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A Simple and Efficient Approach to a Rigid Diphosphine Ligand Containing Two Phosphorus and Three Carbon Stereogenic Centers by Means of a Palladium Complex Promoted Asymmetric Diels−Alder Reaction

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Introduction

The synthetic application of enantiomerically pure diphosphines is an important subject which has been highlighted by numerous leading articles.[1] These bidentate ligands have undoubtedly been the key to many spectacular achievements in homogeneous asymmetric catalysis. To date, optically active diphosphines with chirality residing within their carbon skeletons are conventionally prepared from their corresponding chirons.[2] Due to the limitation in the natural pool of chirality, however, this approach generally produces only one particular enantiomeric form of the desired diphosphine. Furthermore, this synthetic methodology is rarely applied efficiently to the important class of P-chiral bidentate ligands.[3] On the other hand, although both racemic C-chiral and P-chiral diphosphines can often be separated into their enantiomers by means of optical resolutions,[4] the procedures involved are somewhat tedious and inefficient. To a significant extent, the difficulties associated with ligand synthesis have restricted the number and the variety of optically active P-chiral diphosphines available for application in asymmetric catalysis. Hence the potential of this class of bidentate ligands as chiral auxiliaries has not been fully explored or exploited. Herein we describe a simple and efficient route to both of the enantiomerically pure forms of a rigid diphosphine ligand containing two phosphorus and three carbon stereogenic centers.

Results and Discussion

The target diphosphine was obtained from the asymmetric Diels−Alder reaction between phenyldivinylphosphine and 1-phenyl-3,4-dimethylphosphole (DMPP) using the organopalladium complex **1** as the reaction promoter (Scheme 1). In this approach, phenyldivinylphosphine was coordinated regiospecifically[5] to (+)-**1** in dichloromethane to give the monomeric complex (+)-**2** as stable yellow prisms in 80% isolated yield, $[\alpha]_D$ +81.0° (CH_2Cl_2). The neutral complex (+)-**2** is soluble in most noncoordinating solvents. In $CDCl_3$, the ^{31}P NMR spectrum of the complex exhibited a sharp singlet at δ 25.0. Treatment of (+)-**2** with silver perchlorate yielded the intermediate nonconducting perchlorato complex (+)-**3** in essentially quantitative yield with $[\alpha]_D$ +86.7° (CH_2Cl_2).[6] This highly reactive species was not isolated and, upon removal of silver chloride, the dichloromethane solution of the complex was treated directly with a stoichiometric amount of DMPP. The cycloaddition reaction was monitored by ^{31}P NMR spectroscopy and was found to be complete within 2 h at room temperature. Removal of the solvent gave the complex (+)-**4** as a colorless viscous oil; attempts at crystallization from a wide range of solvents were unsuccessful. The ^{31}P NMR spectrum of this material in $CDCl_3$ exhibited two doublets at δ 50.6 and 116.0 ($^2J_{PP}$ = 43.9 Hz). Treatment of (+)-**4** with concentrated hydrochloric acid in acetone[7] gave the dichloro complex (−)-**5**, $[\alpha]_D$ −86.3° (CH_2Cl_2). In this reaction, the ^{31}P NMR spectrum of the crude product precipitated from the reaction mixture was recorded prior to recrystallization. In accord with the spectrum observed for (+)-**4**, the ^{31}P NMR spectrum of crude (−)-**5** in $CDCl_3$ exhibited only two strong doublets at δ 36.4 and 124.5 ($^2J_{PP}$ = 4.5 Hz), hence confirming that only one isomer is formed in the asymmetric Diels−Alder reaction. However, this observation is in contrast to a previous report in which two stereochemically distinct isomers were generated simultaneously during the synthesis of **5** by using $PdCl_2$ as the reaction promoter.[8] Clearly, in this earlier work, the two pairs of internally diastereomeric racemates arising from the nonequivalent phosphorus stereogenic centers, (*R**,*R**)-, (*R**,*S**)-**5**, were both generated in the absence of a chiral directing agent, although it was observed to be a 20:1 diastereomeric excess in favor of the (*R**,*S**) isomer.[8] The dichoro complex (−)-**5** was subsequently crystallized from chloroform as stable yellow prisms in 70% yield. The optical rotation value of the complex remained unchanged after the slow recrystallization process.

The X-ray analysis of (−)-**5** reafirms that, as desired, an enantiomerically pure complex has been formed (Figure 1). Five new chiral centers have been generated with *S* and *R* absolute stereochemistries at P(1) and P(2) respectively and *S*, *R*, and *R* stereochemistries at C(1), C(2), and C(5) respectively. An implied prior claim to have achieved spontaneous resolution of **5** on crystallization[8] is incorrect; although crystallization occured

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[1] For selected examples, see: Barnhart, R. W.; Wang, X.; Noheda, P.; Bergens, S. H.; Whelan, J.; Bosnich, B. *J. Am. Chem. Soc.* **1994**, *116*, 1821. Knowles, W. S.; *Acc. Chem. Res.* **1983**, *16*, 106. Noyori, R.; Ohta, M.; Hsaio, Y.; Kitamura, M.; Ohta, T.; Takaya, H. *J. Am. Chem. Soc.* **1986**, *108*, 7117. Brunner, H.; Becker, R.; Gauder, S. *Organometallics* **1986**, *5*, 739. Hayashi, T.; Kanashi, M.; Kumada, M. *J. Chem. Soc., Chem. Commun.* **1984**, 107. Brown, J. M.; McIntyre J. F. *J. Chem. Soc., Perkin Trans.* **1985**, 961. Hiyama, T.; Wakasa, N. *Tetrahedron Lett.* **1985**, *26*, 3259. Tani, K.; Yamagata, T.; Tatsuno, Y.; Yamagata, Y.; Tomita, K.; Akutagawa, S.; Otsuka, S.; Kumobayashi, H. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 217. Landis, C. R.; Halpern, J. *J. Am. Chem. Soc.* **1987**, *109*, 1746. Parinello, G.; Stille, J. K. *J. Am. Chem. Soc.* **1987**, *109*, 7122. Allen, D. G.; Wild, S. B.; Wood, D. L. *Organometallics* **1986**, *5*, 1009.

[2] For examples, see: Fryzuk, M. D.; Bosnich, B. *J. Am. Chem. Soc.* **1978**, *100*, 5491. Stille, J. K.; Amma, J. P. *J. Org. Chem.* **1982**, *47*, 468. Kyba, E. P.; Davies, R. E.; Juri, P. N.; Shirley, K. R. *Inorg. Chem.* **1981**, *20*, 3616. Brown, J. M.; Murrer, B. A. *Tetrahedron Lett.* **1980**, *21*, 581. Takaya, H.; Mashima, K.; Koyano, K.; Yagi, M.; Kumobayashi, H.; Taketomi, T.; Akutagawa, S.; Noyori, R. *J. Org. Chem.* **1986**, *51*, 629. Ojima, I.; Kogure, T.; Yoda, Y. *Org. Synth.* **1985**, *63*, 18. Nagel, U.; Kinzel, E. *J. Chem. Soc., Chem. Commun.* **1986**, 1098.

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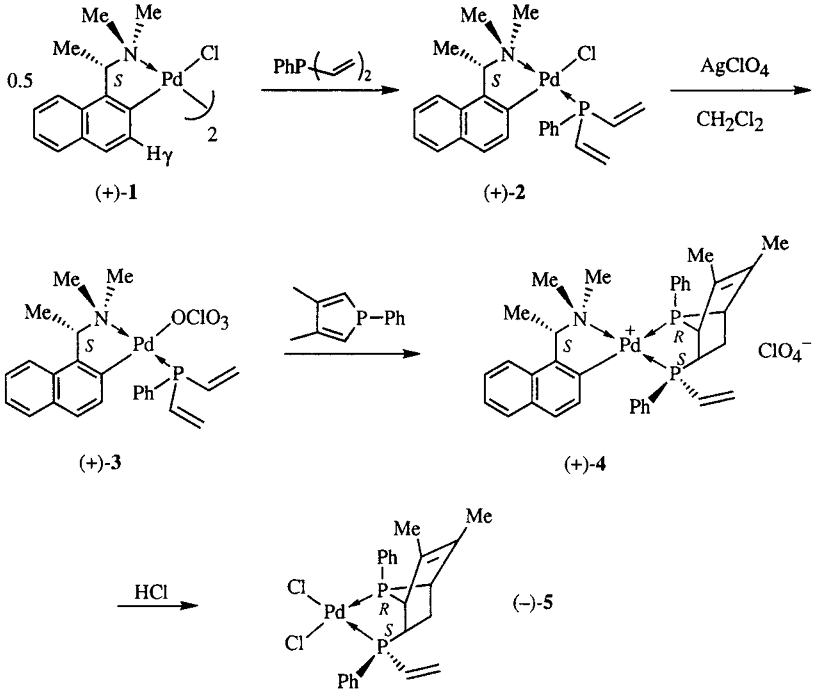
Scheme 1



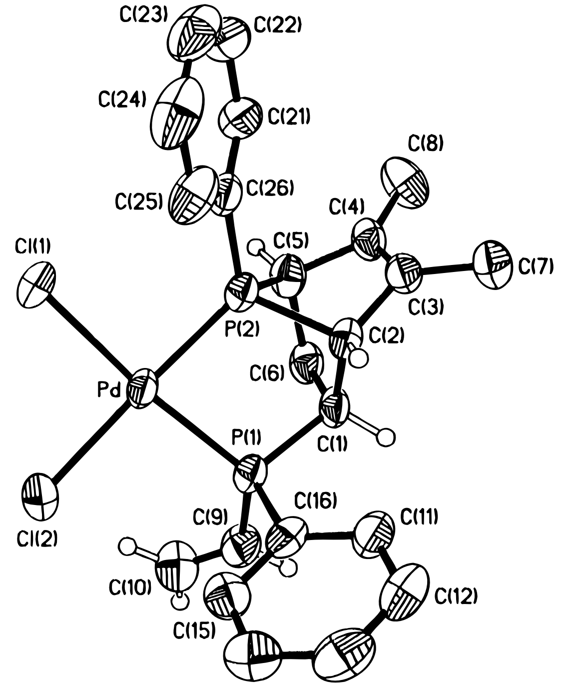


Figure 1. The molecular structure of (−)-**5** showing the five new chiral centers formed from the Diels−Alder reaction (70% probability ellipsoids).

in the noncentrosymmetric polar space group *Fdd*2, this space group contains glide planes and hence equal numbers of (+) and (−) molecules—thus resolution was not achieved. The relative stereochemistries, however, of the five chiral centers are the same as we observe for (−)-**5**.

The palladium has slightly distorted square-planar geometry comprising a contraction in the P−Pd−P ligand bite angle to 83.0(1)° and a small enlargement of the Cl−Pd−Cl angle at 92.0(1)°. There are significant out of plane deviations of the coordinated atoms, the Pd, Cl, and P atoms having deviations of up to 0.08 Å from their mean plane. The coordinated bond lengths Pd−Cl(1) and −Cl(2) = 2.357(1), 2.361(1) Å and Pd−P(1) and −P(2) = 2.247(1), 2.228(1) Å are unexceptional, though it is noticeable that the bond length from the palladium to the more sterically hindered phosphorus P(2) is 0.02 Å shorter than that to the less hindered P(1). There are no significant differences in the bond lengths observed here and those reported for the racemic structure.[8] The principal difference is in the orientation of the vinylic group which has a *syn* relationship to the palladium in (−)-**5** compared with an *anti* geometry in the racemate. There are no strong intermolecular interactions in (−)-**5**, though there is evidence for weak CH···π bonding.

It is noteworthy that enantiomerically pure (+)-**5** is also obtained in similar yield and optical purity when the equally accessible (−)-**1** is used as the reaction promoter. It has been reported in the earlier nonenantioselective work that the formation of the thermodynamically unstable *exo*−*syn* isomer in this particular Diels−Alder reaction required both the diene and the dienophile to be coordinated simultaneously on the metal template during the course of the cycloaddition.[8] From a stereochemical standpoint, however, the present enantiospecific synthesis of **5** requires an additional control of the absolute stereochemistry at both template sites. We have previously observed that the two prochiral *N*-methyl groups and the γ naphthylene proton (H_γ) which is adjacent to the metalated carbon of the 5-membered organometallic naphthylamine ring are sensitive to the stereochemical environment of their neighboring coordination sites in square-planar palladium(II) complexes.[9] We are currently investigating the influence of these groups on the enantioselectivities of this particular Diels−Alder reaction.

Experimental Section

Reactions involving air-sensitive compounds were performed under a positive pressure of purified nitrogen. NMRs were recorded at 25 °C on Bruker ACF 300 and AMX 500 spectrometers. Optical rotations were measured on the specified solutions in a 1-dm cell at 25 °C with a Perkin-Elmer Model 341 polarimeter. Elemental analyses were performed by the Microanalytical Laboratory of the Department of Chemistry at the National University of Singapore.

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Both of the enantiomerically pure forms of bis(μ-chloro)bis[(*R/S*)-1-[1-(dimethylamino)ethyl]-2-naphthalenyl-*C,N*]dipalladium(II) dichloromethane solvate, (±)-**1**, were prepared as previously described.[10]

[*SP*-4-4-(*S*)-Chloro[1-[1-(dimethylamino)ethyl]-2-naphthalenyl-*C,N*][phenyldivinylphosphine-*P*]palladium(II) [(+)-2]. A mixture of phenyldivinylphosphine (2.1 g) and (+)-**1** (4.4 g) in dichloromethane (300 mL) was stirred at room temperature until all the reaction promoter had dissolved (ca. 1 h). The solvent was removed from the reaction mixture and the residue was recrystallized from dichloromethane-*n*-hexane mixture, forming beautiful yellow prisms: mp 106−108 °C; $[\alpha]_D$ +81.0° (*c* 1.1, CH_2Cl_2); 5.2 g (80% yield). Anal. Calcd for $C_{24}H_{27}ClNPPd$: C, 57.4; H, 5.4; N, 2.8. Found: C, 57.4; H, 5.4; N, 2.8. ^{31}P NMR ($CDCl_3$): δ 25.0(s); ^1H NMR ($CDCl_3$): δ 1.97 (d, 3H, $^3J_{HH}$ = 6.4 Hz, CH*Me*), 2.93 (d, 3H, $^4J_{PH}$ = 1.7 Hz, NMe), 2.95 (d, 3H, $^4J_{PH}$ = 3.5 Hz, NMe), 4.35 (qn, 1H, $^3J_{HH} = {}^4J_{PH}$ = 6.4 Hz, C*H*Me), 5.58−6.21 (m, 4H, 2 × CH═CH_2), 6.60−6.87 (m, 2H, 2 × C*H*═CH_2), 7.10−7.92 (m, 2H, 2 × C═C*H*), 6.80−7.80 (m, 11H, aromatics).

[*SP*-4-3-[1α,4α,5α(*S*),7*R*]]-Dichloro[5-(ethenylphenylphosphino)-2,3-dimethyl-7-phenyl-7-phosphabicyclo[2.2.1]hept-2-ene-*P*^{5},*P*^{7}]-palladium(II) [(−)-5]. A solution of (+)-**2** (5.1 g) in dichloromethane (200 mL) was stirred for 2 h in the presence of a solution of silver perchlorate (2.1 g) in water (1 mL). The colorless organic layer, after the removal of AgCl and dried ($MgSO_4$), was treated with DMPP (1.8 g) at room temperature for 2 h. Removal of the solvent gave (+)-**4** as a colorless oil that could not be crystallized from any of the solvents tried: $[\alpha]_D$ +75.4° (*c* 0.4, CH_2Cl_2). ^{31}P NMR ($CDCl_3$): δ 50.6 (d, 1P, $^2J_{PP}$ = 43.9 Hz, P^5), 116.0 (d, 1P, $^2J_{PP}$ = 43.9 Hz, P^7). Crude (+)-**4** was redissolved in acetone (130 mL) and was treated with hydrochloric acid (10 M, 15 mL). The reaction mixture was then refluxed for 15 min. The bright yellow microcrystals of (−)-**5** precipitated out during this period. The product was then filtered and recrystallized from chloroform: mp >300 °C dec; $[\alpha]_D$ −86.3° (*c* 0.5, CH_2Cl_2); 3.7 g (70% yield). Anal. Calcd for $C_{22}H_{24}Cl_2P_2Pd$: C, 50.1; H, 4.6. Found: C, 49.9; H, 4.5. ^{31}P NMR ($CDCl_3$): δ 36.4 (d, 1P, $^2J_{PP}$ = 4.5 Hz, P^5), 124.5 (d, 1P, $^2J_{PP}$ = 4.5 Hz, P^7); ^1H NMR ($CDCl_3$) was similar to that of its racemic analogue.[8]

Crystal Structure Determination of (−)-5. Yellow prisms were obtained as described above, and a crystal of approximate dimensions 0.53 × 0.50 × 0.50 mm was used for the diffraction study. Crystallographic data are summarized in Table 1. Intensity data were collected in the ω-scan mode on a Siemens P4/PC diffractometer using Mo Kα radiation to a maximum 2θ value of 55°. The structure was solved by direct methods and the non-hydrogen atoms refined anisotropically. H atoms for the two methyl groups were located from a ΔF map and their positions idealized while the remaining H atoms were included in calculated positions. The H atoms were assigned isotropic thermal parameters, $U(H) = 1.2U_{eq}(C)$ [$U(H) = 1.5U_{eq}(C{-}Me)$] and allowed to ride on their parent carbon atoms. Both phenyl rings were refined as idealized rigid bodies. Computations (SHELXTL PC version 5.03) were by the full-matrix least-squares method to give $R_1 = 0.0293$, $wR_2 = 0.0761$ for 2634 independent observed reflections [$|F_o| > 4\sigma(|F_o|)$]. The absolute configuration was determined unambiguously both by an *R*-factor test [$R^+ = 0.0293$, $R^- = 0.0316$] and by the Flack parameter, which refined to an *x* value of 0.11(5). Selected bond lengths and angles are given in Table 2.

Table 1. Crystallographic Data for (−)-**5**

formula: $C_{22}H_{24}Cl_2P_2Pd$	fw = 527.7
a = 7.280(1) Å	orthorhombic
b = 15.428(1) Å	space group: $P2_12_12_1$
c = 19.224(3) Å	λ = 0.710 73 Å
V = 2159.1(3)	μ(Mo Kα) = 1.261 mm^{-1}
Z = 4	$F(000)$ = 1064
ρ_{calc} = 1.623 g cm^{-3}	T = 223 K
R_1 = 0.0293[a]	wR_2 = 0.0761[b]

[a] $R_1 = \sum||F_o| - |F_c||/\sum|F_o|$. [b] $wR_2 = \{\sum[w(F_o^2 - F_c^2)^2]/\sum[w(F_o^2)^2]\}^{1/2}$; $w^{-1} = \sigma^2(F_o^2) + (aP)^2 + bP$.

Table 2. Selected Bond Lengths (Å) and Angles (deg) for (−)-**5**

Pd−P(2)	2.228(1)	Pd−P(1)	2.247(1)
Pd−Cl(1)	2.357(1)	Pd−Cl(2)	2.361(1)
P(1)−C(9)	1.810(4)	P(1)−C(16)	1.814(2)
P(1)−C(1)	1.829(4)	P(2)−C(26)	1.796(2)
P(2)−C(5)	1.841(4)	P(2)−C(2)	1.851(4)
C(3)−C(4)	1.330(6)		
P(2)−Pd−P(1)	83.00(4)	P(2)−Pd−Cl(1)	90.78(4)
P(1)−Pd−Cl(1)	172.38(4)	P(2)−Pd−Cl(2)	175.64(4)
P(1)−Pd−Cl(2)	94.49(4)	Cl(1)−Pd−Cl(2)	91.98(4)
C(9)−P(1)−C(16)	104.4(2)	C(9)−P(1)−C(1)	105.9(2)
C(16)−P(1)−C(1)	107.0(2)	C(9)−P(1)−Pd	118.5(2)
C(16)−P(1)−Pd	115.2(1)	C(1)−P(1)−Pd	105.0(1)
C(26)−P(2)−C(5)	111.6(2)	C(26)−P(2)−C(2)	112.3(2)
C(5)−P(2)−C(2)	81.7(2)	C(26)−P(2)−Pd	117.5(1)
C(5)−P(2)−Pd	118.2(1)	C(2)−P(2)−Pd	110.0(1)

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Supporting Information Available: For (−)-**5**, a figure showing a different view of the structure and tables of crystal data, data collection, solution and refinement, final positional parameters, bond distances and angles, thermal parameters of non-hydrogen atoms, and calculated hydrogen parameters (6 pages). Ordering information is given on any current masthead page.

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