and 2 mol % phosphine employed.

Scheme 1
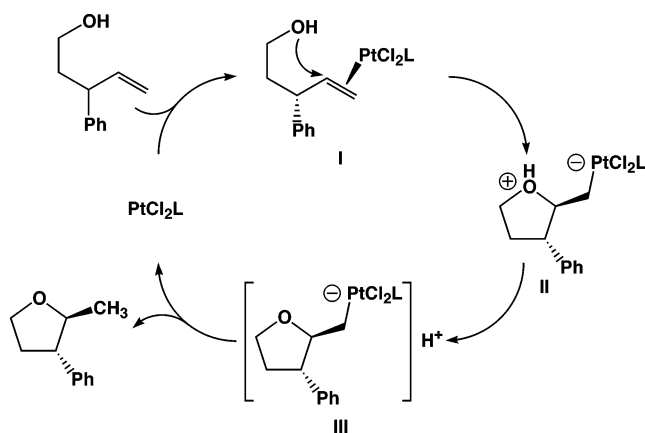
synthesis of fused- and spirobicyclic ethers (Table 2, entries 13−15) and was effective for the hydroalkoxylation of δ-hydroxy olefins to form substituted tetrahydropyran derivatives (Table 2, entries 16−19).

Both the regio- and stereoselectivity of platinum-catalyzed hydroalkoxylation parallels the selectivity observed for the oxymercuration/reduction of γ- and δ-hydroxy olefins,[2] which suggests that C−O bond formation occurs by a similar mechanism in both processes. On the basis of this analogy and by analogy to the mechanism established for the platinum-catalyzed cyclization of

Table 2. Hydroalkoxylation of γ- and δ-hydroxy Olefins (2.0 M) Catalyzed by a Mixture of [PtCl₂(H₂C=CH₂)]₂ (**1**) (1 mol %) and P(4-C₆H₄CF₃)₃ (2 mol %) in Cl₂CHCHCl₂ at 70 °C for 16−48 h

entry	alkenyl alcohol	heterocycle(s)	yield (%)[a]
1			66 (8:1)[b]
2	R = Bn		91
3	R = (CH₂)₂OH		91
4	R = (CH₂)₃OBn		79
5	R = –CH₂CH₂N(phthalimide)		73[b]
6	R¹ = Piv, R² = H		71 (1.7:1)
7	R¹ = Ac, R² = Me		92[c]
8	R¹ = TBDMS, R² = Me		75[c]
9	R¹ = TBDPS, R² = Me		84[c]
10			98[d]
11			47[b]
12	E:Z = 6:1		63 (3.6:1)[d,e]
13			87
14			98
15			69
16	R¹ = H, R² = H		92[f]
17	R¹ = Ph, R² = H		90
18	R¹ = Ph, R² = Me		50
19			60 (≥50:1)[c]

[a] Isolated product of >95% purity. [b] Reaction time = 64 h. [c] 0.5 mol % **1** and 1 mol % P(4-C₆H₄CF₃)₃ employed. [d] Reaction temperature = 80 °C. [e] 2 mol % **1** and 4 mol % P(4-C₆H₄CF₃)₃ employed. [f] NMR yield versus internal standard.

2-alkenyl indoles,[13] we propose a mechanism for platinum-catalyzed hydroalkoxylation involving outer-sphere attack of the pendant hydroxyl group on the platinum-complexed olefin of **I** to form

zwitterion **II** (Scheme 1). Although a number of pathways can be envisioned for proton transfer, we favor a mechanism involving ionization to form a contact or solvent-separated ion pair (**III**), followed by protonolysis of the Pt−C bond (Scheme 1). A similar proton-transfer pathway has been proposed for the Wacker oxidation[17] and would obviate the need to break a strong Pt−Cl bond prior to protonolysis.

In summary, we have developed a mild and efficient platinum-catalyzed protocol for the hydroalkoxylation of γ- and δ-hydroxy olefins. Our current efforts are directed toward expanding the scope and improving the efficiency of platinum-catalyzed olefin hydroalkoxylation.

Supporting Information Available: Experimental procedures and spectroscopic data for products. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) Elliot, M. C. *J. Chem. Soc., Perkins Trans 1* **2000**, 1291. (b) Elliot, M. C.; Williams, E. *J. Chem. Soc., Perkins Trans 1* **2001**, 2303. (c) Alali, F. Q.; Liu, X. X.; McLaughlin, J. L. *J. Nat. Prod.* **1999**, *62*, 504.

(2) (a) Kotsuki, H. *Synlett* **1992**, 97. (b) Koert, U. *Synthesis* **1995**, 115. (c) Cardillo, G.; Orena, M. *Tetrahedron* **1990**, *46*, 3321. (d) Larock, R. C.; Leong, W. W. In *Comprehensive Organic Synthesis*; Trost. B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol 4. (e) Boivin, T. L. B. *Tetrahedron* **1987**, *43*, 3309.

(3) Pellicciari, R.; Castagnino, E.; Fringuelli, R.; Corsano, S. *Tetrahedron Lett*. **1979**, *5*, 481.

(4) Bartlett, P. A. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1984; Vol 3, pp 411−454.

(5) (a) Sheng, Y.; Musaev, D. G.; Reddy, K. S.; McDonald, F. E.; Morokuma, K. *J. Am. Chem. Soc.* **2002**, *124*, 4149. (b) Utimoto, K. *Pure Appl. Chem.* **1983**, *55*, 1845.

(6) Hoffmann-Röder, A.; Krause, N. *Org. Lett.* **2001**, *3*, 2537.

(7) (a) Jolly, P. W.; Kokel, N. *Synthesis* **1990**, 771. (b) Utsunomiya, M.; Kawatsura, M.; Hartwig, J. F. *Angew. Chem., Int. Ed.* **2003**, *42*, 5865.

(8) (a) Hosokawa, T.; Shinohara, T.; Ooka, Y.; Murahashi, S.-I. *Chem. Lett.* **1989**, 2001. (b) Miller, K. J.; Kitagawa, T. T.; Abu-Omar, M. M. *Organometallics* **2001**, *20*, 4403.

(9) The lone example of transition metal-catalyzed olefin hydroalkoxylation is the Ru-catalyzed cyclization of *o*-alkenyl phenols, which is both inefficient and of limited scope: Hori, K.; Kitagawa, H.; Miyoshi, A.; Ohta, T.; Furukawa, I. *Chem. Lett.* **1998**, 1083.

(10) Although palladium(II) complexes activate olefins toward attack by oxygen nucleophiles, facile β-hydride elimination precludes hydroalkoxylation: (a) Hosokawa, T.; Murahashi, S.-I. *Heterocycles* **1992**, *33*, 1079. (b) Semmelhack, M. F.; Bodurow, C. *J. Am. Chem. Soc.* **1984**, *106*, 1496.

(11) For a recent examples of Pd-catalyzed olefin alkoxylation see: (a) Trend, R. M.; Ramtohul, Y. K.; Ferreira, E. M.; Stoltz, B. M. *Angew. Chem., Int. Ed.* **2003**, *42*, 2892. (b) Arai, M. A.; Kuraishi, M.; Arai, T.; Sasai, H. *J. Am. Chem. Soc.* **2001**, *123*, 2907. (c) Wolfe, J. P.; Rossi, M. A. *J. Am. Chem. Soc.* **2004**, *126*, 1620.

(12) Wang, X.; Widenhoefer, R. A. *Chem. Commun.* **2004**, 660.

(13) Liu, C.; Han, X.; Wang, X.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **2004**, *126*, 3700.

(14) Wang, X.; Widenhoefer, R. A. *Organometallics* **2004**, *23*, 1649.

(15) Olefin isomerization represented the primary side reaction in these transformations.

(16) The possibility of a significant acid-catalyzed background reaction was ruled out through control experiments (see Supporting Information).

(17) Bäckvall, J. E.; Akermark, B.; Ljunggren, S. O. *J. Am. Chem. Soc.* **1979**, *101*, 2411.

JA0477773