CHEMISTRY LETTERS, pp. 1775-1776, 1986.

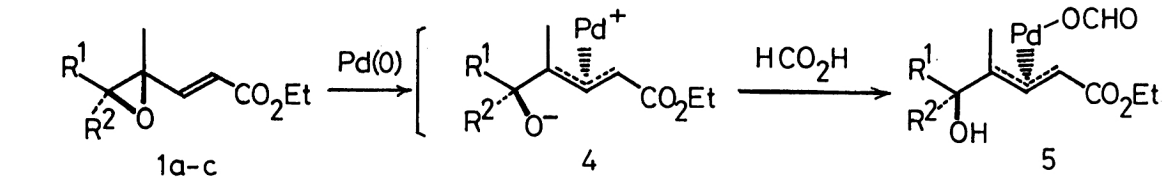
Stereoselective Synthesis of (*E*)-5-Hydroxy-4-methyl-2-alkenoates by Palladium-Catalyzed Stereospecific Hydrogenolysis of (*E*)-4,5-Epoxy-4-methyl-2-alkenoates with Ammonium Formate

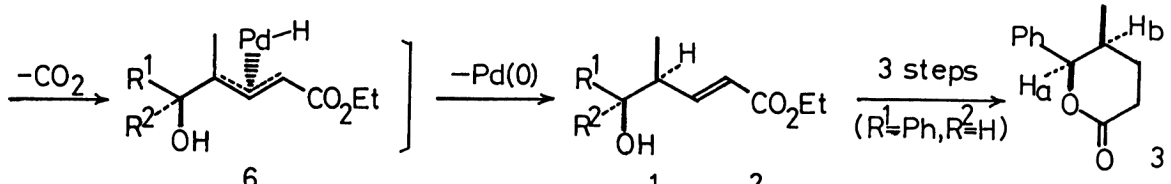
Isao SHIMIZU,* Masato OSHIMA, Mohammad NISAR,† and Jiro TSUJI†

School of Science and Engineering, Waseda University,
Ookubo 3-4-1, Shinjuku-ku, Tokyo 160
†Tokyo Institute of Technology,
Ookayama 2-12-1, Meguro-ku, Tokyo 152

Palladium-catalyzed hydrogenolysis of (*E*)-4,5-epoxy-4-methyl-2-alkenoates with HCO_2H-Et_3N gave (*E*)-5-hydroxy-4-methyl-2-alkenoates in good yields with inversion of stereochemistry.

We have reported that hydrogenolysis of butadiene monoepoxide with ammonium formate in the presence of palladium catalyst gave homoallyl alcohol with high regioselectivity.[1,2] However, stereochemistry of the palladium-catalyzed hydrogenolysis of allylic compounds with ammonium formate has not been reported.[3] Due to the practical utility of 5-hydroxy-4-methyl-2-alkenoates (2) for the synthesis of natural products such as macrocyclic antibiotics,[4] we examined both regio- and stereoselectivity of the hydrogenolysis of (*E*)-4,5-epoxy-4-methyl-2-alkenoates (1).[5] We wish to report here a facile stereoselective synthesis of (*E*)-5-hydroxy-4-methyl-2-alkenoates by palladium-catalyzed hydrogenolysis of 1 with HCO_2H-Et_3N under mild conditions.





2a R^1=Ph, R^2=H, 78%
2b R^1=Et, R^2=H, 85%
2c R^1=H, R^2=Et, 82%

In a typical experiment, (*E*)-(4S*,5S*)-4,5-epoxy-4-methyl-5-phenyl-2-pentenoate (**1a**) (2 mmol) was added to a solution of $Pd_2(dba)_3CHCl_3$ (0.05 mmol)-PBu_3 (0.05 mmol), Et_3N (0.3 cm^3) and HCO_2H (0.2 cm^3) in dioxane (10 cm^3). The mixture was stirred for 4 hours at room temperature to give the hydroxy ester **2a** in 78% yield after chromatographic purification. The hydroxy ester **2a** was hydrogenated (H_2,Pd/C), followed by subsequent hydrolysis and lactonization to give the *cis*-lactone **3a** [^{1}H NMR (CCl_4) δ 5.33 ppm (d, J_{ab}=3.0 Hz, H_a)], which proved the *syn* stereochemistry of **2a**. Similarly, **1b** was converted to the *syn*-alcohol **2b** in 85% yield. On the contrary, reaction of **1c** (as a 5:1 mixture of **1c** and **1b**)[6] gave the *anti*-alcohol **2c** (**2c**:**2b**=5:1) in 82% yield. Thus, the reaction was all stereospecific with inversion of the stereochemistry.

The reaction can be explained as follows. At first, Pd(0)-phosphine complexes coordinating the olefin **1** displace the oxide of **1** with inversion to form π-allylpalladium alkoxide complex **4**. Addition of the formic acid to the palladium complex **4** gives the π-allylpalladium formate **5**, which decarboxylates to give π-allylpalladium hydride complex **6**. Internal attack of the hydride to the more substituted carbon of the π-allylpalladium **6** gives the homoallyl alcohol **2** and Pd(0) is reproduced.

Since optically active esters can be prepared by Sharpless epoxidation of allylic alcohols,[8] the reaction presented here provides a useful method for natural product synthesis. Further mechanistic investigations and application to natural product synthesis are in progress.

This research was financially supported by the Grant-in-Aid for Encouragement of Young Scientist (No.61750830) from the Ministry of Education, Science and Culture of Japan, and the Kawakami Memorial Foundation.

References

1) J. Tsuji, I. Shimizu, and I. Minami, Chem. Lett., 1984, 1017.
2) A recent work for the palladium catalyzed reduction of allylic compounds, M. Mohri, H. Kinoshita, K. Inomata, H. Kotake, H. Takagaki, K. Yamazaki, Chem. Lett., 1986, 1177, and other references therein.
3) Inversion stereochemistry in the palladium catalyzed reduction of allylic compounds with $NaBD_4$ or Bu_3SnH has been reported. E. Keinan, and N. Greenspoon, Tetrahedron Lett., 23, 241 (1982).
4) Recent works: M. Honda, T. Katsuki, and M. Yamaguchi, Tetrahedron Lett., 25, 3857 (1984); A. I. Meyers, R. F. Spohn, and R. J. Linderman, J. Org. Chem., 50, 3633 (1985).
5) Vinyl epoxides **1a-c** were prepared from the corresponding allylic alcohols by epoxydation (t-BuOOH, $VO(acac)_2$), followed by Swern oxidation (DMSO, $(COCl)_2$, Et_3N) and subsequent Emmons-Horner reaction ($(EtO)_2P(=O)CH_2CO_2Et$, NaH).
6) Starting (*Z*)-allylic alcohol (*Z*:*E*=5:1) was prepared according to the literature. C. Sreekumer, K. P. Darst, and W. C. Still, J. Org. Chem., 45, 4260 (1980).
7) ^{13}C NMR **2b**:166.60 (s), 151.4 (d), 121.1 (d), 75.7 (d), 60.2 (t), 42.4 (d), 27.41 (t), 14.24 (q), 14.15 (q), and 10.31 (q). **2c**: 166.63 (s), 150.9 (d), 121.6 (d), 76.1 (d), 60.2 (t), 42.3 (d), 27.44 (t), 15.9 (q), 14.27 (q), and 10.18.
8) For a review, see: A. Pfenninger, Synthesis, 1986, 89.

(Received August 5, 1986)