A Palladium Complex Promoted Asymmetric Synthesis of a Novel P-Chiral Diphosphine Containing an Ester Functional Group

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Introduction

The spectacular efficiency of functionalized diphosphines as chiral auxiliaries in homogeneous asymmetric catalysis has been convincingly demonstrated.[1] In most cases, chiral catalysts supported by these functionalized bidentate ligands give significantly higher chemical yields and optical purities than those supported by monodentate or nonfunctionalized auxiliaries. To date, functionalized diphosphines with chirality residing in the carbon skeletons are readily prepared from their corresponding chirons. This approach, however, has been unsuccessful in preparing diphosphines containing stereogenic phosphorus centers. Although functionalized monodentate P-chiral phosphines and nonfunctionalized P-chiral diphosphines can be prepared by asymmetric synthesis,[2] surprisingly, the few reported functionalized P-chiral diphosphines are invariably obtained via tedious optical resolution.[3] These kinetically stable bidentate ligands should be ideal auxiliaries since their chiral donor atoms, which are the primary chirality inducers, are directly coordinated onto the catalytic metal centers while a secondary control is operating simultaneously via the attached functionalities. We herein report the first asymmetric synthesis of a rigid P-chiral diphosphine containing an ester functional group.

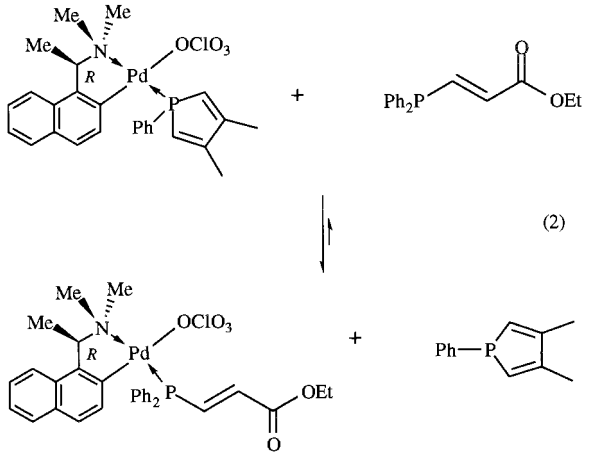
Results and Discussion

The ethyl carboxylate substituted phosphine **1** can be prepared efficiently from the reaction between diphenylphosphine and ethyl propiolate at room temperature in CH_2Cl_2 (eq 1).

$$Ph_2PH + H{-}C{\equiv}C{-}CO_2Et \rightarrow \underset{\mathbf{1}}{\textit{trans}\text{-}Ph_2PCH{=}CH{-}CO_2Et} \quad (1)$$

Purification of the crude product by silica gel chromatography afforded the tertiary phosphine as an air-sensitive colorless oil in 50% yield. The ^{31}P NMR spectrum of **1** in $CDCl_3$ exhibited a sharp singlet at δ −10.9. When treated with the coordinated cyclic diene 1-phenyl-3,4-dimethylphosphole (DMPP) in complex (R_c)-**2**,[4] the ethyl carboxylate substituted phosphine behaved as a typical dienophile in the ensuing [4+2] cycloaddition reaction (Scheme 1). The reaction was carried out at room temperature in CH_2Cl_2 and was found to be complete within 2 h to give (R_c,S_p)-**3** stereospecifically. Prior to crystallization, the 202 MHz ^{31}P NMR spectrum of the crude product exhibited two doublets at δ 52.3 and 128.7 (J_{PP} = 41.5 Hz). No other ^{31}P NMR signal was detected in the spectrum. Upon crystallization from CH_2Cl_2−Et_2O, (R_c,S_p)-**3** was isolated as colorless prisms (90%): mp 224−227 °C dec; $[\alpha]_D$ −4.4° (c = 0.5, CH_2Cl_2).

It is noted that, in addition to the Diels−Alder reaction, a ligand redistribution process was also involved in the formation of (R_c,S_p)-**3** (eq 2). Due to the distinct electronic directing



effects originating from the σ-donating nitrogen and π-accepting aromatic carbon atom of the ortho-metalated naphthylamine ring, it has been well established that the position trans to the NMe_2 group invariably takes up the softest donor atom available.[5] It is therefore clear that the phosphorus donor in **1** is a stronger π-acceptor than its counterpart in DMPP. Furthermore, the ligand redistribution process must occur prior to the cycloaddition reaction, as it has been reported that organopalladium complexes containing the naphthylamine auxiliary and diphosphine ligands are kinetically stable but their monodentate phosphine analogues are kinetically labile.[6] The coordination chemistry and the absolute stereochemistry of (R_c,S_p)-**3** were confirmed by X-ray structural analysis (Figure 1). The studies reveal that the PPh_2 moiety is indeed coordinated trans to the NMe_2 group and the ethyl carboxylate group is attached at the endo position of the phosphanorbornene skeleton. The absolute configurations at the P(1), C(11), C(15), C(18), C(19), and C(20) stereocenters are *S*, *R*, *S*, *S*, *R*, and *S*, respectively.

Treatments of (R_c,S_p)-**3** with concentrated sulfuric acid and lithium chloride at room temperature gave the dichloro complex (S_p)-**4** in 94% isolated yield with $[\alpha]_D$ +76.7° (c = 0.5, CH_2Cl_2). The ^{31}P NMR spectrum of (S_p)-**4** in $CDCl_3$ exhibited a pair of doublets at δ 133.4 and 35.2 (J_{PP} = 4.0 Hz). It is noteworthy that the small phosphorus−phosphorus coupling

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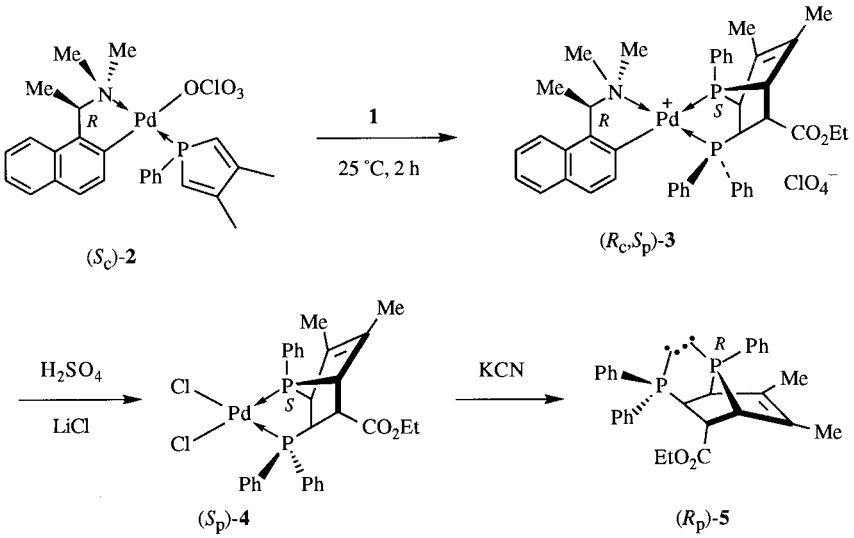
Scheme 1



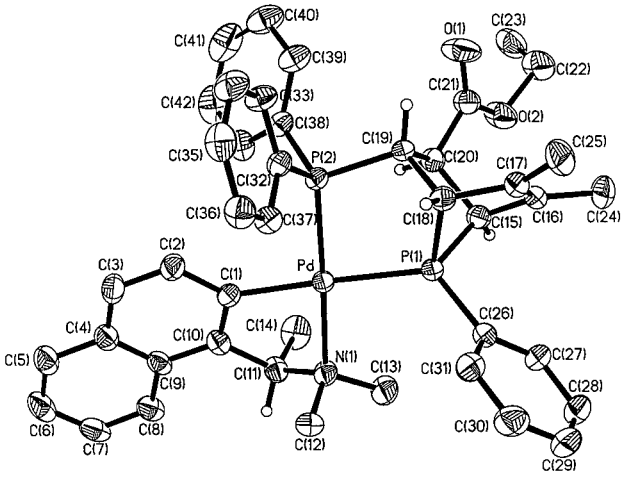


Figure 1. Molecular structure and absolute stereochemistry of (R_c,S_p)-**3**.

constant observed for this dichloro complex is consistent with those recorded for similar diphosphine palladium complexes containing chloro ligands.[7,8] Indeed, the unusually strong P−P coupling (41.5 Hz) observed in the ^{31}P NMR spectrum of (R_c,S_p)-**3** can be attributed to a strong P−Pd−P′ electronic interaction triggered by the organopalladium−naphthylamine unit.[8] We recently suggested that the strong P−P interactions on the chiral template complexes are the major electronic factors for the activation of this class of cycloaddition reactions.[8] Stereospecific liberation of the functionalized diphosphine ligand from (S_p)-**4** can be achieved by the treatment of the dichloro complex with aqueous cyanide. The free ligand (R_p)-**5** was thus obtained as a colorless oil in 86% yield with $[\alpha]_D$ +204.5° (*c* = 0.5, CH_2Cl_2). The ^{31}P NMR spectrum of the free diphosphine in $CDCl_3$ exhibited a pair of doublets at δ 103.8 and −4.4 (J_{PP} = 70.5 Hz). The low-field ^{31}P resonance indicates that the exo-syn stereochemistry is retained.[7] It is noteworthy that the apparent inversion of configuration that takes place at the phosphorus stereogenic center during the liberation reaction is merely a consequence of the Cahn−Ingold−Prelog (CIP) rules.[9] Furthermore, the enantiomeric forms of (S_c,R_p)-**3**, (R_p)-**4**, and (S_p)-**5** can be prepared similarly from the ethyl carboxylate substituted phosphine **1** and the equally accessible cyclic diene complex (S_c)-**2**. Investigations on the catalytic properties of transition metal complexes containing these optically active functionalized diphosphines are currently in progress.

Experimental Section

Reactions involving air-sensitive compounds were performed under a positive pressure of purified nitrogen. NMR spectra 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.

Both of the enantiomerically pure forms of chloro{(*R*/*S*)-1-[1-(dimethylamino)ethyl]-2-naphthyl-C^2,*N*}[3,4-dimethyl-1-phenylphosphole-*P*]palladium(II), (R/S_c)-**2**, were prepared according to literature methods.[4]

Diphenyl[(*E*)-2-(ethoxycarbonyl)vinyl]phosphine. A mixture of ethyl propiolate (0.98 g, 10 mmol), diphenylphosphine (1.86 g, 10 mmol), and glacial acetic acid (0.6 g, 10 mmol) in dichloromethane (30 mL) was stirred at room temperature for 2 d. The solvent was removed under reduced pressure to give a black residue. This material was chromatographed on a silica gel column (50 g, 40−63 μm) with dichloromethane−hexane (1:1 v/v) as the eluent, giving the tertiary phosphine as a highly air-sensitive colorless oil: 1.40 g (50% yield). ^{31}P NMR ($CDCl_3$): δ −10.9.

{(*R*)-1-[1-(Dimethylamino)ethyl]naphthyl-C^2,*N*}{(1α,4α,5α(*R*),6β-(*S*),7*S*)-[5-(diphenylphosphino)-2,3-dimethyl-6-(ethoxycarbonyl)-7-phenyl-7-phosphabicyclo[2.2.1]hept-2-ene-P^5,P^7}palladium(II) Perchlorate [(R_c,S_p)-3]. A solution of the perchlorato complex (R_c)-**2** (0.63 g, 1.06 mmol) in dichloromethane (30 mL) was treated with the ethyl carboxyate substituted phosphine **1** (0.30 g, 1.06 mmol) at room temperature for 2 h. The solution was then concentrated to ca. 10 mL. Upon slow addition of diethyl ether to the concentrated solution, (R_c,S_p)-**3** was obtained as colorless prisms: mp 224−227 °C; $[\alpha]_D$ −4.4° (*c* 0.5, CH_2Cl_2); 0.84 g (90% yield). Anal. Calcd for $C_{43}H_{46}ClNO_6P_2Pd$: C, 58.9; H, 5.3; N, 1.6; P, 7.1. Found: C, 58.7; H, 5.7; N, 1.4; P, 6.9. ^{31}P NMR ($CDCl_3$): δ 52.3 (d, 1 P, $^2J_{PP}$ = 41.5 Hz, P^5), 128.7 (d, 1 P, $^2J_{PP}$ = 41.5 Hz, P^7). ^{1}H NMR ($CDCl_3$): δ 1.20 (t, 3 H, $^3J_{HH}$ = 7.0 Hz, OCH_2Me), 1.41 (s, 3 H, C=C*Me*), 1.67 (s, 3 H, C=C*Me*), 1.99 (d, 3 H, $^3J_{HH}$ = 6.2 Hz, CH*Me*), 2.56 (d, 3 H, $^4J_{PH}$ = 1.7 Hz, N*Me*), 2.73 (d, 3 H, $^4J_{PH}$ = 3.5 Hz, N*Me*), 2.90 (dd, 1 H, $^2J_{PH}$ = $^3J_{HH}$ = 1.8 Hz, H_4), 3.47 (dddd, 1 H, $^3J_{PH}$ = 22.8 Hz, $^3J_{P'H}$ = $^3J_{HH}$ = $^3J_{HH'}$ =

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1.8 Hz, $H_{6(exo)}$), 3.66 (dddd, 1 H, $^3J_{PH}$ = 43.9 Hz, $^2J_{P'H}$ = 8.8 Hz, $^3J_{HH}$ = $^3J_{HH'}$ = 1.8 Hz, H_5), 4.03 (q, 2 H, $^3J_{HH}$ = 7.0 Hz, O*CH*$_2$Me), 4.30 (dd, 1 H, $^2J_{PH}$ = 4.0 Hz, $^3J_{HH}$ = 1.8 Hz, H_1), 4.45 (qn, 1 H, $^3J_{HH}$ = $^4J_{PH}$ = 6.2 Hz, C*H*Me), 6.80−8.24 (m, 21 H, aromatics).

[SP-4-2-(1α,4α,5α(*R*),6β(*S*),7*S*)]-Dichloro{5-(diphenylphosphino)-2,3-dimethyl-6-(ethoxycarbonyl)-7-phenyl-7-phosphabicyclo[2.2.1]-hept-2-ene-*P*^{5},*P*^{7}}palladium(II) [(*S*$_p$)-4]. The naphthylamine auxiliary in (*R*$_c$,*S*$_p$)-**3** was removed chemoselectively by dissolving the complex (0.50 g, 0.57 mmol) in concentrated sulfuric acid (30 mL, 70%). Addition of the acidic solution to crushed ice (100 g) followed by treatment with lithium chloride (0.51 g, 12.0 mmol) gave the dichloro complex (*S*$_p$)-**4** as a white precipitate. The crude complex was subsequently filtered, off, washed with water (3 × 10 mL) and ethanol (3 × 10 mL), and recrystallized from dichloromethane−diethyl ether as pale yellow blocks: mp 272−275 °C; $[\alpha]_D$ +76.7° (*c* 0.5, CH_2Cl_2); 0.35 g (94% yield). Anal. Calcd for $C_{29}H_{30}Cl_2O_2P_2Pd$: C, 53.6; H, 4.7; P, 9.5. Found: C, 53.5; H, 5.0; P, 9.4. ^{31}P NMR ($CDCl_3$): δ 35.2 (d, 1 P, $^2J_{PP}$ = 4.0 Hz, P^5), 133.4 (d, 1 P, $^2J_{PP}$ = 4.0 Hz, P^7). ^{1}H NMR ($CDCl_3$): δ 1.19 (t, 3 H, $^3J_{HH}$ = 7.3 Hz, OCH$_2$*Me*), 1.55 (s, 3 H, C=C*Me*), 1.56 (s, 3 H, C=C*Me*), 3.08 (b s, 1 H, H_4), 3.62 (dddd, 1 H, $^3J_{PH}$ = 20.7 Hz, $^3J_{P'H}$ = $^3J_{HH}$ = $^3J_{HH'}$ = 1.8 Hz, $H_{6(exo)}$), 3.72 (dddd, 1 H, $^3J_{PH}$ = 49.0 Hz, $^2J_{P'H}$ = 7.0 Hz, $^3J_{HH}$ = $^3J_{HH'}$ = 1.8 Hz, H_5), 3.84 (dd, 1 H, $^2J_{PH}$ = 3.6 Hz, $^3J_{HH}$ = 1.8 Hz, H_1), 4.06 (q, 2 H, $^3J_{HH}$ = 7.3 Hz, O*CH*$_2$Me), 7.40−8.20 (m, 15 H, aromatics).

(1α,4α,5α(*R*),6β(*S*),7*S*)-5-(Diphenylphosphino)-2,3-dimethyl-6-(ethoxycarbonyl)-7-phenyl-7-phosphabicyclo[2.2.1]hept-2-ene [(*R*$_p$)-5]. Liberation of (*R*$_p$)-**5** from (*S*$_p$)-**4** was achieved by treating a dichloromethane (20 mL) solution of the dichloro complex (0.32 g, 0.5 mmol) with potassium cyanide (2.5 g, 40 mmol) in water (10 mL) at room temperature for 15 min. The organic layer was separated from the mixture, washed with water (3 × 10 mL), and dried over $MgSO_4$. Upon removal of the solvent, the diphosphine (*R*$_p$)-**5** was obtained as an air-sensitive colorless oil: $[\alpha]_D$ +204.5° (*c* 0.5, CH_2Cl_2); 0.20 g (86% yield). ^{31}P NMR ($CDCl_3$): δ −4.4 (d, 1 P, $^2J_{PP}$ = 70.5 Hz, P^5), 103.8 (d, 1 P, $^2J_{PP}$ = 70.5 Hz, P^7).

Crystal Structure Determination of (*R*$_c$,*S*$_p$)-3. A colorless prism with dimensions 0.33 × 0.33 × 0.22 mm was used for diffraction studies. Crystallographic data are summarized in Table 1. A total of 7358 independent reflections were measured on a Siemens SMART CCD diffractometer with Mo Kα radiation (graphite monochromator) using ω scans. All the non-hydrogen atoms were refined anisotropically. Full-matrix least-squares refinement based on F^2 with absorption-corrected data gave R_1 = 0.0400 and wR_2 = 0.1036. The absolute stereochemistry was determined unambiguously by refining the Flack parameter [x = −0.03(3)]. Selected bond lengths and angles are given in Table 2.

Table 1. Crystallographic Data for (*R*$_c$,*S*$_p$)-**3**

formula	$C_{43}H_{46}ClNO_6P_2Pd$	*Z*	9
fw	876.6	*T*/K	293
space group	*R*3	ρ_{calcd}/g cm^{-3}	1.393
crystal system	trigonal	λ/Å	0.710 73 (Mo)
a/Å	18.464(1)	μ/cm^{-1}	6.31
b/Å	18.464(1)	*F*(000)	4068
c/Å	31.851(1)	R_1 (obs data)[a]	0.0400
V/Å^3	9404.1(2)	wR_2 (obs data)[b]	0.1036

[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 (*R*$_c$,*S*$_p$)-**3**

Pd−P(1)	2.342(1)	Pd−P(2)	2.257(2)
Pd−C(1)	2.050(5)	Pd−N(1)	2.143(5)
P(1)−C(15)	1.867(5)	P(1)−C(18)	1.867(5)
P(1)−C(26)	1.804(5)	P(2)−C(19)	1.869(5)
P(2)−C(32)	1.835(5)	P(2)−C(38)	1.827(5)
C(16)−C(17)	1.326(8)	C(19)−C(20)	1.567(7)
C(21)−O(1)	1.187(7)	C(21)−O(2)	1.332(7)
P(1)−Pd-P(2)	83.1(1)	P(1)−Pd−C(1)	174.5(1)
P(1)−Pd−N(1)	99.8(1)	P(2)−Pd−C(1)	97.2(2)
P(2)−Pd−N(1)	174.0(2)	C(1)−Pd−N(1)	80.3(2)
C(15)−P(1)−C(18)	81.3(2)	P(2)−C(19)−C(20)	108.7(3)

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Supporting Information Available: For (*R*$_c$,*S*$_p$)-**3**, tables of crystal data and data collection, solution, and refinement details, final positional parameters, bond distances and angles, thermal parameters of non-hydrogen atoms, and calculated hydrogen parameters (13 pages). Ordering information is given on any current masthead page.

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