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Rhodium-Catalyzed Ring Opening of Vinyl Epoxides with Alcohols and Aromatic Amines

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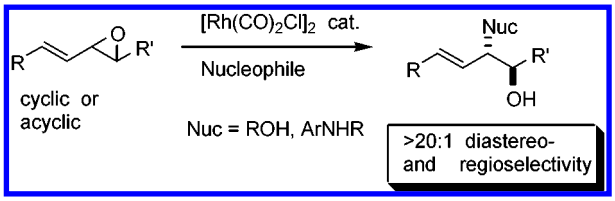
ABSTRACT

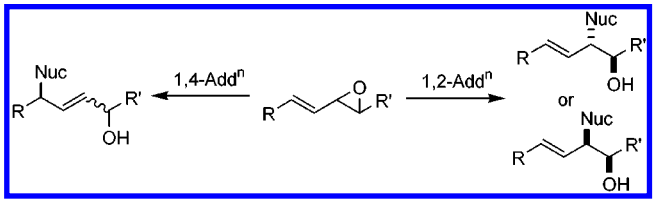


$[Rh(CO)_2Cl]_2$ is an effective catalyst for the ring opening of vinyl epoxides with alcohols and aromatic amines under neutral conditions at room temperature. The reaction occurs with excellent diastereo- and regioselectivity (>20:1) giving the *trans*-1,2-amino alcohols or alkoxy alcohols for a wide range of substrates. The regio- and stereochemistry of these reactions is complementary to that typically obtained with palladium-catalyzed ring openings of vinyl epoxides.

Vinyl epoxides are commonly used starting materials in organic synthesis.[1] Among their most important applications are as electrophiles in transition metal catalyzed reactions. The most frequently used catalysts are palladium based which permit coupling with a wide variety of nucleophiles.[2] A common trend in all of these reactions is a preference for the nucleophilic addition to occur in a 1,4-manner *syn* to the leaving group. This results from a net S_N2' addition with retention of configuration arising from a double inversion pathway.

Transition metal catalyzed reactions giving 1,2-addition products are far fewer in number. To obtain 1,2-addition with palladium, the nucleophile is typically delivered in an intramolecular fashion via a tether to give the *cis* product[3,4] (Scheme 1). While *trans*-1,2-addition products can sometimes be obtained through stoichiometric or catalytic use of Brønsted and Lewis acids, these methods suffer from poor functional group compatibility. In addition, such methods

Scheme 1. Regioselectivity in Vinyl Epoxide Ring Opening



(1) *Comprehensive Organic Synthesis*; Trost, B. M., Flemming, I., Eds.; Permagon Press: New York, 1991; Vol. 6.

(2) For a review on allylic alkylation, see: Trost, B. M.; Van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395 and pertinent references therein. For a review on allylic amination, see: Johannsen, M.; Jorgensen, K. A. *Chem. Rev.* **1998**, *98*, 1689 and pertinent references therein. For a general reference on the chemistry of palladium, see: Tsuji, J. *Palladium Reagents and Catalysis*; Wiley and Sons Ltd.: Toronto, 1995.

(3) For the use of tin alkoxides, see: Trost, B. M.; Tenaglia, A. *Tetrahedron Lett.* **1988**, *29*, 2931. Keinan, E.; Sahai, M.; Roth, Z.; Nudelman, A.; Herzig, J. *J. Org. Chem.* **1985**, *50*, 3558. For the use of cocatalytic trialkylborates with alcohols, see: Trost, B. M.; McEachern, E. J.; Toste, F. D. *J. Am. Chem. Soc.* **1998**, *120*, 12702. For the use of carbon monoxide to give cyclic carbonates, see: Trost, B. M.; Angle, S. R. *J. Am. Chem. Soc.* **1985**, *107*, 6123. For the use of aldehydes to give cyclic acetals, see: Suzuki, S.; Fujita, Y.; Kobayashi, Y.; Sato, F. *Tetrahedron Lett.* **1986**, *27*, 69. For the use of isocyanates to give oxazolidinones, see: Trost, B. M.; Sudhakar, A. R. *J. Am. Chem. Soc.* **1987**, *109*, 3792.

(4) Very recently, a palladium-catalyzed dynamic kinetic asymmetric transformation has been reported with phthalimide and vinyl epoxides giving the 1,2-addition products in good yield and excellent ee's. See: Trost, B. M.; Bunt, R. C.; Lemoine, R. C.; Calkins, T. L. *J. Am. Chem. Soc.* ASAP.

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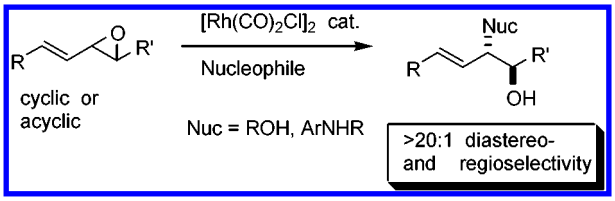
generally fail with amine nucleophiles as a result of their high basicity.[5] Given the synthetic utility of the 1,2-addition products, particularly 1,2-alkoxy alcohols and 1,2-amino alcohols, the development of a mild and selective method for their preparation from vinyl epoxides would be a desirable goal.

We now report a very mild rhodium-catalyzed reaction of vinyl epoxides that occurs at room temperature. The reaction can be conveniently run in an open flask without any special precautions. Both alcohols and aromatic amines are effective nucleophiles, giving the *trans*-1,2-addition products in greater than 20:1 diastereo- and regioselectivity (Scheme 2). Because of the mildness of the reaction

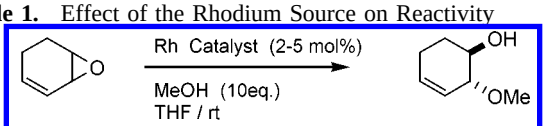
Scheme 2. Rhodium-Catalyzed Alcoholysis and Aminolysis of Vinyl Epoxides



conditions, we believe that this methodology represents an attractive alternative to the traditional Brønsted and Lewis acid mediated routes, especially when substrates contain acid-labile functionalities.

Our initial experiments focused on finding an active catalyst system with alcohol nucleophiles (Table 1). As a

Table 1. Effect of the Rhodium Source on Reactivity

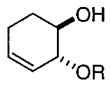
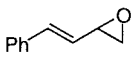
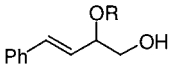
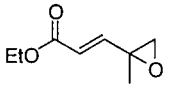
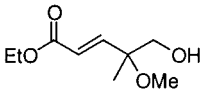
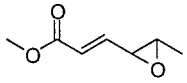
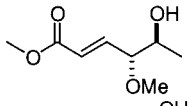
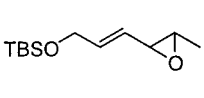
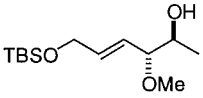


Rhodium Catalyst	Yield
$[Rh(COD)Cl]_2$ / 2DPPF	NR
$[Rh(COD)Cl]_2$ / $4P(OMe)_3$	NR
$[Rh(CO)_2Cl]_2$ / $4P(OMe)_3$	NR
Wilkinson's Cat. / $4P(OMe)_3$	NR
$[Rh(CO)_2Cl]_2$ / $4P(OMe)_3$	<10%
$[Rh(CO)_2Cl]_2$	**94%**

consequence of our ongoing studies on the asymmetric ring opening (ARO) reaction of oxabicyclic alkenes,[6] we focused our attention on rhodium complexes. Neither the catalyst shown to induce reaction in our oxabicyclic alkene studies (entry 1) nor the modified Wilkinson's catalyst used by P. A. Evans in the allylic alkylation,[7] amination,[8] and etherification[9] studies (entry 4) showed any reactivity. $[Rh(CO)_2Cl]_2$ in the absence of any added ligand (entry 6), however, produced the best results, giving the *trans*-1,2-addition product in 94% isolated yield with >20:1 diastereo- and regiselectivity.[10]

The reactivities of other alcohol nucleophiles with this substrate were examined. Both primary and secondary alcohols are effective. Phenol gives lower yields and benzyl alcohol is ineffective, giving very little desired product. The reaction is general for a wide range of vinyl epoxides (Table 2). When the ring-opened products contained a primary

Table 2. Reaction of Various Vinyl Epoxides with Alcohols

Starting Material	Product	Cond.	Yield (R)
		A	94% (Me)
		A	92% (Et)
		A	94% (^{i}Pr)
		A	55% (Ph)
		A	64% (Me)
		B	92% (Me)
		A	62% (Et)
		B	89% (Et)
		B	89% (^{i}Pr)
		B	88%
		A	89%
		B	89%

Conditions A: 1-2mol% $[Rh(CO)_2Cl]_2$, 10eq. ROH, THF
Conditions B: 1-2mol% $[Rh(CO)_2Cl]_2$, neat ROH

alcohol, a significant amount of dimeric and oligomeric byproducts were produced. By running the reactions in neat alcohol, however, the isolated yields were increased to >90%. These reactions are very mild, occurring under neutral conditions and at room temperature.

The compatibility of amine nucleophiles was also investigated. We were gratified to find that aromatic amines are highly reactive nucleophiles providing the *trans*-1,2-amino alcohols with selectivities exceeding 20:1.[10] The reaction occurs with a

(5) For use of diethylaluminum amides, see: Overman, L. E.; Flippin, L. A. *Tetrahedron Lett.* **1981**, 195. For use of amino silanes and stannanes, see: Papini, A.; Ricci, A.; Taddei, M. *J. Chem. Soc., Perkin Trans. 1* **1984**, 2261. Fiorenza, M.; Ricci, A.; Taddei, M.; Tassi, D. *Synthesis* **1983**, 640. For the use of lithium, magnesium, and zinc salts, see: Chini, M.; Crotti, P.; Macchia, F. *Tetrahedron Lett.* **1990**, *31*, 4661. For the use of amino lead reagents, see: Yamada, J.; Yumoto, M.; Yamamoto, Y. *Tetrahedron Lett.* **1989**, *30*, 4255. For the use of cobalt-catalyzed aminolysis, see: Iqbal, J.; Pandey, A. *Tetrahedron Lett.* **1990**, *31*, 575. For the use of lanthanide catalysts, see: Fu, X.-L.; Wu, S.-H. *Synth. Commun.* **1997**, *27*, 1677.

(6) Lautens, M.; Fagnou, K.; Rovis, T. *J. Am. Chem. Soc.* **2000**, *122*, 5650. Lautens, M.; Fagnou, K.; Taylor, M. *Org. Lett.* **2000**, *2*, 1677.

(7) Evans, P. A.; Nelson, J. D. *J. Am. Chem. Soc.* **1998**, *120*, 5581.

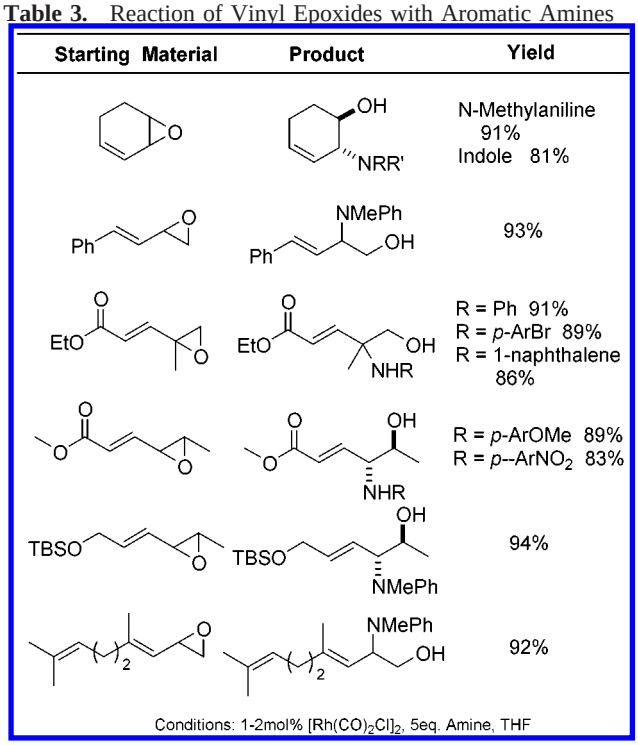
(8) Evans, P. A.; Robinson, J. E.; Nelson, J. D. *J. Am. Chem. Soc.* **1999**, *121*, 6761.

(9) Evans, P. A.; Leahy, D. *J. Am. Chem. Soc.* **2000**, *122*, 5012.

(10) For the establishment of regio- and relative stereochemistry, see Supporting Information.

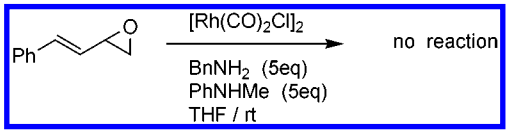
wide variety of aromatic amines, varying in both steric bulk and in basicity (e.g., both *p*-anisidine and *p*-nitroaniline are compatible nucleophiles) (Table 3).

Table 3. Reaction of Vinyl Epoxides with Aromatic Amines



Aliphatic amines fail to react under these reaction conditions. This is likely due to the amine binding strongly to the rhodium metal, resulting in catalyst poisoning. Since aromatic amines are less basic than aliphatic amines, this mode of binding would be significantly reduced. Evidence for this hypothesis is obtained by performing the reaction with 5 equiv of both *N*-methylaniline and benzylamine (Scheme 3).

Scheme 3. Effect of Added Aliphatic Amine on Aromatic Amine Addition



In the presence of the more basic amine, the aromatic amine addition pathway is shut down, indicating that the rhodium is being sequestered from the catalytic cycle.

There are two possible roles that rhodium might be playing; it can act as a mild Lewis acid, or it can insert into the carbon−oxygen bond to produce a π-allyl or enyl[7] rhodium intermediate. Preliminary mechanistic studies have shown that the presence of an olefin is required for the reaction to occur since cyclohexene oxide does not react under these conditions. Furthermore, styrene oxide does not react even after prolonged reaction times, indicating that the rhodium is likely not acting as a Lewis acid.

When vinyl epoxides possessing a terminal olefin are used, a mixture of 1,4- and 1,2-addition products is produced, analogous to the results obtained by Evans with anilines in the allylic amination of allyl carbonates.[8] In contrast to previous reports on rhodium-catalyzed allylic alkylation, amination, and etherification that occur with retention of absolute configuration, $[Rh(CO)_2Cl]_2$ promotes the ring opening of vinyl epoxides with inversion of stereochemistry at the allylic position undergoing nucleophilic attack. In our studies of ARO reactions of oxabicyclic alkenes inversion is also observed, but the reaction proceeds via a net S_N2' displacement contrary to the net S_N2 reaction that occurs with vinyl epoxides. Current studies are focused on elucidating the source of these intriguing differences.

In conclusion, we have demonstrated that $[Rh(CO)_2Cl]_2$ is an effective catalyst for the ring opening of vinyl epoxides with alcohols and aromatic amines under neutral conditions at room temperature. The reaction occurs with excellent diastereo- and regioselectivity (>20:1) giving the *trans*-1,2-addition products for a wide range of substrates. This regio- and stereoselectivity is complementary to that typically observed with palladium catalysis. The simplicity and mildness of this methodology make it an attractive option whenever substrates possess acid-sensitive groups.

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Supporting Information Available: Full characterization details including proton NMR, carbon NMR, IR, HRMS, and proof of regio- and stereochemistry. This material is available free of charge via the Internet at http://pubs.acs.org

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