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# Enantioselective Elimination Reaction of a 6,6-Membered Bicyclic Allylic Carbonate. Importance of Chirality Reversal Depending on the Palladium-Chiral Phosphine Ratio.

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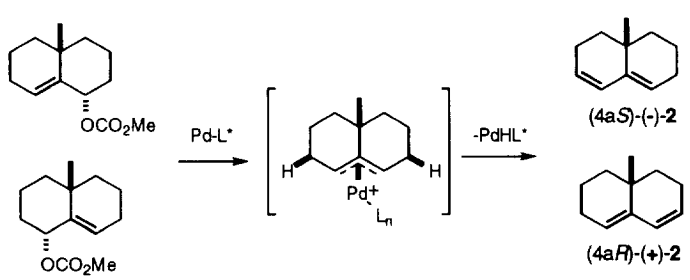
*Abstract*: Reaction of (±)-8α-methoxycarbonyloxy-4aβ-methyl-2,3,4,4a,5,6,7,8-octahydronaphthalene (**1**) in the presence of a palladium-chiral phosphine catalyst gave 4a-methyl-3,4,4a,5,6,7-hexahydronaphthalene (**2**) enantioselectively. When the reaction was carried out using $Pd(OAc)_2$ and (*S*)-(-)-BINAP, the enantioselection was influenced by the phosphine to palladium ratio, because (*S*)-BINAP oxide generated *in situ* acted as a ligand causing the opposite enantioselectivity. High enantioselectivity (86% ee) was obtained when (1-Me-$C_3H_5$-$PdCl)_2$ and (*S*)-(-)-*p*-Tol-BINAP were used.


Various types of palladium-catalyzed methods for enantioselective conversion of achiral or racemic allylic compounds into optically active compounds using chiral phosphine ligands have been reported.[1] Enantioselective nucleophilic substitutions via symmetrical 1,3-disubstituted π-allylpalladium complexes have been realized with high enantioselectivities by using various chiral phosphines. However, less explored among these reactions are enantioselective dehydrogenative elimination to produce 1,3-dienes.[2] We have realized the enantioselective elimination of the allylic bicyclic carbonate **1** to a diene **2** using a Pd-chiral phosphine catalyst (Scheme 1). In the course of our investigation, we have found that the ratio of BINAP to $Pd(OAc)_2$[3] influences the enantioselection dramatically. We now report the accomplishment of the enantioselective dehydrogenative elimination of a bicyclic allylic carbonate **1** to give **2**, and importance of the palladium-chiral phosphine ratio.




(±)-(4a*R**, 8*S**)-**1**

**Scheme 1**

The elimination reaction of **1**[4] was carried out using 5 mol% of $Pd(OAc)_2$ and various amounts of (*S*)-BINAP as the ligand in dioxane at 100 °C for 14 h. When less than 1.5 equivalents of (*S*)-BINAP to

$Pd(OAc)_2$ was used, (+)-**2**[6] was obtained as the major enantiomer (Runs 1, 2, and 3 in Table 1).[7] However, when 1.8 equivalents of (*S*)-BINAP to $Pd(OAc)_2$ was used, the enantioselection was reversed, thus, (-)-**2** was obtained in 47% ee (Run 4). When the reactions were carried out with a zero valent palladium complex, $Pd_2(dba)_3CHCl_3$, instead of $Pd(OAc)_2$, the ratio of added (*S*)-BINAP to Pd(0) did not influence the enantioselection to give (-)-**2**, even when excess (*S*)-BINAP was used (Runs 6 and 7). The results imply that (*S*)-(-)-BINAP used in combination with a Pd(0) complex gives (4a*S*)-(-)-**2**, whereas (*S*)-BINAP(O) produced during the process of reduction of $Pd(OAc)_2$ to a Pd(0) species[10] affords (4a*R*)-(+)-**2**.

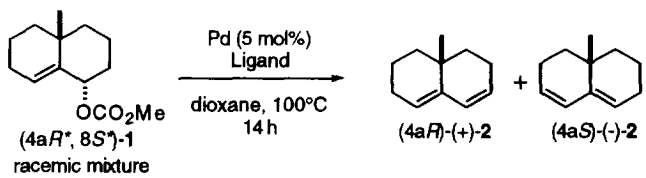
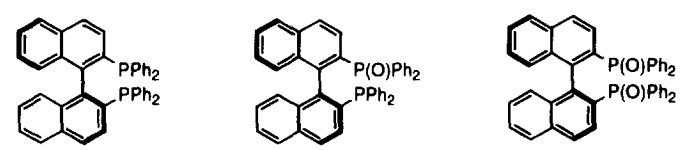



Table 1. Palladium-(*S*)-(-)-BINAP catalyzed reaction of **1**

| Run | Pd | Ligand | Ligand / Pd | Yield (%) | % ee | Rotation |
|---|---|---|---|---|---|---|
| 1 | $Pd(OAc)_2$ | (*S*)-(-)-BINAP | 1.0 | 59 | 35 | (+) |
| 2 | $Pd(OAc)_2$ | (*S*)-(-)-BINAP | 1.2 | 68 | 45 | (+) |
| 3 | $Pd(OAc)_2$ | (*S*)-(-)-BINAP | 1.5 | 60 | 6 | (+) |
| 4 | $Pd(OAc)_2$ | (*S*)-(-)-BINAP | 1.8 | 60 | 47 | (-) |
| 5 | $Pd(OAc)_2$ | (*S*)-(-)-BINAP | 2.0 | 48 | 27 | (-) |
| 6 | $Pd_2(dba)_3CHCl_3$ | (*S*)-(-)-BINAP | 1.0 | 23 | 25 | (-) |
| 7 | $Pd_2(dba)_3CHCl_3$ | (*S*)-(-)-BINAP | 2.0 | 36 | 40 | (-) |
| 8 | $Pd_2(dba)_3CHCl_3$ | (*S*)-BINAP(O) | 2.0 | 40 | 37 | (+) |
| 9 | $Pd_2(dba)_3CHCl_3$ | (*S*)-BINAP(O)$_2$ | 2.0 | 0 | - | - |




(*S*)-(-)-BINAP (*S*)-(-)-BINAP(O) (*S*)-(-)-BINAP(O)$_2$

In fact when the zero valent palladium compound, $Pd_2(dba)_3CHCl_3$, and (*S*)-BINAP(O)[11] were used, (+)-**2** was obtained with 37% ee (Run 8). No reaction proceeded when (*S*)-BINAP(O)$_2$ was used as the ligand instead of (*S*)-BINAP(O) (Run 9). These results indicate that Pd(0)-(*S*)-BINAP and Pd(0)-(*S*)-BINAP(O) have opposite enantiomeric selectivities.

Among several palladium species examined for the palladium(0)-phosphine precursors, $(1\text{-Me-}C_3H_5PdCl)_2$ gave the most satisfactory results in the presence of $Et_3N$. The results using a combination of $(1\text{-Me-}C_3H_5PdCl)_2$ and several chiral bidentate ligands are shown in Table 2. Here again, reversal of the optical activity of the diene **2** from (+)- to the (-)- enantiomer was observed when (-)-BINAP was used in 1 : 1 and

2 : 1 ratios to the palladium precursor (Runs 1 and 2). Although the reversal of the optical activity was not observed when the other chiral phosphines were used, considerable influence of the phosphine to Pd(II) ratio on the yields and ee was observed (Runs 3 to 8). The high enantioselectivity of 86 % ee was achieved when two equiv. of (-)-*p*-Tol BINAP[12] was used per 1 equiv. of Pd(II). The present results indicate that the ratio of the phosphine ligand to the Pd(II) catalyst precursor gives a critical influence in controling the asymmetric reactions. The phosphine oxide ligand produced from the initially used chiral phosphine in the process of *in situ* reduction of Pd(II) precursors to Pd(0) species can act as a non-innocent chiral ligand causing the opposite enantioselectivity from that of the unoxidized chiral phosphine systems. More attention should be paid to the chemical transformation of chiral ligands during the Pd(II) to Pd(0) reduction of Pd(II) precursors.

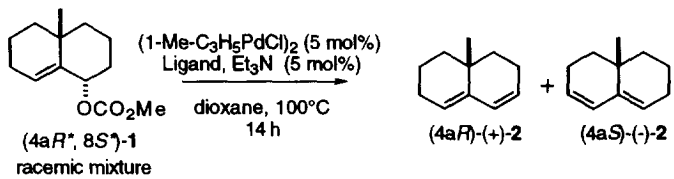



Table 2. Reaction of **1** by palladium-chiral ligand catalyst.

| Run | Ligand | Ligand / Pd | Time | Yield (%) | % ee | Rotation |
|---|---|---|---|---|---|---|
| 1 | (-)-BINAP | 1 | 8 | 41 | 28 | (+) |
| 2 | (-)-BINAP | 2 | 2 | 61 | 78 | (-) |
| 3 | (-)-DIOP | 1 | 7 | 8 | 0 | |
| 4 | (-)-DIOP | 2 | 3 | 57 | 28 | (+) |
| 5 | (-)-Chiraphos | 1 | 14 | 10 | 31 | (-) |
| 6 | (-)-Chiraphos | 2 | 5 | 54 | 44 | (-) |
| 7 | (-)-*p*-Tol-BINAP | 1 | 14 | 23 | 5 | (-) |
| 8 | (-)-*p*-Tol-BINAP | 2 | 2 | 65 | 86 | (-) |

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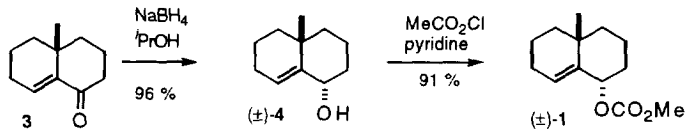
4. **1** was prepared from ketone **3**[5] as shown in the following scheme. Alcohol **4** is known: J. M. Coxon and J. R. Gibson, *Aust. J. Chem.* **1979**, *32*, 2223.

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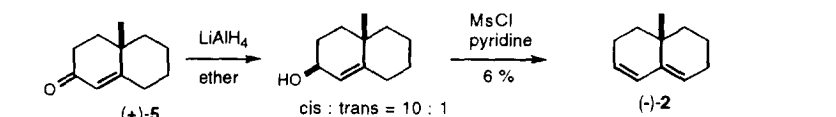
6. **2**; $^1$H NMR (270 MHz, $CDCl_3$) δ 5.94 (dd, 1H, J=2.3, 10.2 Hz), 5.67-5.55 (m, 1H), 5.40 (t, 1H, J=3.6 H), 2.36-1.23 (m, 10H), 1.02 (s, 3H); $^{13}$C NMR (67.9 MHz, $CDCl_3$) δ 140.9, 128.8, 125.7, 123.3, 37.6, 37.0, 32.2, 25.7, 23.2, 23.0, 18.5.
7. The enantiomeric excess (ee) was calculated[8] by comparing with the maximum rotation of (-)-**2**, which was prepared from the optically active (+)-**5**[9] (purchased from Kanto Chemical Company) as shown in the following scheme.




8. Optical rotations were measured on a JASCO DIP-1000 digital polarimeter using a sodium lamp (589 nm, D line).
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11. (*S*)-BINAP(O) was prepared from (*S*)-BINAP by the procedure of reference 10a. Synthesis of a cationic π-allylpalladium complex with (2-(diphenylphosphino)ethyl)diphenylphosphine oxide was reported: S. Mecking, W. Keim, *Organometallics* **1996**, *15*, 2650.
12. (*S*)-(-)-*p*-Tol-BINAP was donated by *Takasago Perfumery Co. Ltd.*

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