

Negative nonlinear effect in aquo palladium catalysis depending on *tropos* biphenylphosphine ligand chirality controlled by chiral diaminobinaphthyl activator*

Koichi Mikami[‡], Kohsuke Aikawa, and Masahiro Yamanaka

Department of Applied Chemistry, Tokyo Institute of Technology, O-okayama, Meguro-ku, Tokyo 152-8552, Japan

Abstract: Asymmetric activation of aquo Pd catalysts with *tropos* biphenylphosphine (BIPHEP) ligands by a chiral diaminobinaphthyl (DABN) activator exhibits a remarkable negative nonlinear effect, (–)-NLE, with higher catalytic efficiency than that achieved by enantiopure *atropos* BINAP- or *tropos* BIPHEP-Pd catalysts without DABN activator.

In asymmetric catalysis [1], the design of chirally rigid *atropisomeric* (*atropos*) [2] ligand has long been considered to be the key to establish high enantioselectivity and to increase the catalytic activity from the achiral metal pre-catalyst (“ligand-accelerated catalysis” [3]). The chiral metal catalyst is prepared from the pre-catalyst via ligand exchange with usually *atropos* ligands, such as binaphthylphosphines (BINAP). The asymmetric catalysts thus prepared can be further transformed into highly activated catalysts by association with chiral activators (“asymmetric activation” [4]). This process is particularly useful in racemic catalysis, through enantiomer-selective activation of the racemic catalyst [5]. A “chiral activator” selectively activates one enantiomer of a racemic catalyst, which can then attain an enantioselectivity higher than that achieved with the enantiopure catalyst, in addition to higher catalytic efficiency. We report here a further advanced strategy for asymmetric activation using chirally flexible *tropos* biphenylphosphine (BIPHEP) ligands by a chiral diaminobinaphthyl (DABN) activator to give higher catalytic efficiency than that using enantiopure *atropos* BINAP or *tropos* BIPHEP catalysts without DABN activator (Fig. 1). Aquo palladium complex bearing, at the outset, racemic but *tropos* BIPHEP ligands [BIPHEP-Pd(OH₂)₂] was eventually converted to an enantiopure (*R*)-BIPHEP-Pd

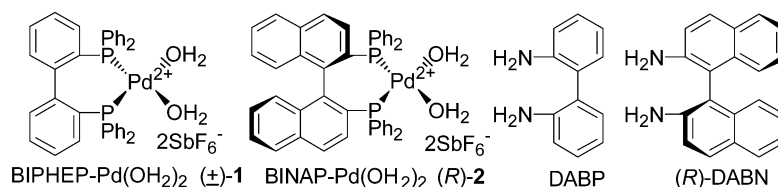


Fig. 1 *Tropos* and *atropos* aquo Pd complexes and chiral activators.

*Plenary and invited lectures presented at the 12th IUPAC International Symposium on Organometallic Chemistry Directed Towards Organic Synthesis (OMCOS-12), Toronto, Ontario, Canada, 6–10 July 2003. Other presentations are published in this issue, pp. 453–695.

[‡]Corresponding author: E-mail: kmikami@o.cc.titech.ac.jp

complex [6] with (*R*)-DABN. A remarkable level of negative nonlinear effect, (–)-NLE [7], is shown depending on BIPHEP chirality in the Diels–Alder (DA) reaction [8].

The selectivity in complexation of BIPHEP-Pd(OH₂)₂ with a diamine activator was first examined. With 0.5 equiv of DABN, 9:1 mixture of BIPHEP-Pd/DABN complexes was observed, with (*R*)-BIPHEP-Pd/(*R*)-DABN as the major. The *tropo*-inversion, inversion of chirality of the *tropos* ligand, was next examined on the enantiomeric BIPHEP-Pd complexes obtained upon addition of an equimolar amount of (*R*)-DABN to racemic BIPHEP-Pd(OH₂)₂ complexes (Fig. 2). No isomerization was seen at room temperature (r.t.); the 1:1 mixture of enantiomeric DABN complexes did not epimerize at r.t. over 8 days, but exhibited *tropo*-inversion at 80 °C after 12 h, leading exclusively to the favorable (*R*)-BIPHEP-Pd/(*R*)-DABN. The (*R*)/(*R*)-configuration of Pd(biphep)(dabn) was confirmed by ¹H and ³¹P NMR comparison with the Pd[(*R*)-biphep][(*R*)-dabn](SbF₆)₂ obtained from the Pd[(*R*)-biphep][(CH₃CN)₂](SbF₆)₂ [6].

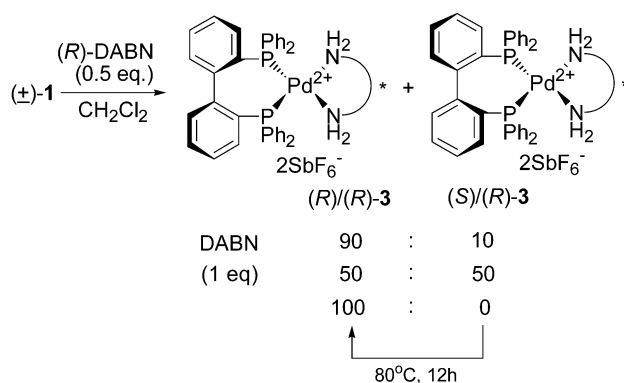


Fig. 2 *Tropo*-inversion of BIPHEP-Pd/DABN complex.

The BIPHEP-Pd/DABN complexes can be readily formed by ligand exchange between OH₂ and DABN on the Pd center. We theoretically estimated the ease of such a ligand-exchange process. The BIPHEP-Pd(OH₂)₂ and BIPHEP-Pd/DABN complexes were optimized using ONIOM method, which has been proven to be a powerful tool for the theoretical treatment of large molecular systems [9,10]. The optimized BIPHEP moieties were slightly changed by coordination of DABN instead of OH₂; the distance of P-Pd was lengthened, and the dihedral angle around the chiral axis was increased (Fig. 3). The interaction energy (ΔE) between (*R*)-BIPHEP-Pd fragment and two molecules of OH₂ or

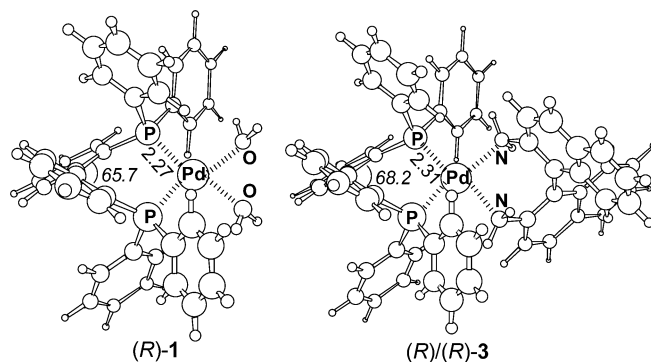


Fig. 3 3D structures of (*R*)-BIPHEP-Pd(OH₂)₂ and (*R*)-BIPHEP-Pd/(*R*)-DABN.

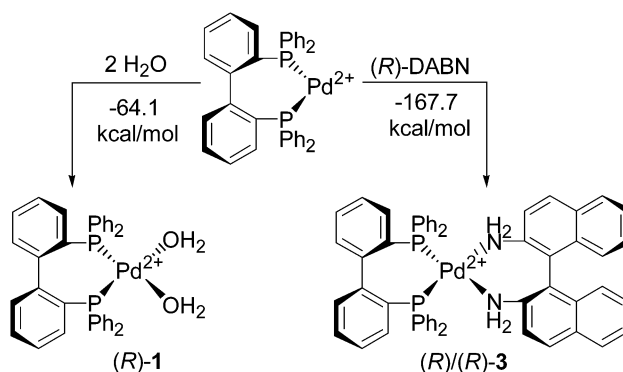


Fig. 4 Interaction energies of (R) -BIPHEP-Pd(OH₂)₂ and (R) -BIPHEP-Pd/ (R) -DABN at the B3LYP/631SDD level.

(R) -DABN were estimated by single point energy calculation at the B3LYP/631SDD level (Fig. 4). The ΔE in the case of DABN (-167.7 kcal/mol) is much larger than that in the case of OH₂ (-64.1 kcal/mol). This indicates that DABN can readily exchange OH₂ in agreement with the experimental results.

The BIPHEP-Pd/DABN complexes showed a remarkable ($-$)-NLE, depending on the enantiopurity of the *tropos* BIPHEP ligands. The 1:1 diastereomeric mixture of Pd[(R) -biphep][(R) -dabn] and Pd[(S) -biphep][(R) -dabn] (racemic in BIPHEP ligand) with DABN activator can be used as an activated catalyst for the DA reactions to give $(1S)$ -DA product in a higher chemical yield (64 %) but with a very low level of enantioselectivity (9 % ee) (Table 1, entry 1). Even with a 50 % ee of BIPHEP, a very low enantioselectivity (10 % ee) was again obtained to give further the enantiomeric $(1R)$ -DA product (entry 2). These results imply a remarkable level of ($-$)-NLE, depending on the enantiopurity of the BIPHEP ligand controlled by DABN activator.

Table 1 ($-$)-NLE in glyoxylate-DA reaction.

entry	(R) -BIPHEP : (S) -BIPHEP	yield (%)	% ee (<i>endo</i>) ^{a)}
1	50 : 50	64	9 ($1S,3R,4R$)
2	75 : 25	81	10 ($1R,3S,4S$)
3	100 : 0	75	94 ($1R,3S,4S$)

a) *exo* product was not observed.

In the presence of water, aquo palladium complexes are generally formed and often show very low Lewis acidity [11]. However, upon addition of diamines, water was found to be replaced with diamines to allow complexation of substrates and hence to increase the catalytic activity of the aquo Pd catalyst. This asymmetric activation was exemplified by the higher chemical yields and enantioselectivity (94 % ee) in the DA reaction between ethyl glyoxylate and cyclohexadiene attained by BIPHEP-Pd/DABN complex (Table 1, entry 3) than those attained by the *atropos* and enantiopure BINAP-Pd catalyst without DABN activator, which gave only trace amount of products (Table 2, entry 1). Indeed,

Table 2 Asymmetric activation of (*R*)-**2** by diamines.

entry	activator	yield (%)	% ee (<i>endo</i>)
1	none	trace	-
2	DABP	71	>99 (1 <i>R</i> ,3 <i>S</i> ,4 <i>S</i>)
3	(<i>R</i>)-DABN	70	>99 (1 <i>R</i> ,3 <i>S</i> ,4 <i>S</i>)
4 ^a)	(<i>R</i>)-DABN	86	>99 (1 <i>S</i> ,3 <i>R</i> ,4 <i>R</i>)

a) (*S*)-**2** was employed instead of (*R*)-**2**

(*R*)-DABN activated the enantiopure (*R*)-BINAP-Pd catalyst to give the DA adduct in an enantiopure form (>99 % ee 1*R*) (entries 1 vs. 3) but in lower chemical yield (70 %) than that with (*S*)-BINAP-Pd catalyst (86 %, >99 % ee 1*S*) (entries 3 vs. 4).

Asymmetric activation thus provides a strategy for the use of *tropos* ligands without asymmetric synthesis or resolution even in the presence of water to establish a remarkable (–)-NLE in DA reactions. Higher enantioselectivity and catalytic efficiency are attained by aquo BIPHEP-Pd complexes with DABN than those achieved by enantiopure BINAP-Pd catalysts without DABN activator.

REFERENCES

- (a) R. Noyori. *Asymmetric Catalysis in Organic Synthesis*, John Wiley, New York (1994); (b) *Transition Metals for Organic Synthesis*, M. Beller and C. Bolm (Eds.), VCH, Weinheim (1998); (c) E. N. Jacobsen, A. Pfaltz, H. Yamamoto. *Comprehensive Asymmetric Catalysis*, Vols. 1–3, Springer, Berlin (1999); (d) *Catalytic Asymmetric Synthesis*, Vols. I and II, I. Ojima (Ed.), VCH, New York (1993, 2000).
- (a) K. Mikami, K. Aikawa, Y. Yusa, J. Jodry, M. Yamanaka. *Synlett* 1561 (2002); (b) K. Mikami and M. Yamanka. *Chem. Rev.* In press.
- D. J. Berrisford, C. Bolm, K. B. Sharpless. *Angew. Chem., Int. Ed. Engl.* **34**, 1059 (1995).
- K. Mikami, M. Terada, T. Korenaga, Y. Matsumoto, M. Ueki, R. Angelaud. *Angew. Chem., Int. Ed. Engl.* **39**, 3532 (2000).
- K. Mikami and S. Matsukawa. *Nature* **8**, 815 (1997); *Enantiomer* **1**, 69 (1996).
- K. Mikami, K. Aikawa, Y. Yusa, M. Hatano. *Org. Lett.* **4**, 91 (2002).
- (a) C. Girard and H. B. Kagan. *Angew. Chem., Int. Ed. Engl.* **37**, 2923 (1998); (b) R. Noyori and M. Kitamura. *Angew. Chem., Int. Ed. Engl.* **30**, 49 (1991); (c) K. Mikami and M. Terada. *Tetrahedron* **48**, 5671 (1992).
- The DA reactions can recently be carried out using not only main-group but also transition-metal complexes; recent reviews: K. A. Jorgensen. *Angew. Chem., Int. Ed. Engl.* **34**, 3557 (2000); D. A. Evans and J. S. Johnson, in ref. 1a, Vol. III, p. 1178.
- (a) F. Maseras and K. Morokuma. *J. Comp. Chem.* **16**, 1170 (1995); (b) S. Dapprich, I. Komáromi, K. S. Byun, K. Morokuma, M. J. Frisch. *J. Mol. Struct. (Theochem)* **461–462**, 1 (1999); (c) T. Vreven and K. Morokuma. *J. Comp. Chem.* **21**, 1419 (2000); (d) T. Vreven, K. Morokuma, Ö. Farkas, H. B. Schlegel, M. J. Frisch. *J. Comp. Chem.* **24**, 760 (2003).
- All calculations were performed by Gaussian 98 package. Basis set denoted as 631SDD consists of Stuttgart effective core potential for Pd and 6-31G(d) basis set for the rest. For the details of computational method, see: M. Yamanaka and K. Mikami. *Organometallics* **21**, 5847 (2002).
- A. Fujii, E. Hagiwara, M. Sodeoka. *J. Synth. Org. Chem. Jpn.* **58**, 728 (2000). Also see: D. Ferraris, B. Young, T. Dudding, T. Lectka. *J. Am. Chem. Soc.* **120**, 4548 (1998).