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Tropos or *Atropos* Nature of Rhodium Complexes Bearing a Tetrakis(phosphanyl)terphenyl Ligand: Highly Enantioselective Catalysis of Ene-Type Cyclization

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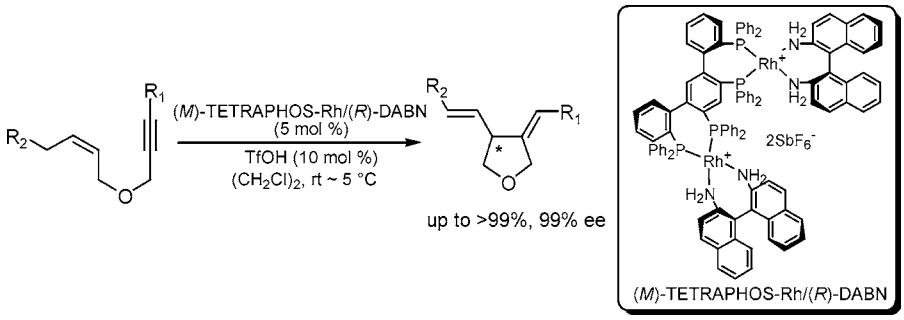
ABSTRACT



Not only axial but also helical chirality of *tropos* TETRAPHOS–Rh complexes can be controlled by chiral diamines. The flexibility of the TETRAPHOS–Rh complex is increased by association of DABN. In contrast, the diamine-free complex is chirally more stable than the BIPHEP counterpart. The higher levels of enantioselectivity in ene-type cyclization of 1,6-enynes can thus be achieved even at room temperature by the diamine-free TETRAPHOS–Rh complex.

Asymmetric catalysts for organic reactions are generally metal complexes bearing chiral and atropisomeric ligands such as BINAP and BINOL, which can provide the C_2-symmetric reaction centers to achieve asymmetric catalysis.[1] Enantiopure atropisomeric ligands usually require the enantioresolution or synthetic transformation from chiral pools. Since the word *atropos* consists of "*a*" meaning "not" and "*tropos*" meaning "turn" in Greek, the chirally rigid or flexible nature of axis, planar, center, and helicity on chiral ligands can be called *atropos* or *tropos*, respectively.[2] We have already reported Rh complexes bearing *tropos* 2,2′-bis(diphenylphosphino)biphenyl (BIPHEP) ligands,[2,3] of which the axial chirality can be controlled by a chiral diamine.[4] We have also reported Pd complexes with *tropos* 2,4′,6′,2″-tetrakis(diphenylphosphino)[1,1′;3′,1″]terphenyl (TETRAPHOS) ligand, which shows nonplanar helicity[5] proven by X-ray analysis (Scheme 1).[6] Herein, we report that the TETRAPHOS−Rh complex with aromatic 2,2′-diamino-1,1′-binaphthyl (DABN) diamine is more flexible

(1) Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H. *Comprehensive Asymmetric Catalysis*; Springer: Berlin, 1999; Vols. 1−3.

(2) (a) Mikami, K.; Aikawa, K.; Yusa, Y.; Jodry, J. J.; Yamanaka, M. *Synlett* **2002**, *10*, 1561−1578. Oki has discussed the borderline between *tropos* and *atropos* nature. A half-life of 1000 s (16.7 min) is considered as the minimum requirement for *atropos* biphenyl. The free energy of activation is necessary more than ca. 22.3 kcal/mol (93.2 kJ/mol) to isolate it at room temperature (300 K): (b) Oki, M.; Yamamoto, G. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 266−270. (c) Oki, M. *Top. Stereochem.* **1983**, *14*, 1−81.

(3) (a) Desponds, O.; Schlosser, M. *Tetradedron Lett.* **1996**, *37*, 47−48. (b) Desponds, O.; Schlosser, M. *J. Organomet. Chem.* **1996**, *507*, 257−261.

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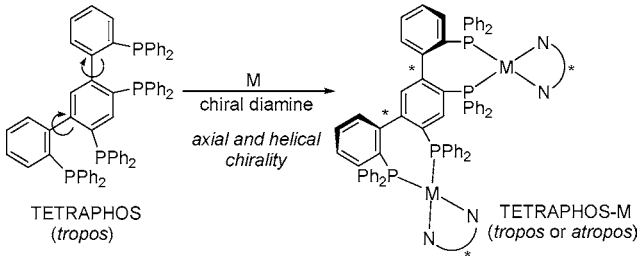
Scheme 1. Control of Axial and Helical Chirality



than the BIPHEP counterpart with DABN to isomerize to the single diastereomer much faster. In sharp contrast, the diamine-free TETRAPHOS−Rh complex is more rigid than the BIPHEP counterpart. The single enantiomer of TETRAPHOS complex thus controlled can be used efficiently for an asymmetric ene-type cyclization even at room temperature.

TETRAPHOS−Rh complex **1** was readily obtained from TETRAPHOS ligand and 2.0 equiv of $[Rh(nbd)_2]SbF_6$ in CH_2Cl_2.[7] When the axial chirality of racemic complex **1** is *S*,*S*, the helical chirality is *P* (plus), namely clockwise around the helix axis.[6] In the case of *R*,*R*, the helical chirality is *M* (minus). The *meso* diastereomer complex having axial chirality of *S*,*R* was not obtained, apparently due to steric repulsion between two diphenylphosphine units.

The dynamic behavior of the TETRAPHOS−Rh complex with diamines was thus examined (Figure 1). The combination of the racemic TETRAPHOS−Rh complex **1** and 2.0 equiv of (*R*)-DABN in CD_2Cl_2 under hydrogen (1 atm) gave a mixture of diastereomers in 67:33 ratio ((*M*)/(*R*)/(*R*)-**2** : (*P*)/(*R*)/(*R*)-**2**) though in a selective manner at room temperature for 30 min. The isomerization took place in CD_2Cl_2 at room temperature, leading eventually to the single diastereomer (*M*)/(*R*)/(*R*)-**2** within 24 h.[8] The results indicate that TETRAPHOS−Rh/DABN complex **2** is *tropos* at room temperature. Significantly, complex **2** isomerized much faster at room temperature than BIPHEPs-Rh/(*R*)-DABN complexes, which converged on the single diastereomer over 17 days.[4a]

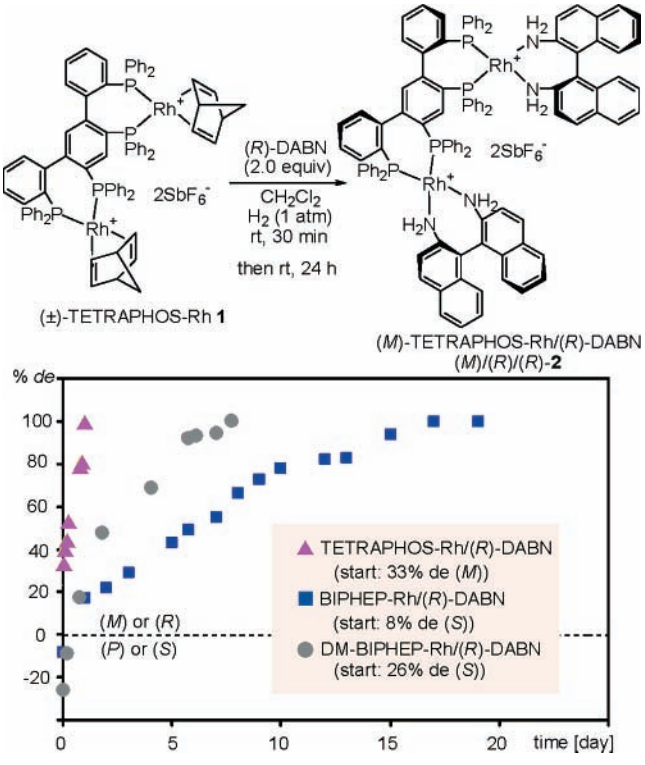
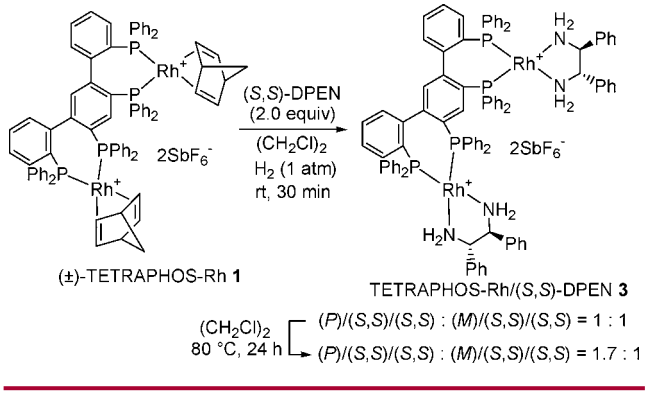


Figure 1. Isomerizaton of TETRAPHOS− and BIPHEPs−Rh/DABN complexes in CD_2Cl_2 at room temperature. The diastereomeric ratios were determined by ^{31}P NMR.

The *tropos* nature of the TETRAPHOS−Rh/DPEN complex **3** was next investigated. The treatment of the racemic complex **1** and 2.0 equiv of (*S*,*S*)-DPEN under the same conditions gave a mixture of diastereomers in 1:1 ratio ((*P*)/(*S*,*S*)/(*S*,*S*)-**3** : (*M*)/(*S*,*S*)/(*S*,*S*)-**3**) in nonselective manner at room temperature (Scheme 2). No change was observed in the diastreomeric ratio (1:1) at room temperature. The results imply that TETRAPHOS−Rh/(*S*,*S*)-DPEN complex **3** is *atropos* at room temperature. However, the isomerization proceeded at 80 °C in $(CH_2Cl)_2$ to give the 1.7:1 diastereomer mixture. (*P*)- or (*M*)-helicity of the TETRAPHOS moiety

Scheme 2. Chirality Control of Complex **1** by (*S*,*S*)-DPEN



(4) For the BIPHEP−Rh complex: (a) Mikami, K.; Kataoka, S.; Yusa, Y.; Aikawa, K. *Org. Lett.* **2004**, *6*, 3699−3701. For the BIPHEP−Ru complex: (b) Mikami, K.; Korenaga, T.; Terada, M.; Ohkuma, T.; Pham, T.; Noyori, R. *Angew. Chem., Int. Ed.* **1999**, *38*, 495−497. (c) Mikami, K.; Aikawa, K.; Korenaga, T. *Org. Lett.* **2001**, *3*, 243−245. For the BIPHEP−Pd complex: (d) Mikami, K.; Aikawa, K.; Yusa, Y.; Hatano, M. *Org. Lett.* **2002**, *4*, 91−94. (e) Mikami, K.; Aikawa, K.; Yusa, Y. *Org. Lett.* **2002**, *4*, 95−97. For the BIPHEP−Pt complex: (f) Tudor, M. D.; Becker, J. J.; White, P. S.; Gagne, M. R. *Organometallics* **2000**, *19*, 4376−4484. (g) Becker, J. J.; White, P. S.; Gagne, M. R. *J. Am. Chem. Soc.* **2001**, *123*, 9478−9479. (h) Mikami, K.; Kakuno, H.; Aikawa, K. *Angew. Chem., Int. Ed.* **2005**, in press. For the use of different chirally flexible (*tropos*) NUPHOS ligands, see: (i) Doherty, S.; Newman, C. R.; Rath, R. K.; Luo, H.; Nieuwenhuyzen, M.; Knight, J. G. *Org. Lett.* **2003**, *5*, 3863−3866. (j) Doherty, S.; Knight, J. K.; Hardacre, C.; Lou, H.; Newman, C. R.; Rath, R. K.; Campbell, S.; Nieuwenhuyzen, M. *Organometallics* **2004**, *23*, 6127−6133.

(5) (a) Schmuck, C. *Angew. Chem., Int. Ed.* **2003**, *42*, 2448−2452. (b) Urbano, A. *Angew. Chem., Int. Ed.* **2003**, *42*, 3986−3989.

(6) Aikawa, K.; Mikami, K. *Angew. Chem., Int. Ed.* **2003**, *42*, 5458−5461.

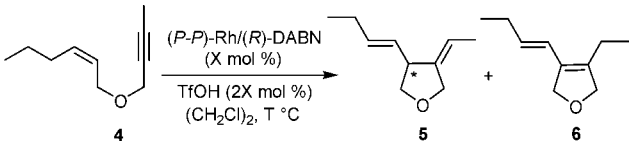
(7) For the BINAP−Rh complex: (a) Takaya, H.; Miyashita, A.; Souchi, T.; Noyori, R. *Tetrahedron* **1984**, *40*, 1245−1253. (b) Halpern, J.; Rily, D. P.; Chan, A. S. C.; Pluth, J. J. *J. Am. Chem. Soc.* **1977**, 8055−8057.

(8) The single diastereomer (*M*)/(*R*)/(*R*)-**2** could also be obtained at 80 °C in dichloroethane for 30 min.

was determined by ligand exchange through addition of (*S*,*S*)-DPEN (2.0 equiv) to the (*R*)-DABN counterpart (*M*)/(*R*)/(*R*)-**2**.

The diastereopure (*M*)-TETRAPHOS−Rh/(*R*)-DABN complexes **3** obtained via pretreatment[8] were efficient catalysts for asymmetric ene-type cyclization[9] of 1,6-enyne substrate **4** (Table 1). The (*R*)-BIPHEP−Rh/(*R*)-DABN complex, upon

Table 1. Enantioselective Ene-Type Cyclization of 1,6-Enyne **4**[a]



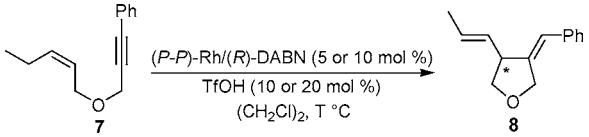
					yield[c] (%)		
entry	*P-P*	X	*T* (°C)	time	**5**	**6**	ee[d] (%)
1[b]	(*R*)-BIPHEP	10	rt	30 min	84		59 (−)
2[b]	(*R*)-DM-BIPHEP	10	rt	5 min	70	23	85 (−)
3	(*M*)-TETRAPHOS	5	rt	15 min	91	3	91 (−)
4	**(*M*)-TETRAPHOS**	**5**	**5**	**3 h**	**92**		**99 (−)**

[a] All reactions were examined after being preheated at 80 °C for 5 h or 30 min. [b] Reference 4a. [c] Yield of isolated product. [d] Enantiopurity was determined by chiral GC analysis on a CP Chirasil Dex CB column.

addition of TfOH to dissociate DABN, afforded the desired cyclic product **5** in moderate enantioselectivity (entry 1). (*R*)-DM-BIPHEP−Rh/(*R*)-DABN (DM = 3,5-dimethyphenyl) complex increased both the catalytic activity and enantioselectivity (entry 2). Using TETRAPHOS ligand instead of BIPHEPs ligands, both the activity and enantioselectivity of the Rh catalyst were increased, however, along with the formation of *achiral* conjugated 1,3-diene **6** in 3% yield (entry 3). At lower temperature (5 °C), the TETRAPHOS complex gave virtually complete enantioselectivity and high chemical yield of **5** (99% ee, 92%) without undesired **6** (entry 4).[10] The result clearly indicates the advantage of the *tropos* TETRAPHOS ligand.

Since the racemization of the (*M*)-TETRAPHOS moiety might proceed during the course of the reaction, the change in enantiomeric excess (% ee) of the product was examined with progress of the reaction by choosing substrate **7** not to give an undesired achiral 1,3-diene product (Table 2). In the

Table 2. Enantiomeric Excess (% ee) Changes with Time



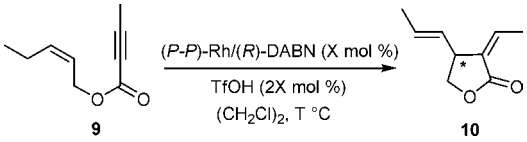
			time				
P-P	*T* (°C)		<1 min	5 min	30 min	1 h	14 h
DM-BIPHEP[a]	rt	conv (%)[b]	15	28	47	56	>99[c]
		ee (%)[d]	94	91	89	86	61
TETRAPHOS	rt	conv (%)[b]	24	79	>99[c]		
		ee (%)[d]	91	91	91		

[a] Reference 4a. [b] Conversion was determined by ^{1}H NMR analysis. [c] Isolated yields were 99%. [d] Enantiopurity was determined by HPLC analysis using Daicel CHIRALCEL OJ-H.

TETRAPHOS case, the change of enantioselectivity (91% ee) was not observed at all, even at room temperature (94% ee at 5 °C), in sharp contrast to the DM-BIPHEP complex to show the decrease in enantioselectvity.[4a] Furthermore, the cyclic product **8** of 91% ee did not racemize under the reaction conditions even at room temperature. It can be seen that diamine-free TETRAPHOS−Rh complex after the treatment of TfOH is more rigid than the BIPHEPs−Rh complex and *atropos* at room temperature. In sharp contrast to diamine-free TETRAPHOS−Rh complex, TETRAPHOS−Rh/DABN complex is more flexible through the association of diamine.

The other substrate **9** was examined to produce the lactone product **10** (Table 3).[9b] The reaction did not proceed by (*R*)-

Table 3. Enantioselective Ene-Type Cyclization of 1,6-Enyne **9**[a]



entry	*P-P*	X	*T* (°C)	time (h)	yield[b] (%)	ee[c] (%)
1	(*R*)-DM-BIPHEP	10	5	16	0	
2	(*M*)-TETRAPHOS	5	5	6	17	88
3	(*M*)-TETRAPHOS	5	rt	16	50	88

[a] All reactions were examined after being preheated at 80 °C for 5 h or 30 min. [b] Yield of isolated product. [c] Enantiopurity was determined by chiral GC analysis on a CP-Cyclodextrin-β-2,3,6-M-19 column.

BIPHEP−Rh/(*R*)-DABN complex (entry 1). However, when TETRAPHOS ligand instead of DM-BIPHEP ligand was used, the activity of the Rh catalyst was significantly enhanced and a high level of enantioselectivity was obtained even at room temperature (entries 2 and 3).

In summary, we have succeeded in chirality control at room temperature over not only axial but also helical chirality of the Rh complexes that bear the *tropos* TETRAPHOS

(9) (a) Cao, P.; Zhang, Xumu *Angew. Chem., Int. Ed.* **2000**, *39*, 4104−4106. (b) Lei, A.; He, M.; Zhang, X. *J. Am. Chem. Soc.* **2002**, *124*, 8198−8199. (c) Lei, A.; He, M.; Wu, S.; Zhang, X. *Angew. Chem., Int. Ed.* **2002**, *41*, 3457−3460. (d) Lei, A.; Waldkirch, J. P.; He, M.; Zhang, X. *Angew. Chem., Int. Ed.* **2002**, *41*, 4526−4529. (e) Lei, A.; He, M.; Zhang, X. *J. Am. Chem. Soc.* **2003**, *125*, 11472−11473.

(10) **Typical Experimental Procedure (Table 1, Entry 4).** To a mixture of $[Rh_2(tetraphos)(nbd)_2](SbF_6)_2$ (0.01 mmol) and (*R*)-DABN (0.021 mmol) in a 10 mL Schlenk tube was added dry dichloroethane (0.70 mL) under Ar atmosphere. The mixture was frozen and charged with hydrogen gas using a balloon (1 atm) and then stirred for 30 min at room temperature. After being charged with argon atmosphere once more, the mixture was stirred at 80 °C for 30 min and then cooled to 5 °C. 1,6-Enyne substrate **4** (0.2 mmol) and TfOH (0.04 mmol) were added, and the reaction mixture was stirred at 5 °C for 3 h and directly loaded onto a silica gel column to give cyclic product as a colorless oil (yield 92%). The enantiomeric excess (% ee) was determined by GC analysis (99% ee).

ligand. Significantly, the flexibility of diamine-free TETRAPHOS−Rh complex can be increased by association of the chiral diamine DABN. In contrast, the diamine-free TETRAPHOS−Rh complex is chirally more stable than the BIPHEP counterpart and hence affords a high level of enantioselectivity in asymmetric ene-type cyclization.

Supporting Information Available: Typical experimental procedures and spectral data for TETRAPHOS−Rh complexes **1**−**3**. This material is available free of charge via the Internet at http://pubs.acs.org.

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