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Resolution of Pd Catalyst with *tropos* Biphenylphosphine (BIPHEP) Ligand by DM-DABN: Asymmetric Catalysis by an Enantiopure BIPHEP–Pd Complex[1]

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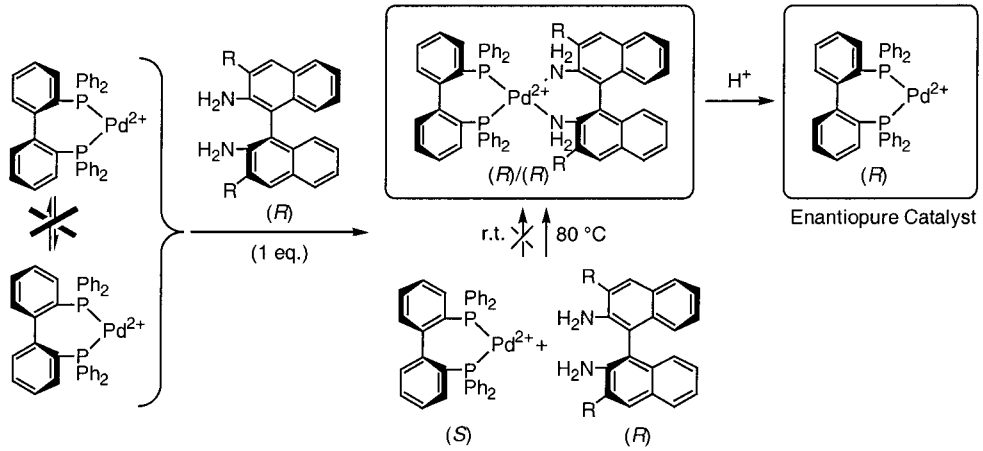
ABSTRACT



The racemic Pd complex with the chirally flexible (*tropos*) biphenylphosphine (BIPHEP) ligand can be resolved with enantiopure 3,3′-dimethyl-2,2′-diamino-1,1′-binaphthyl (DM-DABN) as a resolving agent at room temperature. The enantiopure BIPHEP–Pd complex is obtained from complexation with enantiopure DABN followed by *tropo*-inversion into the single BIPHEP–Pd diastereomer at 80 °C and protonation at 0 °C. The enantiopure BIPHEP–Pd complex can be used as an efficient Lewis acid catalyst for the Diels–Alder reaction at room temperature to give high enantioselectivity (82% ee, 60%).

Development of asymmetric catalysts for organic reactions is of central importance in modern science and technology.[2] Such asymmetric catalysts are generally metal complexes bearing chiral and often atropisomeric (*atropos*) ligands such as binaphthylphosphine (BINAP).[3] The word *atropos* is found in Greek mythology of the "Moirai", the three sisters who personificate the inescapable destiny of man. The youngest is Ατροπος (Atropos), whose name means "She who cannot (*a*) be turned (*tropos*)", and who restrictively cuts the thread of life. Thus, atropisomer covers isomers originated by stopping the turn around the bonds,[4] where

(1) This work has been presented at the Annual Meeting of the Chemical Society of Japan, March 31, 2001, no. 4H315.

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(3) We are honored to dedicte this paper to the Nobel Laureates in Chemistry, 2001.

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the isomers can be actually isolated.[5] The resolution of atropisomers[6] antedates by several years the concept of conformation[7] and the discovery of the rotational barrier in ethane.[8] The early examples of atropisomers are all biphenyl derivatives, and hence atropisomerism is called biphenyl isomerism. The tethering effect of 2,2′-positions has been studied in a latent *atropos* biphenyl (Figure 1).[9] In the case

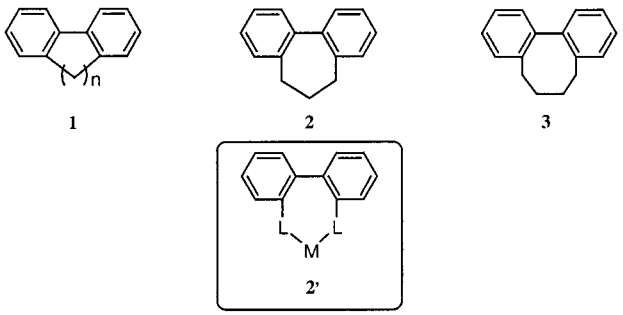

Figure 1.

of $n = 2$, **1** has been resolved but its chiral stability is not so high. Stability increases when the tether is lengthened to three but not up to four. A four-atom bridge in **3** leads to chiral lability. Compound **2** with a three-atom tether has been resolved, even without 6,6′-substituents. Therefore, a biphenyl−metal complex of type **2′** could be resolved and hence employed as a chirally stable *atropos* catalyst. We herein report the Pd complex with the *tropos* biphenylphosphine (BIPHEP)[10] ligand as an enantiopure *atropos* catalyst,[11] though in the same row as Ru. We have already reported that racemic BIPHEP−$RuCl_2$ and (*S*,*S*)-diphenylethylenediamine (DPEN) initially provide both diastereomers, $RuCl_2$[(*S*)-biphep][(*S*,*S*)-dpen] and $RuCl_2$[(*R*)-biphep][(*S*,*S*)-dpen], in an equal amount, which eventually evolved in a 2:1 diastereomer ratio, because of the *tropos* nature of the BIPHEP−Ru complex even at room temperature or below.[12,13]

A highly effective resolving agent not giving a mixture of diastereomers was thus employed for the racemic BIPHEP−Pd complex (Figure 2) to clarify whether the remaining BIPHEP−Pd enantiomer shows a *tropo*-inversion at room temperature. By using 3,3′-dimethyl-2,2′-diamino-1,1′-binaphthyl (DM-DABN)[14] with sterically demanding

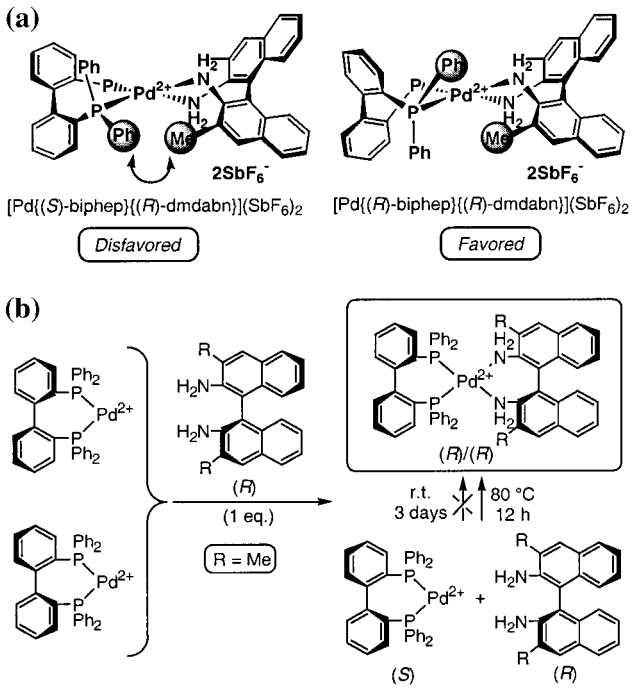

Figure 2. (a) CAChe molecular modeling study for enantiomer discrimination of racemic BIPHEP−Pd. (b) Resolution of BIPHEP−Pd using (*R*)-DM-DABN and *atropos* nature of BIPHEP−Pd complex at room temperature or below.

methyl substituents in the 3,3′-positions of diaminobinaphthyl (DABN),[15] resolution and *tropo*-inversion of the BIPHEP−Pd complex was examined (Figure 2b). Combination of racemic BIPHEP−$Pd(SbF_6)_2$[16] even with an equimolar amount of (*R*)-DM-DABN gave the single (*R*)-BIPHEP−Pd/(*R*)-DM-DABN diastereomer[17] along with the remaining (*S*)-BIPHEP−Pd and (*R*)-DM-DABN. There was no *tropo*-

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(17) [Pd{(*R*)-biphep}{(*R*)-dmdabn}]$(SbF_6)_2$: ^{1}H NMR (300 MHz, CD_2Cl_2) δ 1.68 (s, 6H) 3.44 (br, 2H), 4.83 (br, 2H), 6.60−6.62 (m, 2H), 6.74−6.78 (m, 2H), 7.12−7.23 (m, 6H), 7.33−7.60 (m, 14H), 7.71−7.87 (m, 12H) 7.91−7.95 (m, 2H). ^{31}P NMR (109 MHz, CD_2Cl_2) δ 25.1.

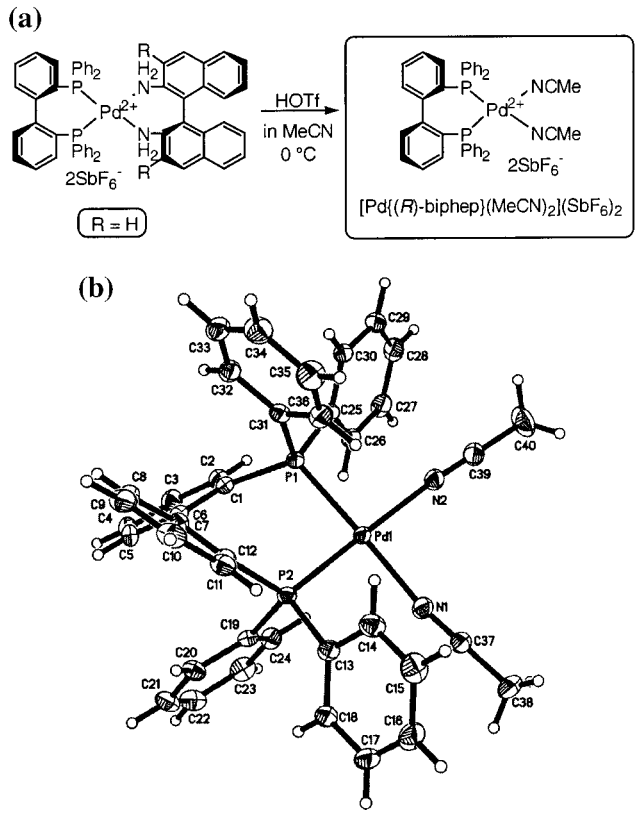


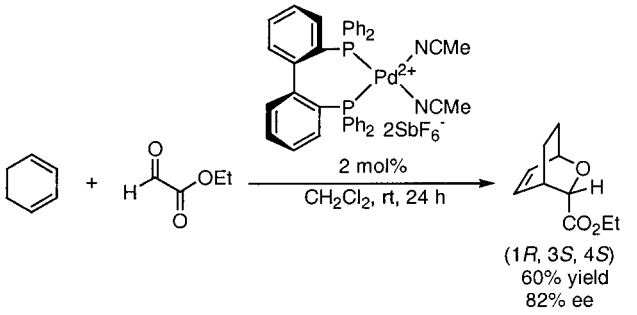
Figure 3. (a) Enantiopure [Pd{(*R*)-biphep}(MeCN)$_2$](SbF$_6$)$_2$ after *tropo*-inversion and protonation without racemization. (b) ORTEP drawing of [Pd{(*R*)-biphep}(MeCN)$_2$](SbF$_6$)$_2$.

inversion of the remaining (*S*)-BIPHEP−Pd enantiomer, which did not complex with (*R*)-DM-DABN at room temperature even after 3 days. At 80 °C for 12 h, however, the *tropo*-inversion of (*S*)-BIPHEP−Pd was indeed observed to give the single diastereomer (*R*)-BIPHEP−Pd/(*R*)-DM-DABN without any remaining (*S*)-BIPHEP−Pd. We thus clarified that BIPHEP−Pd species could be resolved as an *atropos* metal complex without *tropo*-inversion even after reasonable periods of time (>3 days) at room temperature or below.

With this success in proving the *atropos* nature of BIPHEP−Pd species at room temperature, we tried to isolate the enantiopure BIPHEP−Pd complex. However, protonation of the single (*R*)-BIPHEP−Pd/(*R*)-DM-DABN diastereomer was found to be sluggish presumably because of the steric shielding effect of the 3,3′-dimethyl substituents in DM-DABN. Therefore, the less sterically demanding DABN complex, (*R*)-BIPHEP−Pd/(*R*)-DABN (see the following paper) was employed to provide the enantiopure BIPHEP−Pd complex. Enantiopure [Pd{(*R*)-biphep}(MeCN)$_2$] (SbF$_6$)$_2$ was obtained by treatment of [Pd{(*R*)-biphep}{(*R*)-dabn}]-(SbF$_6$)$_2$ with trifluoromethanesulfonic acid in acetonitrile at 0 °C for 30 min without racemization (Figure 3a). The (*R*)-configuration of [Pd(biphep)(MeCN)$_2$](SbF$_6$)$_2$ was determined by X-ray analysis of a single crystal obtained from dichloromethane−hexane (Figure 3b).[18] There was indeed no racemization observed, as confirmed by ^{31}P and ^{1}H NMR analyses after complexation with (*S*,*S*)- and (*R*,*R*)-DPEN.[19]

The enantiopure [Pd{(*R*)-biphep}(MeCN)$_2$](SbF$_6$)$_2$ thus obtained can be employed as an *atropos* asymmetric catalyst at room temperature or below but not at 80 °C (Scheme 1).

Scheme 1. HDA Reaction Catalyzed by Enantiopure [Pd{(*R*)-biphep}(MeCN)$_2$](SbF$_6$)$_2$



Indeed, the hetero-Diels−Alder (HDA) reaction of glyoxylate could be catalyzed by enantiopure [Pd{(*R*)-biphep}(MeCN)$_2$]-(SbF$_6$)$_2$ (2 mol %) as a highly efficient Lewis acid catalyst.[20] The HDA adduct[21] was obtained with high enantioselectivity even at room temperature (82% ee, 60%).

In summary, we have proven that the racemic Pd complex even with the *tropos* BIPHEP ligand can be resolved as the *atropos* complex at room temperature or below and converted at higher temperature into the enantiopure catalyst. In carbon−carbon bond forming reactions, the enantiopure

(18) The single-crystal growth was carried out in a dichloromethane/hexane mixed solvent at room temperature. X-ray crystallographic analysis was performed with a Bruker SMART 1000 diffractometer (graphite monochromator, Mo Kα radiation, $\lambda = 0.71073$). Crystal data for [Pd{(*R*)-biphep}(MeCN)$_2$](SbF$_6$)$_2$: $C_{40}H_{34}F_{12}N_2P_2PdSb_2$, yellow, crystal dimension $0.47 \times 0.29 \times 0.18$ mm^3, monoclinic, space group $P2_1$, $a = 11.2119(5)$ Å, $b = 23.6164(10)$ Å, $c = 16.7911(7)$ Å, $V = 4249.9(3)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.848$ gcm^{-3}, μ(Mo Kα) =1.84 mm^{-1}, $T = 100$ K; 13128 reflections were independent and unique, and 571 with $I > 2\sigma(I)$ ($2\theta_{max} = 31.52°$) were used for the solution of the structure. $R = 0.0336$, w$R2 = 0.0617$. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-173072. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, U.K. (Fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk). Selective bond lengths [Å], bond angles [deg], and torsion angle [deg]: Pd1−P1 2.2502(5), Pd1−P2 2.2496(5), Pd1−N1 2.0882(17), Pd1−N2 2.0866(17); P1−Pd1−P2 90.152(18), N1−Pd1−N2 87.79(7): C1−C6−C7−C12 62.92.

(19) Mixture of [Pd{(*R*)-biphep}{(*R*,*R*)-dpen}](SbF$_6$)$_2$ and [Pd{(*R*)-biphep}{(*S*,*S*)-dpen}](SbF$_6$)$_2$: ^{1}H NMR (300 MHz, CD$_2$Cl$_2$) δ 2.01 (m, 2H, NH$_2$), 2.49 (m, 2H, NH$_2$), 3.41 (m, 2H, NH$_2$), 4.25 (m, 2H, NH$_2$), 4.63 (m, 2H, C*H*-NH$_2$), 4.72 (m, 2H, C*H*-NH$_2$). ^{31}P NMR (109 MHz, CD$_2$Cl$_2$) δ 23.0 (*R*)/(*R*,*R*), 23.3 (*S*)/(*R*,*R*).

(20) **Typical Experimental Procedure.** To a solution of [Pd{(*R*)-biphep}{(*R*)-dabn}](SbF$_6$)$_2$ (0.01 mmol, 2 mol % of ethyl glyoxylate) in CH$_2$Cl$_2$ (1 mL) was added ethyl glyoxylate (0.5 mmol) and 1,3-cyclohexadiene (0.75 mmol) at room temperature under argon atmosphere. The reaction mixture was stirred at room temperature for 24 h, directly loaded onto a silica gel column, and elutedd with hexane/ether (3:2) to give HDA product as an colorless oil.

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BIPHEP−Pd complex thus obtained can be used as an *atropos* and efficient asymmetric catalyst to give high enantioselectivity even starting from the racemic BIPHEP−Pd complex.

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