Articles

Asymmetric Synthesis of a (P-Chiral) As−P Bidentate Ligand *via* an Organopalladium Complex Promoted Asymmetric Diels−Alder Reaction between $Ph_2AsCH{=}CH_2$ and 1-Phenyl-3,4-dimethylphosphole

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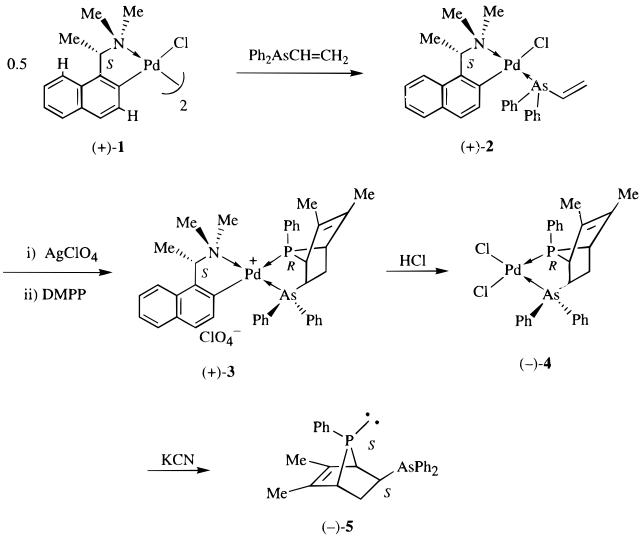
Convenient access to the enantiomerically pure rigid bidentate ligand (−)-[5-(diphenylarsino)-2,3-dimethyl-7-phenyl-7(*S*)-phosphabicyclo[2.2.1]hept-2-ene is established via an asymmetric [4 + 2] cycloaddition between diphenylvinylarsine and 1-phenyl-3,4-dimethylphosphole using the chiral organopalladium(II) complex containing ortho-metalated dimethyl[1-(2-naphthyl)ethyl]amine as the reaction promoter. The absolute configurations of the four newly generated stereocenters have been assigned by single-crystal X-ray analysis.

Introduction

In keeping with our studies concerning the stereochemistry of chelating arsine and phosphine ligands with resolved chiral donor atoms, we have resolved several asymmetric As−S[2,3] and P−S[3,4] bidentate ligands by the metal complexation technique. Recently, we have also reported the asymmetric syntheses of a sulfinyl-substituted P-chiral phosphine[5] and a rigid P-chiral diphosphine.[6] These stereochemically well-defined metal sequesters have been shown to have a rich coordination chemistry.[7] Here we present the first asymmetric synthesis of a rigid As−P hetero-bidentate species with one phosphorus and three carbon stereogenic centers. This class of unsymmetrical bidentates has important implication in enantioselective synthesis.[8] The only two documented optically active As−P bidentate ligands have been obtained by optical resolutions, however.[9]

Scheme 1



Results and Discussion

Asymmetric Synthesis. Diphenylvinylarsine is obtained in 92% isolated yield from the thermolysis of [2-(methylsulfinyl)ethyl]diphenylarsine.[3] As illustrated in Scheme 1, the tertiary arsine is a powerful ligand which splits the chloro bridges in the chiral dimeric complex (+)-**1** regiospecifically[10] to give the monomeric neutral compound (+)-**2** in 88% yield: $[\alpha]_D$ +75.2° (CH_2Cl_2). The asymmetric [4 + 2] cycloaddition reaction is achieved by first treating (+)-**2** with a stoichiometric quantity of silver perchlorate in dichloromethane; upon removal of silver chloride, the cyclic diene 1-phenyl-3,4-

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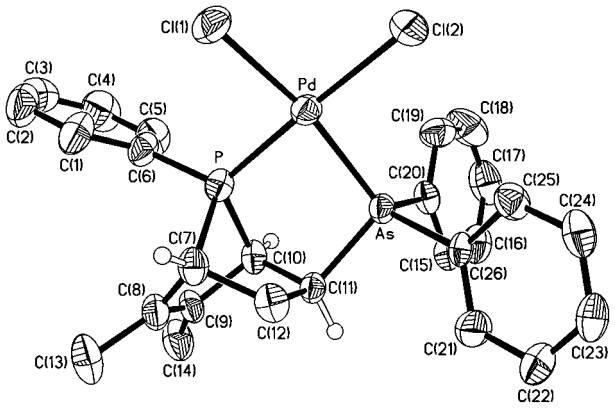

Figure 1. Crystal structure of (−)-**4**. Hydrogen atoms, other than those at chiral centers, have been omitted for clarity, and the thermal ellipsoids are drawn at the 50% probability level.

Table 1. Selected Bond Lengths (Å) and Angles (deg) for (−)-4

Pd−As	2.349(1)	Pd−P	2.218(2)
Pd−Cl(1)	2.345(2)	Pd−Cl(2)	2.360(2)
As−C(11)	1.950(7)	As−C(20)	1.921(3)
As−C(26)	1.920(3)	P−C(6)	1.830(4)
P−C(7)	1.849(7)	P−C(10)	1.834(7)
As−Pd−P	83.1(1)	As−Pd−Cl(1)	168.3(1)
As−Pd−Cl(2)	93.6(1)	P−Pd−Cl(1)	89.1(1)
P−Pd−Cl(2)	175.0(1)	Cl(1)−Pd−Cl(2)	94.78(9)
C(7)−P−C(10)	80.8(3)	C(7)−P−Pd	115.3(2)
C(10)−P−Pd	113.8(2)	C(6)−P−Pd	120.4(2)
C(11)−As−Pd	101.9(2)	C(20)−As−Pd	117.6(2)
C(26)−As−Pd	120.6(1)	C(20)−As−C(26)	103.4(2)
C(11)−C(10)−P	98.1(5)	C(12)−C(7)−P	100.9(5)
C(9)−C(10)−P	101.2(5)	C(8)−C(7)−P	100.7(5)

dimethylphosphole (DMPP) is then added directly into the complex solution. The Diels−Alder reaction is complete in 3 days at room temperature to give (+)-**3** as pale yellow microcrystals in 50% isolated yield: $[\alpha]_D$ +136.0° ($CHCl_3$). It should be note that, prior to purification, the ^{31}P NMR spectrum of the crude Diels−Alder product in $CDCl_3$ exhibits a sharp singlet at δ 118.1. No other ^{31}P resonance signals can be detected in the 202 MHz NMR spectra, thus indicating that only a single diastereomer is formed in the Diels−Alder reaction. The chiral amine auxiliary on (+)-**3** can be removed from the template complex chemoselectively using concentrated hydrochloric acid. The resultant dichloro complex (−)-**4** is thus obtained as yellow prisms in 91% isolated yield: $[\alpha]_D$ −34.1° (CH_2Cl_2).

The X-ray analysis of (−)-**4** confirms that the desired As−P coordination complex has been formed (Figure 1) and establishes the absolute stereochemistries of the four chiral centers created: *R* at P, C(7), and C(10) and *S* at C(11). Selected bond lengths and angles are listed in Table 1. With reference to the ^{31}P NMR spectra, this X-ray analysis also established the absolute stereochemistries for the four equivalent chiral centers in (+)-**3**. In (−)-**4** the geometry at Pd is slightly distorted (tetrahedrally) square-planar with angles at Pd in the ranges 83.1(1)−94.8(1) and 168.3(1)−175.0(1)°, the smallest of these former angles being associated with the bite of the diphenylarsino-phosphole ligand. The Pd−P (2.218(2) Å) and Pd−As (2.349(1) Å) distances are unexceptional. The two Pd−Cl distances differ significantly, with that *trans* to As (2.345(2) Å) being shorter than that *trans* to P (2.360(2) Å), reflecting the greater

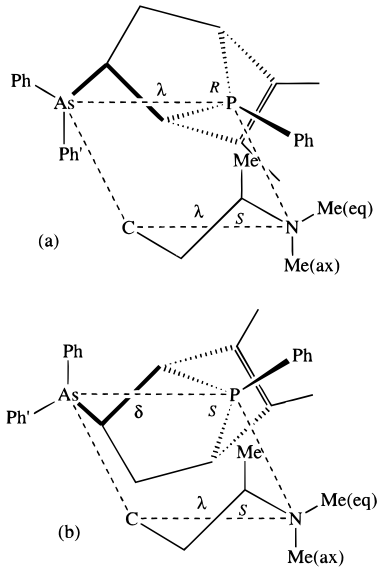

Figure 2. Interchelate interactions (a) in (+)-**3** and (b) in the unfavored diastereomer.

trans influence of the phosphorus donor atom. There is a noticeable contraction from tetrahedral of both the Pd−As−C(11) (101.9(2)°) and C(20)−As−C(26) (103.4-(2)°) angles. The angles at P are similar to those in a related racemic complex.[11]

Treatment of a dichloromethane solution of (−)-**4** with aqueous potassium cyanide liberates the optically active bidentate ligand (−)-**5** as a white solid in 82% isolated yield: $[\alpha]_D$ −54.9° (CH_2Cl_2). Significantly, the ^{31}P NMR spectrum of (−)-**5** in $CDCl_3$ exhibits a sharp singlet at δ 95.3. This low-field signal confirms that the *exo-syn* stereochemical relationship is retained.[11] Owing to the configurational instability of the uncoordinated bridgehead phosphorus stereogenic center,[12] the liberated ligand cannot be stored for longer than *ca.* 30 min and was therefore recoordinated immediately to selected metal ions. These optically active ligand complexes are stereodynamically stable.

Origins of Stereoselectivity. It is well established that the five-membered (*S*)-metalated naphthylamine ring adopts a λ absolute conformation with the methyl substituent on the chiral carbon invariably taking up the axial position above the PdCN ring.[7,10] This axial rather than equatorial geometry for the methyl group is attributed to the extreme steric congestion that would otherwise be present between the proximal H(8) naphthyl proton and the methyl group.[13] Due to the fixed ring conformation, the prochiral N−Me groups are locked into the stereochemically nonequivalent axial and equatorial positions (Figure 2). The N−Me(ax) group projects perpendicularly below the square plane, and N−Me(eq) is somewhat above the plane and quite close to the phosphorus donor atom. It is important to

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note that, due to their relative proximities, equatorially located donor substituents in rigid five-membered rings generally experience much more direct and severe interchelate repulsive forces than their axial counterparts. On the other hand, due to the rigid skew ring conformation and the strict planarity of the naphthyl ring, the H(3) naphthyl proton protrudes invariably toward the space just below the arsenic donor. This naphthyl proton, together with the stereochemically well-defined N−Me groups, are powerful chirality inducers and, in many instances, are able to control the stereochemistry of their neighboring coordination sites.[13a]

It has been well documented that Diels−Alder reactions involving DMPP require both the cyclic diene and the selected dienophiles to be coordinated simultaneously on a transition-metal template during the course of a cycloaddition reaction.[11] Interestingly, the thermodynamically unstable *exo-syn* products are invariably produced from these processes. Figure 2a shows the interchelate interactions in the cationic complex (+)-**3**. In this structure, the As−C−C−P linkage may be viewed as part of the rigid five-membered As−Pd−P chelate ring which adopts the rigid λ conformation. Hence, As−Ph occupies a pseudoequatorial position above the CNAsP square plane and As−Ph′ is in an axial position below the plane. The bridgehead substituent, P−Ph, projects toward the space below the plane. Model studies indicate that there is no major steric repulsion between the two metal chelates. Figure 2b, on the other hand, shows the structure of the unfavored diastereomer that was not formed in the Diels−Alder reaction. In this unfavored complex, the absolute configuration at P is *S* and the As−C−C−P ring adopts the δ conformation. Accordingly, As−Ph occupies the axial position above the square plane and As-Ph′ is equatorially disposed below it. In contrast to its counterpart in (+)-**3**, P−Ph in this unfavored diastereomer projects to the space above the plane. Model studies clearly indicate that two major interchelate repulsions exist within this isomer: one exists between the sterically protruding H(3) naphthyl proton and the equatorial As−Ph′ group; another severe steric constraint is observed between the proximal N−Me(eq) steric group and P−Ph. Interestingly, both repulsive forces are effective at equatorial positions. We believe that these interchelate repulsive forces are the discriminating factors that hinder the formation of this unfavored diastereomer in the Diels−Alder reaction.

Finally, it is noteworthy that no Diels−Alder reaction is observed between free diphenylvinylarsine and free DMPP. Interestingly, the chiral palladium complex activated cycloaddition is found to be at least 15 times slower than the analogous process involving diphenylvinylphosphine.[6] To our knowledge, this is the first example of a metal ion activated reaction involving tertiary arsine ligands.

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. The enantiomerically pure form of bis(μ-chloro)bis{(*S*)-1-[1-(dimethylamino)ethyl]-2-naphthyl-*C,N*}-dipalladium(II) dichloromethane solvate ((±)-**1**)[14] and diphenylvinylarsine[3] were prepared as previously described. Elemental analyses were performed by the microanalytical laboratory of the Department of Chemistry at the National University of Singapore.

Table 2. Crystallographic Data for (−)-4

mol formula	$C_{26}H_{26}AsCl_2PPd\cdot Me_2CO$
mol wt	679.7
cryst syst	triclinic
space group	*P*1
a, Å	8.790(2)
b, Å	8.830(2)
c, Å	10.422(2)
α, deg	97.02(1)
β, deg	112.63(1)
γ , deg	100.75(2)
T, K	293(2)
V, Å^3	716.6(2)
Z	1
d(calcd), g cm^{-3}	1.58
F(000), e	342
cryst size, mm	0.23 × 0.23 × 0.23
total no. of observns	2705
total no. of unique observns	2705
no. of data used in refinement	2534
no. of params	280
λ(Mo Kα), Å	0.7107 3
m, cm^{-1}	20.6
hkl limits	0−10, −10 to 10, −12 to 11
R1[a]	0.035
wR2[b]	0.085

[a] $R1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$. [b] $wR2 = \{\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2}$, $w^{-1} = \sigma^2(F_o^2) + (aP)^2 + bP$.

Chloro{(*S*)-1-[1-(dimethylamino)ethyl]-2-naphthyl-*C*^{2},*N*}(diphenylvinylarsine-*As*)palladium(II) ((+)-2). A mixture of diphenylvinylarsine (2.0 g) and (+)-**1** (3.0 g) in dichloromethane (200 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 a dichloromethane−ethanol mixture, forming bright yellow prisms: yield 4.1 g (88%); mp 200 °C dec; $[\alpha]_D$ +75.2° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.02 (d, 3H, $^3J_{HH}$ = 6.3 Hz, CH*Me*), 2.84 (s, 3H, N*Me*), 2.98 (s, 3H, N*Me*), 4.35 (q, 1H, $^3J_{HH}$ = 6.3 Hz, C*H*Me), 5.54 (d, 1H, $^3J_{HH}$ = 18.2 Hz, *cis* AsCC*H*), 6.14 (d, 1H, $^3J_{HH}$ = 11.2 Hz, *trans* AsCC*H*), 7.10 (dd, 1H, $^3J_{HH}$ = 18.2 Hz, $^3J_{HH'}$ = 11.2 Hz, AsC*H*), 6.70−7.90 (m, 16H, aromatics). Anal. Calcd for $C_{28}H_{29}AsClNPd$: C, 56.4; H, 4.9; N, 2.3; Cl, 5.9. Found: C, 56.3; H, 4.8; N, 2.2; Cl, 5.8.

{(*S*)-1-[1-(dimethylamino)ethyl]naphthyl-*C*^{2},*N*}-{(1α,4α,5α,7R**)-[5-(diphenylarsino)-2,3-dimethyl-7-phenyl-7-phosphabicyclo[2.2.1]hept-2-ene-*As*^{5},*P*^{7}}palladium(II) Perchlorate ((+)-3).** A solution of (+)-**2** (3.0 g) in dichloromethane (100 mL) was stirred for 2 h in the presence of a solution of silver perchlorate (1.0 g) in water (1 mL). The colorless organic layer, after the removal of AgCl and drying ($MgSO_4$), was treated with DMPP (1.0 g) at room temperature for 3 days. Removal of the solvent gave (+)-**3** as a colorless oil, which was then crystallized from dichloromethane−diethyl ether to give the complex as pale yellow crystals: yield 2.1 g (50%); mp 188 °C dec; $[\alpha]_D$ +135.5° (*c* 0.6, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.39 (s, 3H, C=C*Me*), 1.98 (s, 3H, C=C*Me*), 2.08 (d, 3H, $^3J_{HH}$ = 6.2 Hz, CH*Me*), 2.30 (ddd, 1H, $^3J_{PH}$ = 28.0 Hz, $^2J_{HH}$ = 13.4 Hz, $^3J_{HH}$ = 8.9 Hz, $H_{6,endo}$), 2.70 (d, 3H, $^4J_{PH}$ = 1.3 Hz, N*Me*), 2.78 (s, 1H, H_1), 2.88 (d, 1H, $^2J_{HH}$ = 13.4 Hz, $H_{6,exo}$), 3.06 (d, 3H, $^4J_{PH}$ = 3.6 Hz, N*Me*), 3.10 (dd, 1H, $^3J_{PH}$ = 38.0 Hz, $^3J_{HH}$ = 8.9 Hz, H_5), 3.77 (s, 1H, H_4), 4.42 (qn, 1H, $^3J_{HH}$ = $^4J_{PH}$ = 6.2 Hz, C*H*Me), 6.80−7.80 (m, 21H, aromatics); ^{31}P NMR ($CDCl_3$, 36 MHz) δ 118.1. Anal. Calcd for $C_{40}H_{42}AsClNO_4PPd$: C, 56.6; H, 5.0; N, 1.7; Cl, 4.2; P, 3.7. Found C, 56.3; H, 5.1; N, 1.9; Cl, 4.4; P, 3.7.

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Dichloro-{[1α,4α,5α(*S*),7*R*]-[5-(diphenylarsino)-2,3-dimethyl-7-phenyl-7-phosphabicyclo[2.2.1]hept-2-ene-*As*^{5},*P*^{7}}palladium(II) ((−)-4). The Diels−Alder template complex (+)-**3** (1.5 g) was redissolved in acetone (40 mL) and was treated with hydrochloric acid (10 M, 2 mL). The reaction mixture was then refluxed for 15 min. The bright yellow microcrystals of (−)-**4** precipitated out during this period. The product was then filtered and recrystallized from dichloromethane−diethyl ether: Yield 1.0 g (91%); mp >280 °C dec; $[\alpha]_D$ −34.1° (*c* 0.6, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.49 (s, 3H, C=C*Me*), 1.60 (s, 3H, C=C*Me*), 1.95 (ddd, 1H, $^3J_{PH}$ = 23.0 Hz, $^2J_{HH}$ = 13.8 Hz, $^3J_{HH}$ = 9.1 Hz, $H_{6,endo}$), 2.47 (d, 1H, $^2J_{HH}$ = 13.4 Hz, $H_{6,exo}$), 3.04 (dd, 1H, $^3J_{PH}$ = 45.8 Hz, $^3J_{HH}$ = 9.1 Hz, H_5), 3.07 (s, 1H, H_1), 3.45 (s, 1H, H_4), 7.40−8.10 (m, 15H, aromatics); ^{31}P NMR ($CDCl_3$, 36 MHz) δ 129.4. Anal. Calcd for $C_{26}H_{26}AsCl_2PPd$: C, 50.3; H, 4.2; P, 5.0. Found: C, 50.3; H, 4.2; P, 5.0. Treatment of a dichloromethane solution of the dichloro complex with aqueous potassium cyanide for 2 h liberated the free ligand (*S*)-(−)-**5** in 82% yield. Due to its stereodynamic instability, the free ligand was not isolated and was immediately used for recomplexation reactions. The apparent inversion of configuration of the tertiary phosphine that takes place when it is displaced from the metal is consistent with the specification of Cahn et al. for absolute configurations.[15]

Crystal Data for (−)-4. A yellow prism of dimensions 0.23 × 0.23 × 0.23 mm obtained from an acetone solution of the complex was used. The compound crystallized as an acetone solvate. Crystallographic details are given in Table 2. Data were measured on a Siemens P4/PC diffractometer with Mo Kα radiation (graphite monochromator) using ω scans. The structure was solved by direct methods, and the non-hydrogen atoms were refined anisotropically using full-matrix least squares based on F^2 to give R1 = 0.035, and wR2 = 0.085 for 2534 independent, observed reflections ($|F_o| > 4\sigma(|F_o|)$, $2\theta \leq 50°$) and 280 parameters.[16] The absolute stereochemistry of (−)-**4** was determined unambiguously by both an *R*-factor test and the Flack parameter: $R^+ = 0.035$, $R^- = 0.043$, $x = 0.04(2)$. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.

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Supporting Information Available: Tables of crystallographic data, positional and thermal parameters, and bond distances and angles for (−)-**4** (5 pages). Ordering information is given on any current masthead page.

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