Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron Letters
Tetrahedron Letters 46 (2005) 2879–2882

Evidence for the importance of conformational equilibria in Rh-diphosphine complexes for the enantioselection in Rh-catalyzed asymmetric hydrogenation

Hideyuki Tsuruta,[a] Tsuneo Imamoto,[a,*] Kentaro Yamaguchi[b] and Ilya D. Gridnev[c,*]

[a]*Department of Chemistry, Faculty of Science, Chiba University, Yayoi-cho, Inage-ku, Chiba 263-8522, Japan*
[b]*Chemical Analysis Center, Chiba University, Yayoi-cho, Inage-ku, Chiba 263-8522, Japan*
[c]*COE Laboratory, Department of Chemistry, Graduate School of Science, Tohoku University, Aoba-ku, Sendai 980-8578, Japan*

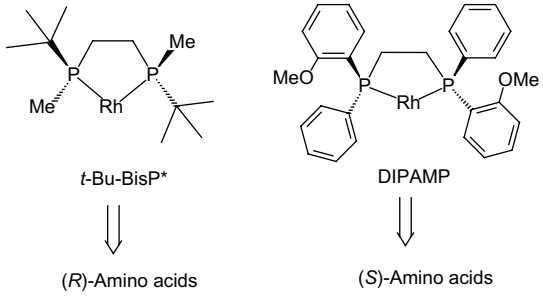
Received 31 January 2005; accepted 18 February 2005

Abstract—The conformations of the chelate cycles in the X-ray structures of norbornadiene- and cyclooctadiene-rhodium complexes of (*R*,*R*)-1,2-bis[(*o*-methylphenyl)phenylphosphino]ethane are dramatically different. Nevertheless, they demonstrate the same sense of enantioselection in asymmetric hydrogenation of dehydroamino acids.

The rhodium-catalyzed asymmetric hydrogenation of activated double bonds has remained a hot research area for over 30 years.[1] The most evident reason for this is the practical importance of this method for the preparation of optically active natural and non-natural amino acids and other non-racemic compounds.[2] However, mechanistic studies of this reaction are probably equally important, since the catalytic cycle of the Rh-catalyzed asymmetric hydrogenation is unique from the point of view of the number of characterized intermediates[3] and detailization of computational studies.[4]

Prediction of the sense of enantioselection is one of the most interesting problems in Rh-catalyzed asymmetric hydrogenation. Although the opposite enantiomers of the chiral diphosphines invariably gave, as expected, the opposite enantiomers of the hydrogenation products, the exact relationship between the structure of the diphosphine and the sense of hydrogenation is a more complicated matter. Several empirical rules for the prediction of enantioselection on the basis of the X-ray structures of the catalytic precursors have been proposed.[5–7] Nowadays only the quadrant rule originally suggested by Knowles and co-workers[6] is widely used due to its straightforwardness and principal applicability to the *P*-stereogenic diphosphine ligands. However, the predictions of the quadrant rule for the various types of diphosphine ligands are often confusing.

Thus, for example, the alkyl-substituted *P*-stereogenic ligands (e.g., (*S*,*S*)-*t*-Bu-bisP*[8]) give (*R*)-hydrogenation products when the bulky substituent occupies the upper left corner of the quadrant diagram (Scheme 1). On the other hand, in the case of the DIPAMP ligand the (*R*,*R*)-enantiomer having the *o*-methoxyphenyl substituent (which is formally larger than unsubstituted phenyl) in the upper left corner affords (*S*)-hydrogenation products in asymmetric hydrogenations catalyzed by its rhodium complexes (Scheme 1).[9]



Scheme 1. Sense of enantioselection in asymmetric hydrogenations of dehydroamino acids catalyzed by Rh-bisP* and Rh-DIPAMP catalysts.

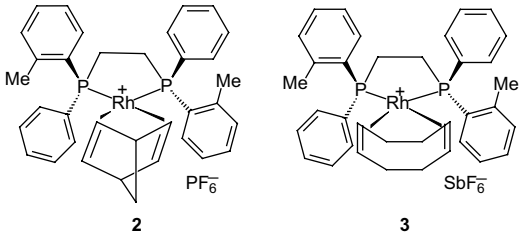
Keywords: Asymmetric hydrogenation; Chiral diphosphines; Chiral rhodium complexes; Sense of enantioselection.
* Corresponding authors. Tel./fax: +81 043 2902791 (T.I.); tel.: +81 022 2173585; fax: +81 022 2176784 (I.D.G.); e-mail addresses: imamoto@faculty.chiba-u.jp; igridnev@mail.tains.tohoku.ac.jp

0040-4039/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2005.02.115

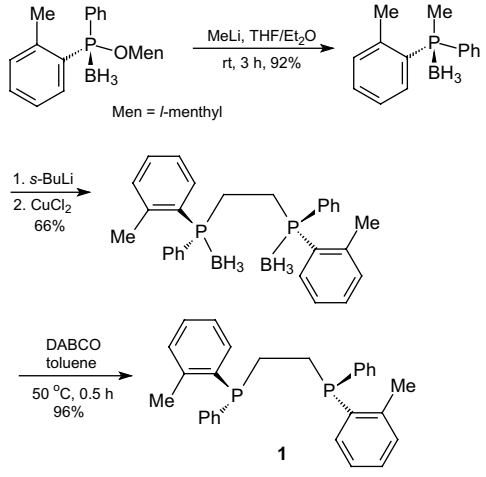
Previously Bakos et al. reported two different solid-state conformations of six-membered chelate cycles in 2,5-norbornadienyl and 1,5-cyclooctadienyl Rh complexes of the (−)-(2*S*,4*S*)-2,4-bis(diphenylphosphino)pentane (BDPP) ligand.[10] These results together with a remarkable dependence of the ee's of the hydrogenation products on the solvent used for their catalytic hydrogenation are an important evidence for the primary importance of the solution conformation of the six-membered chelate cycle for the outcome of the asymmetric hydrogenation. However, most of the successful C_2-symmetric ligands produce five-membered chelate cycles upon coordination to Rh, and the empirical rules for the prediction of the sense of enantioselection are based on the well-defined λ- and δ-conformations of the five-membered chelate cycles.

Hence, we report here two X-ray structures of the 2,5-norbornadienyl (**2**) and 1,5-cyclooctadienyl (**3**) Rh complexes of (*R*,*R*)-1,2-bis[(*o*-methylphenyl)phenylphosphino]ethane (**1**) (Scheme 2), and the results of the asymmetric hydrogenation using these two complexes as catalytic precursors revealing the importance of the solution conformation of the chelate cycle rather than the conformation acquired in the solid state for the sense and order of stereoselection in the Rh-catalyzed asymmetric hydrogenation.

(*R*,*R*)-1,2-Bis[(*o*-methylphenyl)phenylphosphino]ethane (**1**) was prepared by using phosphine–boranes as intermediates according to procedure described in the literature (Scheme 3).[11] The diphosphine ligand **1** was reacted with $[Rh(nbd)_2]PF_6$ or $[Rh(cod)_2]SbF_6$. The resulting complexes **2** and **3** were purified by recrystallization from tetrahydrofuran, and their molecular structures were determined by single crystal X-ray analysis.[12,13] Their ORTEP drawings are shown in Figures 1 and 2.



Scheme 2. Chemical structures of complexes **2** and **3**.



Scheme 3. Synthesis of diphosphine ligand **1**.

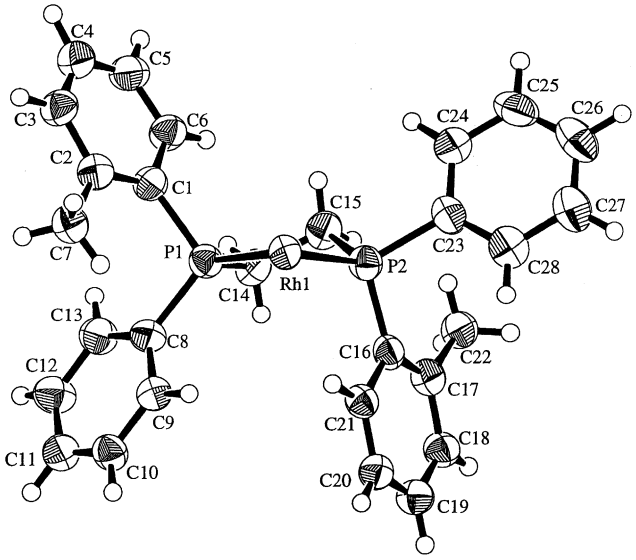


Figure 1. ORTEP diagram of complex **2** (50% thermal ellipsoids, coordinated diene and counter-ion omitted for clarity). Selected bond lengths (Å) and angles (deg): Rh(1)–P(1) 2.300(2), Rh(1)–P(2) 2.284(2), P(1)–C(1) 1.832(7), P(2)–C(23) 1.822(7), P(1)–C(14) 1.838(7), P(2)–C(15) 1.835(8), P(1)–C(8) 1.824(7), P(2)–C(16) 1.810(8), C(14)–C(15) 1.51(1), P(1)–Rh(1)–P(2) 83.92(6), Rh(1)–P(2)–C(16) 111.6(2), Rh(1)–P(2)–C(23) 118.8(3), Rh(1)–P(1)–C(1) 113.5(2), Rh(1)–P(1)–C(8) 121.4(2).

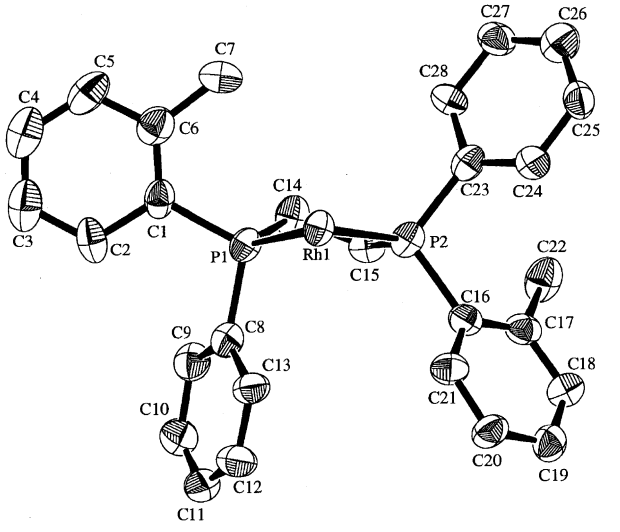
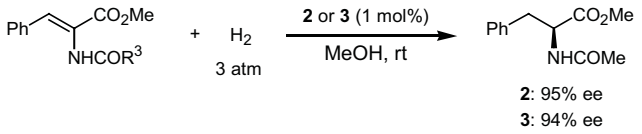
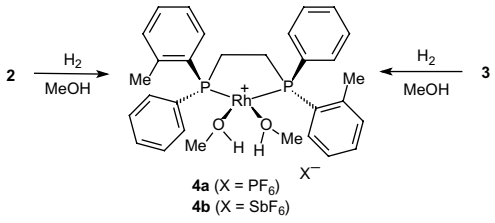


Figure 2. ORTEP diagram of complex **3** (50% thermal ellipsoids, coordinated diene, hydrogens, and counter-ion omitted for clarity). Selected bond lengths (Å) and angles (deg): Rh(1)–P(1) 2.273(3), Rh(1)–P(2) 2.307(3), P(1)–C(1) 1.82(1), P(2)–C(23) 1.79(1), P(1)–C(14) 1.84(1), P(2)–C(15) 1.86(1), P(1)–C(8) 1.82(1), P(2)–C(16) 1.85(1), C(14)–C(15) 1.51(2), P(1)–Rh(1)–P(2) 82.8(1), Rh(1)–P(2)–C(16) 118.0(4), Rh(1)–P(2)–C(23) 112.9(4), Rh(1)–P(1)–C(1) 119.2(4), Rh(1)–P(1)–C(8) 110.7(4).



Scheme 4. Asymmetric hydrogenation of methyl (*Z*)-α-acetamidocinnamate catalyzed by **2** and **3**.



Scheme 5. Structure of active catalyst formed in situ in course of asymmetric hydrogenation catalyzed by **2** and **3**.

Inspection of the Figures 1 and 2 shows that the solid-state conformations of the chelate cycles in **2** and **3** are opposite. The norbornadienerhodium complex **2** has δ-type conformation of the chelate cycle with quasi-equatorial phenyls and quasi-axial *o*-tolyl-substituents. On the other hand, the chelate cycle in the cyclooctadienyl complex **3** apparently has the λ-conformation; the *o*-tolyl-substituents are quasi-equatorial and the phenyls are quasi-axial.

As expected, both complexes **2** and **3** provided the same sense and order of enantioselection when applied as precatalysts in asymmetric hydrogenations of dehydroamino acids (Scheme 4). Notably high ee's (comparable to those reported for DIPAMP) have been observed demonstrating that even the smallest possible difference in the structure of aryl substituents in a C_2-symmetric diphosphine ligand is sufficient to secure high enantioselctivity.[14]

It is clear that after the activation of a precatalyst (hydrogenation of the coordinated diene), the active catalytic species (**4**) generated from **2** and **3** (Scheme 5) differ only by counter-ion, and it is well known that the influence of the counter-ion on the course of asymmetric hydrogenation is minimal, if any. Hence, the different conformations of the same chelate cycle observed for **2** and **3** demonstrate convincingly that the solid-state structures of the conformationally flexible Rh complexes cannot be reliably used as a lead in discussing the mechanism of enantioselection, as it has been accepted previously. Detailed analysis of the conformational equilibria in solution for each important intermediate is required. Such studies are underway in our research group.

Supplementary data

Supplementary data associated with this article can be found, in the online version at doi:10.1016/j.tetlet.2005.02.115. Detailed data for the X-ray analyses of **2** and **3**.

References and notes

1. For representative reviews, see: (a) Knowles, W. S. *Angew. Chem., Int. Ed.* **2002**, *41*, 1998; (b) Noyori, R. *Angew. Chem., Int. Ed.* **2002**, *41*, 2008; (c) Ohkuma, T.; Kitamura, M.; Noyori, R.; In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; 2nd ed. VCH: New York, 2000; pp 1–110; (d) Noyori, R.; Kitamura, M.; Ohkuma, T. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5356.
2. For recent review, see: Tang, W.; Zhang, X. *Chem. Rev.* **2003**, *103*, 3029.
3. (a) Halpern, J.; Riley, D. P.; Chan, A. S. C.; Pluth, J. J. *J. Am. Chem. Soc.* **1977**, *99*, 8055; (b) Brown, J. M.; Chaloner, P. A. *Tetrahedron Lett.* **1978**, 1877; (c) Brown, J. M.; Chaloner, P. A. *J. Am. Chem. Soc.* **1980**, *102*, 3040; (d) Chan, A. S. C.; Pluth, J. J.; Halpern, J. *J. Am. Chem. Soc.* **1980**, *102*, 5952; (e) Landis, C. R.; Halpern, J. *J. Am. Chem. Soc.* **1987**, *109*, 1746; (f) Gridnev, I. D.; Higashi, N.; Asakura, K.; Imamoto, T. *J. Am. Chem. Soc.* **2000**, *122*, 7183; (g) Giernoth, R.; Heinrich, H.; Adams, N. J.; Deeth, R. J.; Bargon, J.; Brown, J. M. *J. Am. Chem. Soc.* **2000**, *122*, 12381; (h) Gridnev, I. D.; Yasutake, M.; Higashi, N.; Imamoto, T. *J. Am. Chem. Soc.* **2001**, *123*, 5268; (i) Gridnev, I. D.; Yamanoi, Y.; Higashi, N.; Tsuruta, H.; Yasutake, M.; Imamoto, T. *Adv. Synth. Catal.* **2001**, *343*, 118; (j) Gridnev, I. D.; Higashi, N.; Imamoto, T. *J. Am. Chem. Soc.* **2001**, *123*, 4631; (k) Gridnev, I. D.; Imamoto, T. *Acc. Chem. Res.* **2004**, *37*, 633.
4. (a) Landis, C. R.; Hilfenhaus, P.; Feldgus, S. *J. Am. Chem. Soc.* **1999**, *121*, 8741; (b) Landis, C. R.; Feldgus, S. *Angew. Chem. Int., Ed.* **2000**, *39*, 2863; (c) Feldgus, S.; Landis, C. R. *J. Am. Chem. Soc.* **2000**, *122*, 12714; (d) Feldgus, S.; Landis, C. R. *Organometallics* **2001**, *20*, 2374; (e) Drexler, H.-J.; Zhang, S.; Sun, A.; Spannenberg, A.; Arrleta, A.; Preetz, A.; Heller, D. *Tetrahedron: Asymmetry* **2004**, *15*, 2139; (f) Gridnev, I. D.; Imamoto, T. *Acc. Chem. Res.* **2004**, *37*, 633; (g) Shimizu, H.; Ishizaki, T.; Fujiwara, T.; Saito, T. *Tetrahedron: Asymmetry* **2004**, *15*, 2169.
5. (a) δ,λ-Rule: Fryzuk, M. D.; Bosnich, B. *J. Am. Chem. Soc.* **1978**, *100*, 5491; (b) Samuel, O.; Couffignal, R.; Lauer, M.; Zhang, S. Y.; Kagan, H. B. *Nouv. J. Chem.* **1981**, *5*, 15; (c) Kagan, H. B. In *Asymmetric Synthesis Using Organometallic Catalysis*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon: Oxford, 1982; Vol. 8, pp 463–498.
6. (a) Quadrant rule: Koenig, K. E.; Sabacky, M. J.; Bachman, G. L.; Christopfel, W. C.; Barnstoff, H. D.; Friedman, R. B.; Knowles, W. S.; Stults, B. R.; Vineyard, B. D.; Weinkauff, D. *Ann. N.Y. Acad. Sci.* **1980**, *333*, 16; (b) Knowles, W. S. *Acc. Chem. Res.* **1983**, *16*, 106.
7. Twist of coordinated diene: Kyba, E. P.; Davis, R. E.; Juri, P. N.; Shirley, K. R. *Inorg. Chem.* **1981**, *20*, 3616.
8. Imamoto, T.; Watanabe, J.; Wada, Y.; Masuda, H.; Yamada, H.; Tsuruta, H.; Matsukawa, S.; Yamaguchi, K. *J. Am. Chem. Soc.* **1998**, *120*, 1635.
9. Vineyard, B. D.; Knowles, W. S.; Sabacky, G. L.; Bachman, G. L.; Weinkauff, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 5946.
10. Bakos, J.; Tóth, I.; Heil, B.; Szalontai, G.; Párkányi, L.; Fülöp, V. *J. Organomet. Chem.* **1989**, *370*, 263.
11. Wada, Y.; Imamoto, T.; Tsuruta, H.; Yamaguchi, K.; Gridnev, I. D. *Adv. Synth. Catal.* **2004**, *346*, 777.
12. Single crystals of **2** suitable for X-ray crystallographic analysis were grown by recrystallization from THF. Crystal data for **2** ($C_{39}H_{44}F_6P_3RhO$ (**2**·THF)): M = 838.59, T = 106 K, monoclinic space group $C2$ (no. 5), a = 15.039(4), b = 11.823(3), c = 20.373(6) Å, β = 97.257(3)°,

$V = 3593(1)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.55$ g cm^{-1}, μ (Mo Kα) = 6.7 cm^{-1}, $2\theta_{max} = 54.2°$, 3814 measured reflections, 3806 unique reflections ($R_{int} = 0.002$), GOF = 1.72 for 3786 reflections with $I > 1\sigma(I)$, $R_1 = 0.067$. CCDC 233230.

13. Single crystals of **3** suitable for X-ray crystallographic analysis were grown by recrystallization from THF. Crystal data for **3** ($C_{36}H_{40}F_6P_2RhSb$): $M = 873.31$, $T = 110$ K, monoclinic space group P_{21} (no. 4), $a = 19.125(4)$, $b = 17.931(9)$, $c = 19.923(5)$ Å, $\beta = 91.970(3)°$, $V = 6828(3)$ Å^3, $Z = 8$, $\rho_{calcd} = 1.70$ g cm^{-1}, μ (Mo Kα) = 14.24 cm^{-1}, $2\theta_{max} = 54.1°$, 13,165 measured reflections, 13,160 unique reflections ($R_{int} = 0.000$), GOF = 1.81 for 13,023 reflections with $I > 1\sigma(I)$, $R_1 = 0.066$. CCDC 233231.
14. Yoshikuni and Bailar, Jr. reported that asymmetric hydrogenation of acetamidoacrylic acid catalyzed by a rhodium complex of optically active bis[(*o*-methylphenyl)phenylphosphine]ethane afforded *N*-acetylalanine with 63.2% ee. However, the enantiomeric excess of the rhodium complex was not given in their paper Yoshikuni, T.; Bailar, J. C., Jr. *Inorg. Chem.* **1982**, *21*, 2129.