Catalytic Asymmetric Reduction of Allylic Esters with Formic Acid Catalyzed by Palladium-MOP Complexes

Tamio Hayashi,* Hiroshi Iwamura, Masaki Naito, Yonetatsu Matsumoto, and Yasuhiro Uozumi

Catalysis Research Center and Graduate School of Pharmaceutical Sciences Hokkaido University, Kita-ku, Sapporo 060, Japan

Misao Miki and Kazunori Yanagi*

Takarazuka Research Laboratory Sumitomo Chemical Company, Limited 4-2-1, Takatsukasa, Takarazuka, Hyogo 665, Japan

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The palladium-catalyzed reduction of allylic esters with formic acid developed by Tsuji and co-workers[1] provides a convenient method for regioselective synthesis of less-substituted olefins. Mechanistic studies[2] on the catalytic reduction have revealed that the olefin is produced by reductive elimination from the key intermediate, Pd(II)(π-allyl)(hydrido)(L), which is generated by the decarboxylation of the palladium formate complex, and that the use of monodentate phosphine ligand is essential for the high regioselectivity. We report here that the catalytic asymmetric reduction forming optically active olefins is attained for the first time by use of the chiral monodentate phosphine ligand, (*R*)-2-(diphenylphosphino)-2'-methoxy-1,1'-binaphthyl ((*R*)-MOP),[3] and its biphenanthryl analog, (*R*)-MOP-phen.

Reaction of geranyl methyl carbonate ((*E*)-**1a**) with formic acid (2.2 equiv) and 1,8-bis(dimethylamino)naphthalene (1.2 equiv) in the presence of 1 mol % of a palladium catalyst generated in situ from $Pd_2(dba)_3$·$CHCl_3$ and (*R*)-MOP (P/Pd = 2/1) in dioxane at 20 °C for 16 h proceeded regioselectively to give a quantitative yield of (*S*)-3,7-dimethyl-1,6-octadiene (**2a**)[4] ($[\alpha]^{20}_D$ +7.0 (*c* 1.2, chloroform)), whose enantiomeric purity was determined to be 76% ee by an HPLC analysis (entry 1 in Table 1) (Scheme 1). The reduction of the (*Z*)-carbonate, neryl methyl carbonate ((*Z*)-**1a**), under the same reaction conditions gave the olefin (*R*)-**2a** that has essentially the same enantiomeric purity (75% ee) but has opposite absolute configuration (entry 2). The use of new chiral phosphine ligand, (*R*)-MOP-phen,[5,6] for the asymmetric reduction of (*E*)-**1a** and (*Z*)-**1a** increased the enantioselectivity to 85% ee and 82% ee, respectively (entries 3 and 4). The reduction is very slow and not regioselective with chelating bisphosphine ligands such as (*R*)-BINAP[7] (entry 5).

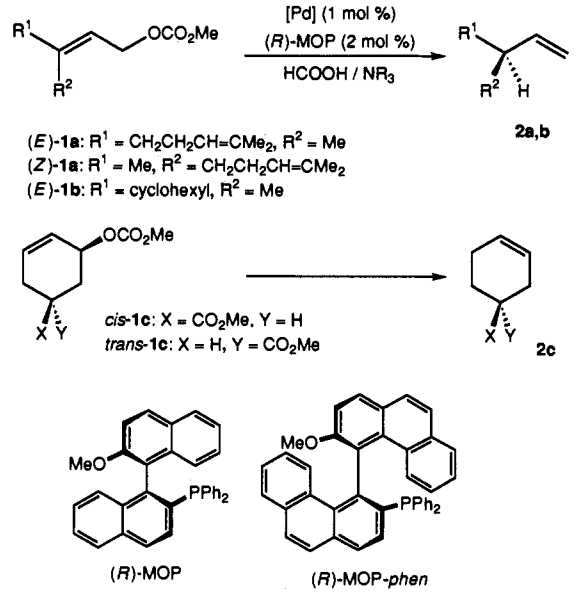
The reduction of **1a** must proceed via π-{1-(4-methyl-3-pentenyl)-1-methylallyl}palladium(II) intermediate **3**, which possibly undergoes *syn–anti* isomerization (*syn*-**3** ↔ *anti*-**3**) and epimerization ((1*R*)-**3** ↔ (1*S*)-**3**) by the σ–π–σ mechanism[8,9] (Scheme 2). The reversal of configuration of **2a** observed for the asymmetric reduction of (*E*)-**1a** and (*Z*)-**1a** demonstrates that the *syn–anti* isomerization of **3** is much slower than reduction forming **2a**. As a model for the key intermediate in the asymmetric reduction, the structure of PdCl(η^3-1,1-dimethylallyl)((*R*)-MOP) (**4**), which is readily obtained by the reaction of [PdCl(η^3-1,1-dimethylallyl)]$_2$ with (*R*)-MOP, was studied in solution and in a crystalline state. ^1H and ^{31}P NMR studies of **4** in $CDCl_3$ reveal

Table 1. Asymmetric Reduction of Allylic Carbonates **1** with Formic Acid Catalyzed by Palladium–MOP[a]

entry	allylic carbonate	ligand	conditions	yield[b] (%)	% ee (config[c])
1	(*E*)-**1a**	(*R*)-MOP	20 °C, 16 h	95 (**2a**)	76[d] (*S*)
2	(*Z*)-**1a**	(*R*)-MOP	20 °C, 14 h	99 (**2a**)	75[d] (*R*)
3	(*E*)-**1a**	(*R*)-MOP-phen	20 °C, 17 h	>99 (**2a**)	85[d] (*S*)
4	(*Z*)-**1a**	(*R*)-MOP-phen	20 °C, 15 h	>99 (**2a**)	82[d] (*R*)
5	(*E*)-**1a**	(*R*)-BINAP	40 °C, 4 days	30[e] (**2a**)	
6	(*E*)-**1b**	(*R*)-MOP-phen	20 °C, 22 h	96 (**2b**)	85[f] (*R*)
7[g]	*cis*-**1c**	(*R*)-MOP	−10 °C, 6 days	>99 (**2c**)	87[h] (*S*)
8[i]	*trans*-**1c**	(*R*)-MOP	20 °C, 13 h	90 (**2c**)	77[h] (*R*)

[a] The reduction was carried out with 2.2 equiv of formic acid in dioxane in the presence of 1.2 equiv of 1,8-bis(dimethylamino)naphthalene and 1.0 mol % of catalyst prepared in situ by mixing $Pd_2(dba)_3$·$CHCl_3$ and a chiral ligand (2 equiv of Pd). [b] Isolated yield by silica gel column chromatography. [c] Determined by the optical rotation of **2**. For **2a** in entry 3, $[\alpha]^{20}_D$ +8.1 (*c* 1.6, chloroform) (ref 4). For **2b** in entry 6, $[\alpha]^{24}_D$ +4.2 (*c* 1.9, chloroform) (Denmark, S. E.; Marble, L. K. *J. Org. Chem.* **1990**, *55*, 1984 and personal communication, (*R*)-**2b** (89% ee) $[\alpha]^{24}_D$ +4.1 (*c* 0.7, chloroform)). For **2c** in entry 7, $[\alpha]^{25}_D$ −71.7 (*c* 1.0, chloroform) (Schwartz, H. M.; Wu, W.-S.; Marr, P. W.; Jones, B. *J. Am. Chem. Soc.* **1978**, *100*, 5199, (*S*)-**2c** $[\alpha]^{25}_D$ −86.3 (*c* 1, chloroform)). [d] Determined by HPLC analysis of dianilide of 2-methylpentanedioic acid, obtained by the oxidation ($NaIO_4$/$KMnO_4$) of **2a**, with Sumichiral OA-4100 (*n*-hexane/dichloroethane/ethanol = 50/15/1). [e] A mixture of **2a** and 3,7-dimethyl-2,6-octadiene in a ratio of 30:70. [f] Determined by HPLC analysis of *N*-phenyl-2-cyclohexylpropanamide, obtained through the oxidation ($NaIO_4$/$KMnO_4$) of **2b**, with Sumichiral OA-2000 (*n*-hexane/dichloroethane/ethanol = 250/20/1). [g] The reaction was carried out with [PdCl(π-C_3H_5)]$_2$ as a catalyst precursor and triethylamine as a base in DMF. [h] Determined by GLC analysis with chiral stationary-phase column, CP Cyclodex β236M. [i] Triethylamine was used as a base.

Scheme 1



(1) (a) Tsuji, J.; Yamakawa, T. *Tetrahedron Lett.* **1979**, 613. (b) Tsuji, J.; Shimizu, I.; Minami, I. *Chem. Lett.* **1984**, 1017. (c) Tsuji, J.; Minami, I.; Shimizu, I. *Synthesis* **1986**, 623. (d) Mandai, T.; Matsumoto, T.; Kawada, M.; Tsuji, J. *J. Org. Chem.* **1992**, *57*, 1326.

(2) Oshima, M.; Shimizu, I.; Yamamoto, A.; Ozawa, F. *Organometallics* **1991**, *10*, 1221.

(3) (a) Uozumi, Y.; Hayashi, T. *J. Am. Chem. Soc.* **1991**, *113*, 9887. (b) Uozumi, Y.; Tanahashi, A.; Lee, S.-Y.; Hayashi, T. *J. Org. Chem.* **1993**, *58*, 1945.

(4) For (*R*)-**2a**: $[\alpha]_D$ −9.82 (*c* 6.18, chloroform): Arigoni, D.; Jeger, O. *Helv. Chim. Acta* **1954**, *37*, 881.

(5) Prepared from (*R*)-(−)-3,3'-dihydroxy-4,4'-biphenanthryl[6] ($[\alpha]^{20}_D$ −67 (*c* 0.13, chloroform)) in a similar manner to the preparation of (*R*)-MOP (ref 3b). (*R*)-MOP-phen: $[\alpha]^{20}_D$ +272 (*c* 1.3, chloroform); mp 209.5–210 °C.

(6) The absolute configuration was determined by its CD spectrum based on Ogoshi's report: Yamamura, K.; Ono, S.; Ogoshi, H.; Masuda, H.; Kuroda, Y. *Synlett* **1989**, 18. The previous assignment by K. Yamamoto is incorrect: Yamamoto, K.; Noda, K.; Okamoto, Y. *J. Chem. Soc., Chem. Commun.* **1985**, 1065.

(7) (*R*)-2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl: Takaya, H.; Mashima, K.; Koyano, K.; Yagi, M.; Kumobayashi, H.; Taketomi, T.; Akutagawa, S.; Noyori, R. *J. Org. Chem.* **1986**, *51*, 629.

(8) For reviews: (a) Consiglio, G.; Waymouth, R. M. *Chem. Rev.* **1989**, *89*, 257. (b) Frost, C. G.; Howarth, J.; Williams, J. M. J. *Tetrahedron: Asymmetry* **1992**, *3*, 1089.

(9) The π-allylpalladium intermediate, where C-1 carbon on the π-allyl is cis to phosphorus, can be excluded because the catalytic reduction produces the terminal olefin selectively.

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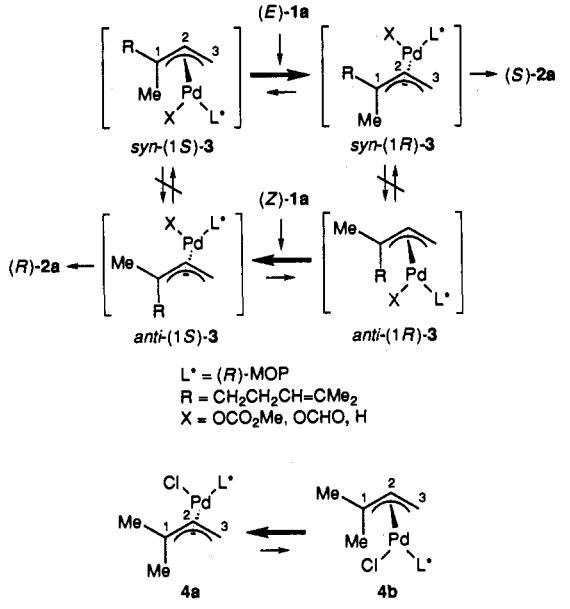
Scheme 2



that the π-allylpalladium **4** exists as a mixture of isomers which are in an equilibrium state between −60 °C and 20 °C, the ratio of major isomer to minor isomer being 4.5:1, 5.1:1, and 6.5:1 at 20 °C, −20 °C, and −60 °C, respectively.[10] Both isomers are determined by the large coupling ($^4J_{H-P}$ = *ca.* 9 and 5 Hz) between methyls on C-1 carbon and phosphorus atom to take the structures **4a** and **4b**, where C-1 carbon on the π-allyl is trans to phosphine. One of the significant features in the ^{1}H NMR[11] spectrum is that the proton on C-2 carbon on the major diastereoisomer **4a** appears at an unusually high field (2.67 ppm) compared with that of the minor isomer **4b** (4.55 ppm) and normal PdCl(π-allyl)(PR_3) complexes.[12] The X-ray crystal structure of the palladium complex **4** (Figure 1)[13] obtained by recrystallization from benzene and ether shows that the C-2 proton is in close proximity to the naphthyl ring substituted with a methoxy group, which will cause the high-field shift of the C-2 proton. Thus, the conformation in the X-ray crystal structure is assumed to be similar to that of the major isomer **4a** in solution. The stereochemical outcome forming (*S*)-**2a** observed in the catalytic asymmetric reduction of (*E*)-**1a** is accounted for by the reductive elimination of the hydrido and π-allyl from the intermediate *syn*-(1*R*)-**3** (X = H) after the equilibration between *syn*-(1*R*)-**3** and *syn*-(1*S*)-**3**, the former taking the same configuration of the π-allyl moiety as **4a**. Similarly, (*R*)-**2a** is formed from *anti*-(1*S*)-**3** after the equilibration with *anti*-(1*R*)-**3**.[14]

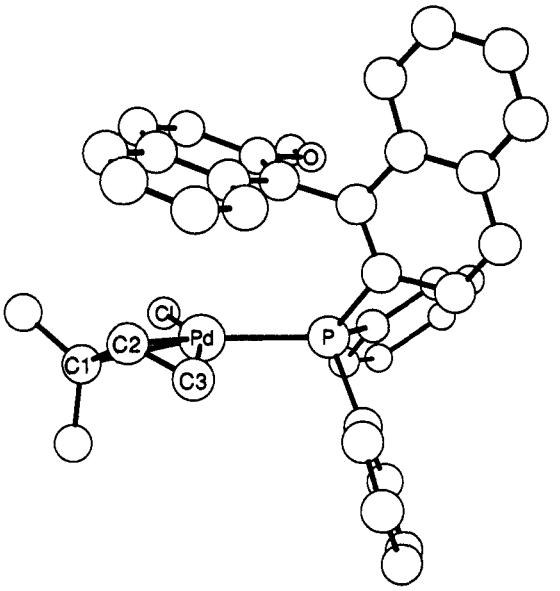


Figure 1. Molecular structure of **4a**. Selected bond distances (Å) and angles (deg): Pd–C1, 2.304(4); Pd–C2, 2.152(5); Pd–C3, 2.110(6); Pd–Cl, 2.387(1); Pd–P, 2.3098(9); C1–C2–C3, 122.6(4); C1–Pd–C2, 36.5-(2); C2–Pd–C3, 38.7(2); C1–Pd–C3, 67.9(2); C1–Pd–Cl, 90.3(2); Cl–Pd–P, 105.26(4); C3–Pd–P, 95.5(1). Twist angle between two naphthyls, 85.2(8)°.

The palladium–MOP catalyst is also effective for the asymmetric reduction of racemic 5-carbomethoxy-2-cyclohexenyl methyl carbonates **1c**, which proceeds through palladium intermediates that have meso-type π-allyl groups, and the reduction of *cis*-**1c** and *trans*-**1c** gave (*S*)-4-carbomethoxycyclohexene (**2c**) (87% ee) and (*R*)-**2c** (77% ee), respectively (entries 7 and 8 in Table 1).

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Supplementary Material Available: Experimental details for the preparation of (*R*)-MOP-phen; Tables of crysal structure data, atomic coordinates, bond lengths, bond angles, and anisotropic parameters for **4** (10 pages); listing of observed and calculated structure factors (18 pages). This material is contained in many libraries on microfiche, immediately follows this article in ordered from the ACS; see any current masthead page for ordering information.

(10) The ratios of main isomer to minor isomer of PdCl(η^3-1,1-dimethylallyl)((*R*)-MOP-phen) in $CDCl_3$ are 6:1, 10:1, and 13:1 at 20 °C, −20 °C, and −60 °C, respectively.

(11) Major isomer **4a**: ^{1}H NMR ($CDCl_3$) δ 0.94 (d, J_{H-P} = 5.2 Hz, 3 H, *anti*-Me on C-1), 1.38 (d, J_{H-P} = 8.6 Hz, 3 H, *syn*-Me on C-1), 1.53 (d, J = 10.5 Hz, 1 H, *anti*-H on C-3), 2.60 (d, J = 7.3 Hz, 1 H, *syn*-H on C-3), 2.67 (dd, J = 7.3 and 10.5 Hz, 1 H, H on C-2), 3.30 (s, 3 H, OMe), 6.96–8.04 (m, 22 H, aromatics); ^{31}P{^{1}H} NMR ($CDCl_3$) δ 20.5 (s). Minor isomer **4b**: ^{1}H NMR ($CDCl_3$) δ 1.12 (d, J_{H-P} = 5.2 Hz, 3 H, *anti*-Me on C-1), 1.66 (d, J_{H-P} = 8.9 Hz, 3 H, *syn*-Me on C-1), 2.38 (d, J = 10.5 Hz, 1 H, *anti*-H on C-3), 2.50 (d, J = 7.3 Hz, 1 H, *syn*-H on C-3), 4.55 (dd, J = 7.3 and 10.5 Hz, 1 H, H on C-2), 3.50 (s, 3 H, OMe), 6.96–8.04 (m, 22 H, aromatics); ^{31}P{^{1}H} NMR ($CDCl_3$) δ 27.3 (s).

(12) For example, the C-2 proton of PdCl(η^3-1,1-dimethylallyl)(PPh_3) appears at 5.22 ppm.

(13) Crystal data for PdCl(η^3-1,1-dimethylallyl)((*R*)-MOP) (**4**): FW 679.52, monoclinic, $P2_1$; a = 18.190(1) Å, b = 8.584(1) Å, c = 10.351(1) Å, β = 102.40(1)°, V = 1578.4 Å^3, Z = 2, D_{calcd} = 1.430 g cm^{-3} μ(Mo Kα) = 7.4 cm^{-1}, crystal dimensions, 0.3 × 0.2 × 0.2 mm^3; R = 0.029, R_w = 0.043 for 379 parameters and 3586 reflections with $I > 3\sigma(I)$. Anal. Calcd for $C_{38}H_{34}ClPdOP$: C, 67.16; H, 5.04; Cl, 5.21. Found: C, 67.04; H, 5.15; Cl, 5.07.

(14) The equilibration causing epimerization is demonstrated by the catalytic asymmetric reduction of racemic linalyl carbonate which gave nonracemic product, (*S*)-**2a** (55% ee), under the same reaction conditions.