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A Simple Route To An Enantiomerically Pure Diphosphine Ligand Containing a Phosphorus Stereogenic Centre.

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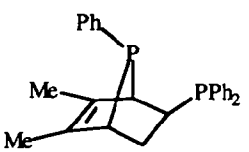
Abstract: The (+)- and (-)- forms of 5-(diphenylphosphino)-2,3-dimethyl-7-phenyl-7-phosphabicyclo[2.2.1]hept-2-ene have been prepared enantioselectively *via* an asymmetric Diels-Alder reaction between diphenylvinylphosphine and 1-phenyl-3,4-dimethylphosphole (DMPP) using 0.5 equiv of (*R*)-(-)- and (*S*)-(+)-bis(μ-chloro)bis[1-[1-(dimethylamino)ethyl]-2-naphthalenyl-*C,N*]dipalladium(II), respectively, as the chiral catalyst. The enantiomeric purity of the diphosphine ligand has been confirmed by ^{1}H and ^{31}P NMR studies.

Optically active phosphine ligands have been successfully employed as metal-based auxiliaries for homogenous asymmetric catalysis.[1] For most of these ligands, the chirality resides either at the phosphorus donor atoms or in the carbon skeleton.[2] The title ligand, **1**, belongs to the rare class of diphosphines which carry both of these desirable structural features. The availability of the enantiomerically pure forms of **1** may therefore have important bearings on the future design of chiral catalysts.



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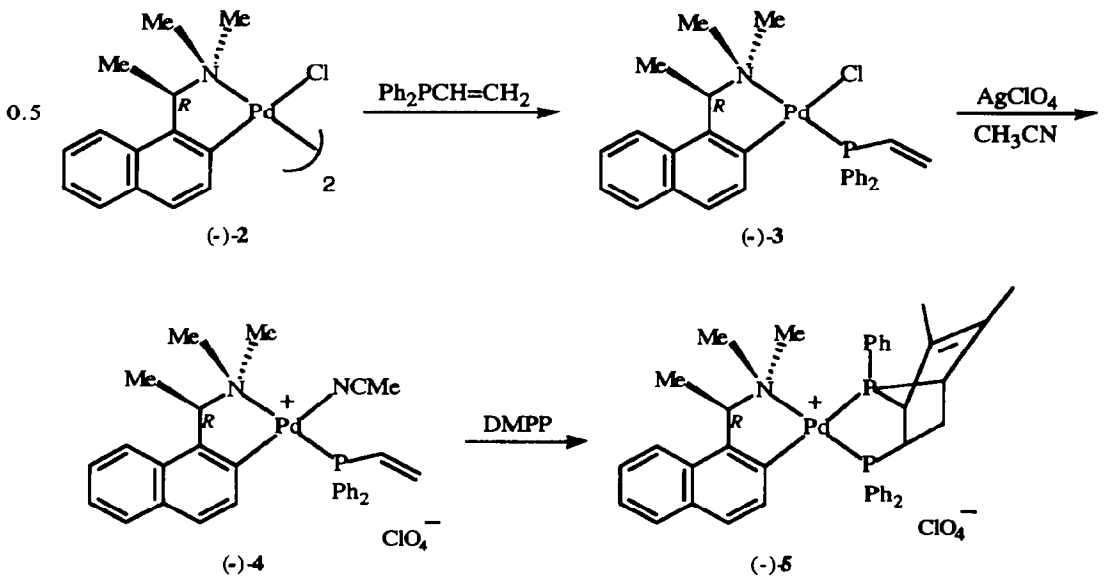
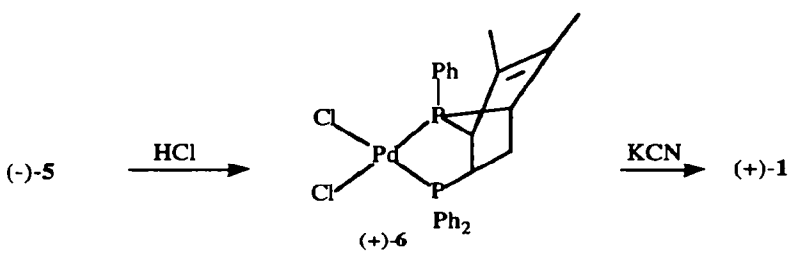
The racemic form of **1** has been prepared diastereoselectively in high yields from the Diels-Alder reaction between $[M(Ph_2PCH{=}CH_2)_2X_2]$ and $[M(DMPP)_2X_2]$ (where M = Pd, Pt; X = Cl, Br, I).[3] In principle, it is possible to resolve this bidentate ligand into its optical antipodes using established methods such as formation of a pair of diastereomeric phosphonium salts[4] or by means of metal complexation.[5] In general, however, resolution is a tedious and inefficient process. In this case, it is further hampered by the thermodynamic instability of the uncoordinated phosphorus stereogenic centre at the bridgehead position.[6] In this paper we offer an attractive approach of generating the optically pure forms of **1** directly from diphenylvinylphosphine and DMPP *via* an asymmetric Diels-Alder reaction mediated by the chiral dipalladium(II) complex **2**[7]. (Scheme 1).



Scheme 1

Diphenylvinylphosphine was coordinated regiospecifically[8] to (-)-**2** to give (-)-**3** in quantitative yield.[9] This mono nuclear complex was isolated as stable yellow needles. Treatment of (*R*)-**3** with silver perchlorate in acetonitrile yielded (-)-**4**. Upon removal of silver chloride and excess acetonitrile, (-)-**4** was redissolved in dichloromethane and then treated with a stoichiometric amount of DMPP at room temperature.[10] The reaction was complete in 5 hours. The resulting complex (-)-**5** was subsequently isolated as pale yellow needles from chloroform-diethyl ether with $[\alpha]_D$ -56.3 (c = 1.0, $CHCl_3$) in 70 % yield.[9]

The free disphosphine ligand (+)-**1** was liberated from (-)-**5** in two steps as illustrated in Scheme 2. The perchlorate salt was first decomposed quantitatively to (+)-**6** with concentrated hydrochloric acid. The dichloro complex was isolated as stable yellow prisms with $[\alpha]_D$ +10.9 (c = 1.0, CH_2Cl_2).[9] Treatment of (+)-**6** with aqueous potassium cyanide afforded the free ligand as a viscous oil with $[\alpha]_D$ +62.5 (c = 0.6, CH_2Cl_2). The overall yield of (+)-**1** from (-)-**5** was 85 %.[11]



Scheme 2

The enantiomeric purity of (+)-**1** was confirmed by the quantitative repreparation of (-)-**5** as its chloride salt from (-)-**2** and the liberated diphosphine ligand: the 500 MHz ^1H and ^{31}P NMR spectra of the crude product in $CDCl_3$ indicated the presence of only one single diastereomer. In the ^{31}P NMR spectrum, two sets of doublets were observed at δ 52.8 and 117.3 ($^3J_{PP}$ = 41.9 Hz). In the ^1H NMR spectrum, the five strong methyl resonances occurred as the expected doublets and singlets at δ 1.40, 1.75, 1.98, 2.57 and 2.67.[9] These signals are identical to that recorded of the perchlorate salt obtained directly from the Diels-Alder reaction.[12] Signals due to the diastereomeric complex product of (-)-**2** and (-)-**1** were not observed.[13] As a further check, a diastereomeric complex was prepared from the liberated (+)-**1** and the equally accessible (+)-**2**. The ^{31}P NMR spectrum of the crude product in $CDCl_3$ showed two entirely new sets of doublets at δ 51.5 and 118.9 ($^3J_{PP}$ = 42.0 Hz). No resonance signals could be detected at δ 52.8 and 117.3. In agreement with the ^{31}P NMR study, the five individual methyl signals in the corresponding ^1H NMR spectrum were observed at clearly different positions (δ 1.40, 1.69, 1.70, 2.39, and 3.06). We therefore concluded that the four stereogenic centres in (+)-**1** were formed stereospecifically in the presence of (-)-**2**. Furthermore, (-)-**1** was obtained in similar yield and optical purity when (+)-**2** was used as the catalyst. Work is in progress in the X-ray structural determination of the various stereoisomeric forms of **5** in order to assign the absolute configurations at the stereogenic centres as well as to determine the stereoelectronic factors that govern this cycloaddition reaction.

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9. Key data: (-)-**3** : ^{31}P NMR (500 MHz, $CDCl_3$) δ 32.88 (s); ^1H NMR (500 MHz, $CDCl_3$) δ 2.02 (3H, d, CH*Me*, $^3J_{HH}$ = 6.4 Hz), 2.75 (3H, d, N*Me*, $^4J_{PH}$ = 1.6 Hz), 2.97 (3H, d, N*Me*, $^4J_{PH}$ = 3.5 Hz), 4.35 (1H, qn, C*H*Me, $^3J_{HH}$ = $^4J_{PH}$ = 6.4 Hz), 5.36 (1H, ddd, *cis*-PCC*H*, $^3J_{HH}$ = $^3J_{PH}$ = 18.1 Hz, $^2J_{HH}$ = 1.4 Hz), 6.05 (1H, ddd, *trans*-PCC*H*, $^3J_{HH}$ = 11.8 Hz, $^3J_{PH}$ = 39.2 Hz, $^2J_{HH}$ = 1.4 Hz), 7.13 (1H, ddd, PC*H*, $^2J_{PH}$ = 22.3 Hz, $^3J_{HH}$ = 18.1 Hz, $^3J_{HH}$ = 11.8 Hz), 6.60-6.90, 7.30-8.00 (18H aromatics). $[\alpha]_D$ -70.3 (c = 1.0, $CHCl_3$).

(-)-**5** : ^{31}P NMR (500 MHz, $CDCl_3$) δ 52.82 (d, $^3J_{PP}$ = 41.9 Hz), 117.29 (d, $^3J_{PP}$ = 41.9 Hz); ^1H NMR (500 MHz, $CDCl_3$) δ 1.40 (3H, s, C=C*Me*), 1.75 (3H, s, C=C*Me*), 1.87 (1H, m, $H_{6,\ ax}$), 1.98 (3H, d, CH*Me*, $^3J_{HH}$ = 6.3 Hz), 2.38 (1H, dd, $H_{6,\ eq}$, $^2J_{HH}$ = 13.2 Hz, $^3J_{PH}$ = 24.1 Hz), 2.57 (3H, d, N*Me*, $^4J_{PH}$ = 1.4 Hz), 2.67 (3H, dd, N*Me*, $^4J_{PH}$ = $^4J_{P'H}$ = 3.5 Hz), 2.82 (1H, s, H_4), 3.14 (1H, ddd, H_5, $^3J_{HH}$ = $^2J_{PH}$ = 8.6 Hz, $^3J_{P'H}$ = 41.0 Hz), 3.78 (1H, m, H_1), 4.45 (1H, qn, C*H*Me, $^3J_{HH}$ = $^4J_{PH}$ = 6.3 Hz), 6.80-8.30 (21H aromatics). $[\alpha]_D$ -56.3 (c = 1.0, $CHCl_3$).

For the diastereomeric complex prepared from (+)-**2** and (+)-**1**: ^{31}P NMR (500 MHz, $CDCl_3$) δ 51.48 (d, $^3J_{PP}$ = 42.0 Hz), 118.89 (d, $^3J_{PP}$ = 42.0 Hz); ^1H NMR (500 MHz, $CDCl_3$) δ 1.40 (3H, s, C=C*Me*), 1.69 (3H, d, CH*Me*, $^3J_{HH}$ = 6.1 Hz), 1.70 (3H, s, C=C*Me*),1.86 (1H, m, $H_{6,\ ax}$), 2.39 (3H, d, N*Me*, $^4J_{PH}$ = 3.7 Hz), 2.63 (1H, dd, $H_{6,\ eq}$, $^2J_{HH}$ = 14.1 Hz, $^3J_{PH}$ = 23.4 Hz), 2.75 (1H, s, H_4), 3.00 (1H, ddd, H_b, $^3J_{HH}$ = $^2J_{PH}$ = 8.0 Hz, $^3J_{P'H}$ = 37.6 Hz), 3.06 (3H, s, N*Me*), 3.91 (1H, m, H_1), 4.40 (1H, qn, C*H*Me, $^3J_{HH}$ = $^4J_{PH}$ = 6.1 Hz), 6.70-8.10 (21H aromatics). $[\alpha]_D$ -6.9 (c = 0.5, CH_2Cl_2).

(+)-**6**: $[\alpha]_D$ +10.9 (c = 1.0, CH_2Cl_2). The ^{31}P and ^1H NMR spectra are identical to that reported for the corresponding racemic materials.[3]

All the complexes were analytically pure.

10. The course of reaction was monitored by ^{31}P NMR spectroscopy. The cycloaddition reaction could be carried out by treating (-)-**3** directly with DMPP. However, the reaction time was longer and the yield was lower.
11. The specific rotation of (+)-**1** changes slowly, presumably due to the configurational instability[6] of the uncoordinated phosphorus stereogenic centre in (+)-**1**. Hence the liberated ligand must be recomplexed to selected metal ions immediately upon liberation.
12. We observed the presence of another isomer (10 %) in the ^{31}P NMR spectrum of the crude cycloaddition product. This compound showed two sets of doublets at δ 29.9 and 119.9 with $^3J_{PP}$ = 42.0 Hz. However, it has been identified in subsequent studies as the diastereomer of (-)-**5** arising from different regio-arrangement of the ortho-metallated naphthylamine and the optically pure (+)-**1** (i.e. *cis* and *trans* isomerism due to the four different donor atoms involved in the square-planar complex). Details concerning the mechanistic aspect of this palladium(II) complex-promoted asymmetric Diels-Alder process and the dynamic properties of the resulting metal chelates will be published in a further paper.
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