## Racemic but *Tropos* (Chirally Flexible) BIPHEP Ligands for Rh(I)-Complexes: Highly Enantioselective Ene-Type Cyclization of 1,6-Enynes

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## ABSTRACT



The *tropos* (chirally flexible) or *atropos* (chirally rigid) nature of BIPHEP–Rh complexes at room temperature critically depends on the amines complexed. The aliphatic DPEN complex is *atropos*, whereas the aromatic DABN complex is *tropos*. BIPHEP–Rh chirality can thus be controlled by DABN at room temperature. The amine-free BIPHEP–Rh complex is *tropos*. At 5 °C, even amine-free BIPHEP–Rh complexes are *atropos* and hence can be used as enantiopure catalysts to give high enantioselectivity in ene-type cyclization of 1,6-enynes.

Despite enantioresolution and synthetic transformation, many enantiopure atropisomeric (*atropos* in Greek; a = not, *tropos* = turn)<sup>1</sup> ligands are synthesized and used in catalytic asymmetric reactions.<sup>2</sup> In sharp contrast, we have succeeded in asymmetric catalysis using racemic but chirally flexible (*tropos*)<sup>1</sup> bis(phosphanyl)biphenyl (BIPHEP) ligand,<sup>3,4a</sup> of which the axial chirality can be controlled by a chiral controller. Thus, the BIPHEPs–Ru and –Pd complexes afford high enantioselectivity in asymmetric hydrogenation and Diels–Alder reactions, respectively.<sup>4</sup> The complexes bearing BIPHEPs are inherently *tropos*, but high levels of enantioselectivity can be achieved under appropriate conditions depending on the central metals employed. Ru complexes are *tropos*, but Pd complexes are, by contrast, *atropos* at room temperature. Thus, the question arises with BIPHEP-complexes of Rh in the same row between Ru and Pd: *tropos* or *atropos* at room temperature?<sup>5</sup>

Herein, we report chiral control of *tropos* BIPHEPs–Rh complexes at room temperature (25 °C) and their application as *atropos* catalysts for highly enantioselective ene-type cyclization of 1,6-enynes at 5 °C.

<sup>(1)</sup> Mikami, K.; Aikawa, K.; Yusa, Y.; Jodry, J. J.; Yamanaka, M. Synlett **2002**, *10*, 1561–1578.

<sup>(2)</sup> Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H. Comprehensive Asymmetric Catalysis; Springer: Berlin, 1999; Vols. 1–3.

<sup>(3)</sup> The activation barrier to axial torsion in selectivity deuterated BIPHEP is measured to be only  $(22 \pm 1)$  kcal, which suggests that axial rotation takes place at room temperature or above: Desponds, O.; Schlosser, M. *Tetradedron Lett.* **1996**, *37*, 47–48.

<sup>(4)</sup> For the BIPHEP-Ru complex: (a) Mikami, K.; Korenaga, T.; Terada, M.; Ohkuma, T.; Pham, T.; Noyori, R. *Angew. Chem., Int. Ed.* **1999**, *38*, 495-497. For the BIPHEP-Pd complex: (b) Mikami, K.; Aikawa, K.; Yusa, Y.; Hatano, M. Org. Lett. **2002**, *4*, 91-94. (c) Mikami, K.; Aikawa, K.; Yusa, Y. Org. Lett. **2002**, *4*, 95-97. For the BIPHEP-Pt complex: (d) Tudor, M. D.; Becker, J. J.; White, P. S.; Gagné, M. R. *J. Am. Chem. Soc.* **2001**, *123*, 9478-9479.

<sup>(5)</sup> A half-life of 1000 s (16.7 min) is considered as the minimum requirement for *atropos* molecules; cf. Oki, M. *Top. Stereochem.* **1983**, *14*, 1–81.



The reaction of racemic BIPHEP–Rh complex<sup>6</sup> in nonpolar solvents such as dichloromethane under hydrogen (1 atm) gave a dimeric BIPHEP–Rh complex (Scheme 1). The dimer complexes<sup>7</sup> consisted of homo- and hetero-chiral ones in a 40:60 ratio, but the hetero-chiral complex isomerized slowly to the homo-chiral one at room temperature over 48 h.<sup>8</sup>

The complexation of the BIPHEP-Rh complex and an equimolar amount of (R,R)-DPEN (1,2-diphenylethylenediamine) as a chiral controller was examined to give a mixture of diastereomers in a 50:50 ratio (eq 1). Unfortunately, no change was observed in the diastereomeric ratio at room temperature regardless of solvents.

Next, an equimolar amount of (R)-DABN (2,2'-diamino-1,1'-binaphthyl) was added under a similar condition, to give a mixture of diastereomers in a R,R/S,R 46:54 ratio (eq 2). However, the isomerization proceeded slowly in dichloro-

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

(8) <sup>31</sup>P NMR (162 MHz, CD<sub>2</sub>Cl<sub>2</sub>): heterochiral  $\delta$  39.8 (dd, J = 193.3, 49.6 Hz), 43.3 (dd, J = 209.5, 49.6 Hz); homochiral  $\delta$  40.8 (dd, J = 192.3, 48.8 Hz), 44.6 (dd, J = 209.5, 48.8 Hz). For the homochiral dimer (*R*)-BINAP-Rh complex: <sup>31</sup>P NMR (162 MHz, CD<sub>2</sub>Cl<sub>2</sub>)  $\delta$  42.7 (dd, J = 195.5, 43.6 Hz), 46.4 (dd, J = 211.4, 43.6 Hz).



**Figure 1.** Solvent effect on chiral control of BIPHEP–Rh/DABN complex. The diastereomeric ratios were determined by <sup>31</sup>P and <sup>1</sup>H NMR at room temperature.

methane at room temperature, leading eventually to the single R,R diastereomer after 17 days (Figure 1). As a solvent effect, the complexation in polar solvents such as methanol gave a different diastereomer ratio R,R/S,R 56:44, and the isomerization was found to be faster to afford the single R,R diastereomer within 72 h. The single R,R diastereomer could also be obtained at 80 °C in dichloroethane within 5 h. However, isomerization was not observed at 5 °C in either solvent.

It is thus clarified that the *tropos* or *atropos* nature of BIPHEP–Rh complexes at room temperature critically depend on the amines complexed. The aliphatic DPEN complex is *atropos*, whereas the aromatic DABN complex is *tropos*. Furthermore, the amine-free BIPHEP–Rh complexes are *tropos*, as proven after amine complexation. However, at 5 °C or below, even amine-free BIPHEP–Rh complexes are *atropos* and hence can be used as chiral catalysts.

The enantiopure Rh-complexes obtained via heat pretreatment (80 °C in dichloroethane for 5 h) could be used as asymmetric catalysts for ene-type cyclization<sup>9</sup> of 1,6-enyne substrate **1** by addition of TfOH to protonate diamines off the Rh metal center (Table 1). BIPHEP–Rh gave the desired cyclic product **2** in good yield but in moderate enantioselectivity at room temperature (entry 1). Without TfOH, the reaction was very slow (12.5 h) (entry 2). Using DM-BIPHEP (DM = 3,5-dimethy-phenyl) instead of BIPHEP,

<sup>(6)</sup> Crystal data for BIPHEP–Rh complex in X-ray analysis: formula C<sub>46</sub>H<sub>44</sub>F<sub>6</sub>P<sub>2</sub>RhSbCl<sub>2</sub>, monoclinic, space group  $P_{1/n}$  (No. 14), a = 14.065-(4) Å, b = 13.737(4) Å, c = 21.407(56) Å,  $\beta = 89.5260(1)^\circ$ , V = 4097.9-(21) Å<sup>3</sup>, Z = 4, and D = 1.732 g cm<sup>-3</sup>. X-ray diffraction data were collected on a Rigaku Saturn 70 CCD system with graphite-monochromated Mo K $\alpha$  ( $\lambda = 0.71070$  Å) at -100 °C and the structure was solved by direct methods (SIR92). The final cycle of full-matrix least-squares refinement on  $F^2$  was based on 12097 observed reflections and 542 variable parameters and converged to R = 0.076 and Rw = 0.179. Goodness of fit = 1.084, shift/error = 0.006. 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 241306. 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.

**Table 1.** Enantioselective Ene-Type Cyclization of1,6-Enyne  $1^a$ 



entry	r-r	$I(\mathbf{C})$	time	~	3	ee (70)
1	(R)-BIPHEP	25	30 min	84		59 (-)
$2^{b}$	(R)-BIPHEP	25	12.5 h	74		56 (-)
3	(R)-DM-BIPHEP	25	5 min	70	23	85 (-)
4	(R)-DM-BIPHEP	5	3 h	83	5	96 (-)

<sup>*a*</sup> All reactions were examined after preheating at 80 °C for 5 h. <sup>*b*</sup> The reaction was examined without TfOH. <sup>*c*</sup> Yield of isolated product. <sup>*d*</sup> Enantiopurity was determined by chiral GC analysis on a CP-Cyclodextrin- $\beta$ -2,3,6-M-19 column.

both the activity and enantioselectivity of the Rh catalyst increased, however, along with the formation of *achiral* conjugated 1,3-diene **3** in 23% yield (entry 3). At lower temperature (5 °C), DM-BIPHEP–Rh complex exhibited high enantioselectivity and chemical yield of **2** (96% ee, 83%) with only 5% yield of undesired **3** (entry 4). After the ene-type reaction, the enantiopure form of the amine-free BIPHEP–Rh complex was confirmed by adding (*R*)-DABN.

Because racemization of the DM-BIPHEP-Rh complex might proceed during the reaction, the change in enantiomeric excess (% ee) was examined with progress of the reaction by choosing substrate 4a not to give a 1,3-diene product.

Table 2. Enantioselective Ene-Type Cyclization of 1,6-Enynes<sup>a</sup>



<sup>*a*</sup> All reactions were examined after preheating at 80 °C for 5 h. <sup>*b*</sup> Yield of isolated product. <sup>*c*</sup> Most of 1,6-enyne substrate **4b** was decomposed. <sup>*d*</sup> Enantiopurity was determined by HPLC analysis.

19

81 (5d)

89 (-)

Et

As expected, at room temperature, enantioselectivity was decreased from 94% ee after 1 min to 86% ee after 1 h. However, at 5 °C, enantioselectivity (94% ee) did not change at all throughout the reaction time. Furthermore, the eneproduct of 94% ee did not racemize under the reaction conditions even at room temperature.

Therefore, 1,6-enyne substrates 4a-d with aromatic terminal substituents were examined at 5 °C (Table 2). All of the reactions were shown to be effective with both electron-withdrawing and -donating substituents except for low yield obtained with MeO-substrate (4b).

In conclusion, we have established the high levels of enantioselectivity in ene-type cyclization of 1,6-enynes catalyzed by BIPHEPs—Rh complexes despite the racemic and *tropos* ligands, through chiral control. Further applications of BIPHEPs-Rh complexes in asymmetric catalysis and chiral control of other metal complexes bearing BIPHEP ligands are now in progress.

**Supporting Information Available:** Typical experimental procedures and spectral data for BIPHEPs-Rh complexes and **1**-**5**, including CIF files. This material is available free of charge via the Internet at http://pubs.acs.org.

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H (4d)

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