

Rational Design of a Chiral Palladium(0) Olefin Complex of Unprecedented Stability

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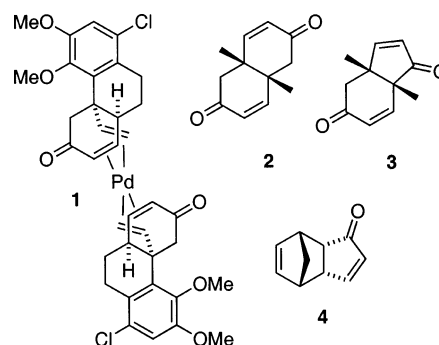
Summary: A chiral bidentate olefin ligand **L** with a 1,4a,5,8a-tetrahydro-naphthalene-2,6-dione framework has been designed, which forms a homoleptic palladium(0) complex L_2Pd of unprecedented stability.

Olefin complexes of palladium(0) such as $Pd_2(dba)_3$ (dba = dibenzylideneacetone)¹ have been widely used as precursors in organometallic synthesis² or as sources for reactive intermediates in palladium-catalyzed transformations.³ In these applications, the olefin usually acts as a weakly coordinating ligand, which is rapidly displaced or easily dissociates. Presumably due to this lability, olefins have received little attention as spectator ligands in palladium-catalyzed reactions.⁴ Their considerable potential as chiral ligands, however, has recently been established by the work of Carreira et al. and Hayashi et al. on Rh(I)- and Ir(I)-catalyzed asymmetric transformations.⁵ Their results indicate that a chiral olefin can remain coordinated strongly enough to the catalytically active metal center to afford high asymmetric induction.

Inspired by these results, we initiated a study on chiral palladium olefin complexes for applications in asymmetric catalysis. As a first step toward this end, we focused on the development of olefin ligands that would show a high affinity toward palladium(0) and remain stably coordinated. We now wish to report the rational design and synthesis of a chiral diene ligand, which forms a palladium(0) complex of unprecedented stability.

Our starting point was the palladium(0) tetraolefin complex **1** (Chart 1), which was recently described by

Chart 1. Structure of Complex 1 and Dienes 2–4



Mulzer et al.⁶ This complex was unexpectedly isolated in racemic form as the product of a Saegusa oxidation.

The ease of formation and relative stability of **1** presumably results from a favorable conformational preorganization of the vinyl phenanthrenone ligand coordinating the metal. Hence, we used the X-ray coordinates of **1** as a search criterion for olefin ligands that would form stable complexes with Pd(0). Computer-assisted modeling led to the identification of a set of rigid bicyclic dienes, compounds **2–4**, that according to our calculations adopt conformations similar to the diene moiety in complex **1** (example in Figure 1).⁷ Among these, the bis(enone) **2** stood out, due to its C_2 symmetry and ease of preparation in enantiomerically pure form.

Apart from its favorable geometry, bis(enone) **2** was chosen as a model ligand for electronic reasons. It has been amply demonstrated that π -back-bonding interactions are a major contributing factor to the stability of d^{10} palladium complexes.⁸ This is reflected partly in the enhanced thermal stability of $Pd_2(dba)_3$ in comparison with labile complexes of palladium with electron-rich olefins such as COD (*cis,cis*-1,5-cyclooctadiene) and 1,6-dienes.⁹ The relatively simple structure of **2** should also allow for substitution to tune the ligands' electronic and steric properties.

(6) Porth, S.; Bats, J. W.; Trauner, D.; Giester, G.; Mulzer, J. *Angew. Chem., Int. Ed.* **1999**, *38*, 2015.

(7) Calculations were conducted using the MM-2 force field, included in: Chem 3-D; CambridgeSoft, 100 CambridgePark Drive, Cambridge, MA, 02140.

(8) (a) Cenini, S.; Ugo, R.; La Monica, G. *J. Chem. Soc. A* **1971**, 416. (b) Yamamoto, G.; Yamamoto, A.; Ikeda, S. *J. Am. Chem. Soc.* **1971**, *93*, 3360. (c) Tolman, C. A. *J. Am. Chem. Soc.* **1974**, *96*, 2780. (d) Ozawa, F.; Ito, T.; Yamamoto, A. *J. Organomet. Chem.* **1979**, *168*, 375.

(9) (a) Green, M.; Howard, J. A. K.; Spencer, J. L.; Stone, F. G. A. *J. Chem. Soc., Chem. Commun.* **1975**, 449. (b) Kraus, J.; Cestari, G.; Haack, K.-J.; Seevogel, K.; Storm, W.; Poerschke, K.-R. *J. Am. Chem. Soc.* **1999**, *121*, 9807.

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(1) Takahashi, Y.; Ito, T.; Sakai, S.; Ishii, Y. *Chem. Commun.* **1970**, 1065.

(2) See for example: (a) Moseley, K.; Maitlis, P. M. *Chem. Commun.* **1971**, 1604. (b) Hashmi, A. S. K.; Naumann, F.; Probst, R.; Bats, J. W. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 104.

(3) Stille, J. R. In *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; Wiley: Chichester, U.K., 1995; Vol. 1, p 482.

(4) For the role of olefin additives in palladium-catalyzed reactions, see: (a) Sustmann, R.; Lau, J.; Zipp, M. *Tetrahedron Lett.* **1986**, *27*, 5207. (b) Tsukada, N.; Yamamoto, Y. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2477. (c) Amatore, C.; Jutand, A. *Coord. Chem. Rev.* **1998**, *178–180*, 511–528.

(5) (a) Fischer, C.; Defieber, C.; Suzuki, T.; Carreira, E. M. *J. Am. Chem. Soc.* **2004**, *126*, 1628. (b) Shintani, R.; Ueyama, K.; Yamada, I.; Hayashi, T. *Org. Lett.* **2004**, *6*, 3425. (c) Defieber, C.; Paquin, J.-F.; Serna, S.; Carreira, E. M. *Org. Lett.* **2004**, *6*, 3873. (d) Tokunaga, N.; Otomaru, Y.; Okamoto, K.; Ueyama, K.; Shintani, R.; Hayashi, T. *J. Am. Chem. Soc.* **2004**, *126*, 13584. (e) Shintani, R.; Okamoto, K.; Otomaru, Y.; Ueyama, K.; Hayashi, T. *J. Am. Chem. Soc.* **2005**, *127*, 54. (f) For a review, see: Glorius, F. *Angew. Chem., Int. Ed.* **2004**, *43*, 3364.

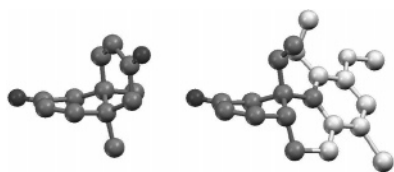
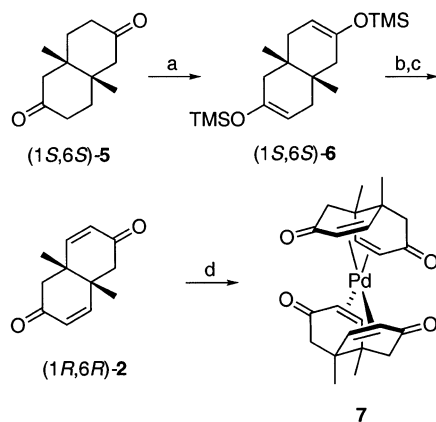


Figure 1. Comparison of the calculated structure of **2** (left) and the phenanthrene ligand in the X-ray crystal structure of **1** (right). Oxygens are colored black, carbons gray, and nonrelevant atoms white. Hydrogen atoms are omitted for clarity.

Scheme 1. Synthesis of Diene (1*R*,6*R*)-2** and Complex **7**^a**



^a Reagents and conditions: (a) TMSCl, LHMDS, THF, -78 °C; (b) NBS, -78 °C; (c) CaCO_3 , DMA, 160 °C (36% over 3 steps); (d) $\text{Pd}(\text{OAc})_2$, (1*R*,6*R*)-**2**, MeOH, 50 °C, 67%.

Bis(enone) **2** was prepared in enantiomerically pure form from the readily available known dione (1*S*,6*S*)-**5** (Scheme 1).¹⁰ Formation of the bis(silyl enol ether) (1*S*,6*S*)-**6**, followed by bromination and dehydrobromination, gave (1*R*,6*R*)-**2** in 36% overall yield. Alternative methods for double unsaturation were found to be less satisfactory.

Treatment of a solution of $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$ in CDCl_3 at room temperature with 2 equiv/Pd of (1*R*,6*R*)-**2** resulted in clean formation of a single product, which precipitates as an orange powder upon trituration with hexanes. MS and HRMS data of the precipitate suggested that two molecules of the ligand (1*R*,6*R*)-**2** are coordinated to palladium. The ^1H NMR shows only five magnetically nonequivalent sets of protons, indicating a symmetric arrangement of the ligands around the metal. Comparison of NMR data of the free ligand **2** and the newly formed complex reveals coordination-induced shifts for the vinylic protons of $\Delta\delta(\text{H}) = -1.8$ and -1.4 ppm and for the coordinated carbon atoms of $\Delta\delta(\text{C}) = -42.4$ and -41.8 ppm, in agreement with expected reduced bonding order due to transfer of electrons from the metal to the π^* molecular orbital of the olefin. These analytical data were consistent with the structure of the D_2 -symmetric, tetracoordinated complex **7**, shown in Scheme 1.

Complex **7** displays an exceptional and unprecedented stability for a Pd(0) olefin complex. It can be handled and stored under air at room temperature and forms stable solutions in normal-grade solvents such as aceto-

nitrile, dichloromethane, and methanol. In contrast to $\text{Pd}_2(\text{dba})_3$, solutions of **7** show no signs of decomposition even after standing at room temperature for days or for hours at elevated temperature (50 °C). Unlike **1**, complex **7** is stable enough to be purified by column chromatography on normal-grade silica gel.

Attempts to grow crystals suitable for X-ray structural analysis from solutions of **7** in various solvents and with varying methods failed, affording only fine powders of the material. However, slow in situ generation of **7** by heating a solution of $\text{Pd}(\text{OAc})_2$ in MeOH to 50 °C in the presence of 3 equiv of (1*R*,6*R*)-**2** led to the formation of large crystals, which were suitable for X-ray crystallographic analysis (Figure 2).^{11,12} Under these conditions, pure **7** was obtained in 67% overall yield.

The X-ray analysis of **7** confirms that all four olefin units of the two ligands are coordinated in a slightly distorted tetrahedral geometry to the palladium center. In comparison with the X-ray structure analysis of the free ligand (1*R*,6*R*)-**2**, coordination only results in a minor change in bond length within the enone units. Average values for the C=C and C=O bonds, respectively, are 1.34 and 1.23 Å in **2** versus 1.38 and 1.22 Å in **7**. While these values do not suggest very strong π -back-bonding, it has to be taken into account that four π -accepting enones are coordinated to the palladium. Similar observations were made for $\text{Pd}_2(\text{dba})_3$.¹³ The dihedral angle C13–C22–C17–C18 in **7** is 62° , a decrease of 12° compared to the corresponding value observed in the crystal of free **2** (74°). Despite the compact arrangement around the metal center, there are no short contacts between the ligands within the complex that would indicate repulsive interactions. Together with the saturated 18-electron configuration of the palladium center and the steric shielding effect of the rigid ligands in **7**, this accounts for the exceptional chemical inertness of the complex.

The catalytic competence of **7** was tested with enyne cyclization **8** \rightarrow **9** under "ligandless conditions":¹⁴ that is, in the absence of phosphines (Scheme 2). The complex showed turnovers at elevated temperature, but no enantiomeric excess has been observed in these preliminary experiments. Though formation of Pd black was not observed under these conditions, the involvement of an achiral catalytically active species

(11) Crystal data for **9**: $\text{C}_{24}\text{H}_{28}\text{O}_4\text{Pd}$, fw 486.90, monoclinic, $P2_1$ (No. 4), $a = 10.783(2)$ Å, $b = 7.306(1)$ Å, $c = 13.147(2)$ Å, $V = 1003.3(3)$ Å³, $\beta = 104.39(2)^\circ$, $Z = 2$, $\mu(\text{Mo K}\alpha) = 9.54$ cm⁻³, Bruker SMART CCD diffractometer, $2\theta_{\text{max}} = 49.4^\circ$, 4464 total reflections measured, $T = -95$ °C, 1981 unique reflections. The data were corrected for Lorentz and polarization effects and were analyzed for agreement and possible absorption. An empirical absorption correction based on comparison of redundant and equivalent reflections was applied ($T_{\text{max}} = 1.00$, $T_{\text{min}} = 0.53$). The structure was solved by direct methods (SIR97).¹⁵ The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. The final cycle of full-matrix least-squares refinement (function minimized $\sum w(|F_o| - |F_c|)^2$) was based on 2321 observed reflections ($I > 3.00\sigma(I)$) and 261 variable parameters and converged with unweighted and weighted agreement factors. $R = 0.043$, $R_w = 0.051$, $R_{\text{all}} = 0.051$, largest difference peaks 0.65 and -1.46 e/Å³.

(12) Farrugia, L. J. *J. Appl. Crystallogr.* **1997**, *30*, 565.

(13) Selvakumar, K.; Valentini, M.; Würle, M.; Pregosin, P. S.; Albinati, A. *Organometallics* **1999**, *18*, 1207.

(14) Trost, B. M.; Lee, D. C.; Rise, F. *Tetrahedron Lett.* **1989**, *30*, 651.

(15) Altomare, A.; Burla, M. C.; Camalli, M.; Casciarano, G.; Giacovazzo, C.; Guagliardi, A.; Moliterni, A. G. G.; Polidori, G.; Spagna, R. *J. Appl. Crystallogr.* **1999**, *32*, 115.

(10) Pfau, M.; Jabin, I.; Reviel, G. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1935.

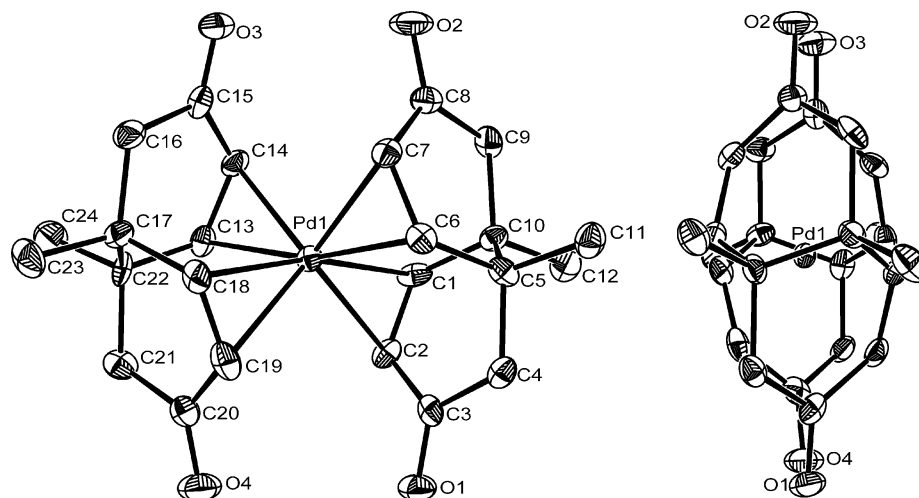
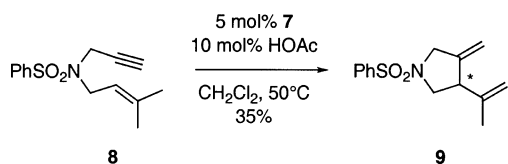


Figure 2. X-ray crystal structure of **7**. Hydrogens are omitted for clarity.

Scheme 2. Enyne Cycloisomerization Catalyzed in the Presence of **7**



formed by partial decomposition of **7** cannot be ruled out.

In summary, we have described the rational design and synthesis of a chiral diene ligand that forms a structurally defined Pd(0) complex of unprecedented stability. Future work will focus on improving the catalytic activity of complexes formed by of this type of ligand and the better definition of the chiral space surrounding the active metal center. To this end, substituted and sterically more demanding derivatives of **2** will be prepared that increase the energy barrier for homoleptic complex formation and should lead to

higher reactivity and asymmetric induction in the reactions catalyzed by their complexes.

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Supporting Information Available: Text giving detailed experimental procedures and analytic data for the preparation of (1*R*,6*R*)-**2** and (1*S*,6*S*)-**7** and crystallographic data, as a CIF file, of the ligand (1*R*,6*R*)-**2** and complex (1*S*,6*S*)-**7**. This material is available free of charge on the Internet at <http://pubs.acs.org>.

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