

Asymmetric synthesis of a rigid diphosphine ligand containing two phosphorus and four carbon stereogenic centres by means of a chiral palladium complex promoted Diels–Alder reaction

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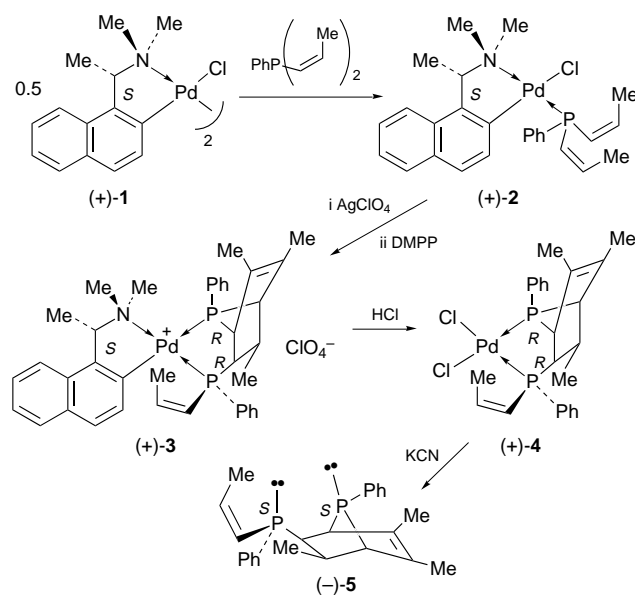
An optically pure diphosphine ligand containing two phosphorus and four carbon stereogenic centres is prepared efficiently by a chiral organopalladium complex promoted asymmetric Diels–Alder reaction between phenyldi[(*Z*)-prop-1-enyl]phosphine and 1-phenyl-3,4-dimethylphosphole.

Despite the critical importance of chiral phosphines in asymmetric catalysis,¹ only a few P-chiral phosphines have been obtained by means of asymmetric synthesis.² The majority of this class of chiral auxiliaries were prepared by optical resolutions which involved the somewhat technically tedious separation of diastereomers. Here we present a simple and highly stereoselective synthesis of a rigid diphosphine that contains two phosphorus and four carbon stereogenic centres.

As illustrated in Scheme 1, the monodentate phenyldi[(*Z*)-prop-1-enyl]phosphine was coordinated regioselectively³ to the chloro-bridged dimer (+)-**1** to give the monomeric compound (+)-**2** as pale yellow prisms, $[\alpha]_D +99.1$ (*c* 1.1, CH₂Cl₂).[†] Upon coordination, the prochiral dienophile is activated and is capable of reacting with an adjacent coordinated cyclic diene, 1-phenyl-3,4-dimethylphosphole (DMPP).⁴ Thus, chloro abstraction from (+)-**2** in CH₂Cl₂ using silver perchlorate followed by treatment with DMPP at room temp. for 6 h gave the corresponding [4 + 2] cycloaddition product (+)-**3** as colourless prisms in 70% isolated yield, mp 151–153°C (decomp.), $[\alpha]_D +10.9$ (*c* 2.0, CH₂Cl₂). X-Ray analysis of (+)-**3** confirmed that the desired diphosphine coordination complex had formed (Fig. 1) and established the absolute stereochemistries of the six

chiral centres created: *R* at P(13), P(20), C(14), C(17) and *S* at C(18), C(19).[‡] In CDCl₃, the two-dimensional ROESY NMR spectrum⁵ of the complex indicated that the new bidentate and the (*S*)-naphthylamine auxiliary interact stereochemically (Fig. 2). For example, Me(23) at the P–vinyl function shows an NOE contact with the protruding aromatic proton at C(2) (signal G). Similarly, the phenyl group at the bridgehead phosphorus shows proximity to both neighbouring N–Me groups (signals H and I). More dramatically, long-range interactions such as Me(24)⋯Me(27) (signal J) and Me(24)⋯Me(29) (signal K) are clearly seen in the spectrum. In the solid state, the C(24)⋯C(27) and C(24)⋯C(29) distances are 4.54 and 4.73 Å, respectively. These interchelate NOE interactions confirm that the new chiral diphosphine is sensitive to the stereochemical environment of the palladium coordination sphere.

The (*S*)-naphthylamine auxiliary can be chemoselectively removed from (+)-**3** by treatment with conc. HCl to give the dichloro species (+)-**4** as stable pale yellow prisms in 85% isolated yield, mp 249–250°C (decomp.), $[\alpha]_D +44.5$ (*c* 1.1, Me₂SO). The free diphosphine can be liberated quantitatively from (+)-**4** by treating a dichloromethane solution of the dichloro complex with aqueous cyanide for 10 min. The



Scheme 1

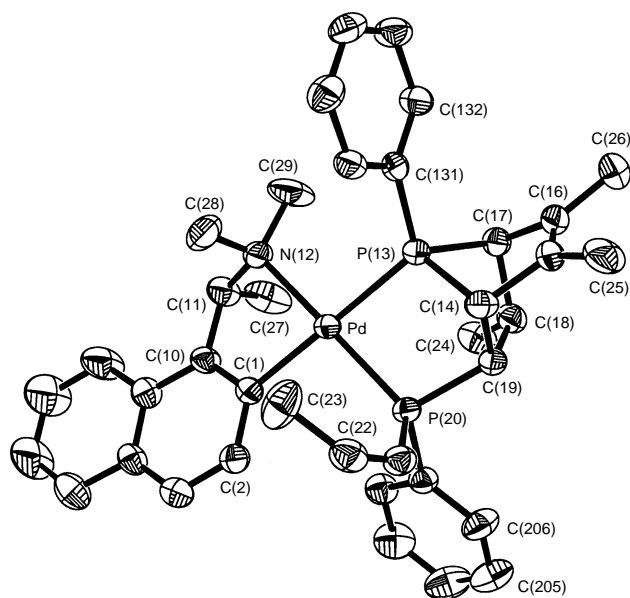


Fig. 1 ORTEP drawing of the cation in (+)-**3** showing the six new chiral centres formed in the Diels–Alder reaction. Selected bond lengths (Å) and angles (°): Pd–C(1) 2.051(5), Pd–N(12) 2.129(4), Pd–P(13) 2.351(1), Pd–P(20) 2.256(2), P(13)–C(14) 1.853(5), P(13)–C(17) 1.843(5), C(15)–C(16) 1.323(7), P(20)–C(19) 1.852(5), P(20)–C(21) 1.806(5), C(21)–C(22) 1.312(7), C(14)–P(13)–C(17) 81.2(2), C(14)–C(19)–P(20) 105.0(3), C(19)–C(18)–C(24) 118.1(5), C(18)–C(19)–P(20) 115.3(3).

optically active diphosphine was obtained as a highly air-sensitive viscous colourless oil with $[\alpha]_D -53.9$ (c 1.3, CH_2Cl_2). The ^{31}P NMR spectrum of free (–)-**5** in CDCl_3 exhibited a pair of doublets at δ 85.7 and 39.6 (J_{PP} 51.3 Hz). The low-field signal confirms that the *exo-syn* stereochemistry is retained.⁴ It is noteworthy that the apparent inversion of configuration that takes place at both phosphorus stereogenic centres when the diphosphine is liberated from the metal is merely a consequence of the Cahn–Ingold–Prelog (CIP) sequence rules.⁶

Investigations on the catalytic properties of transition-metal complexes containing this rigid optically active diphosphine are currently in progress.

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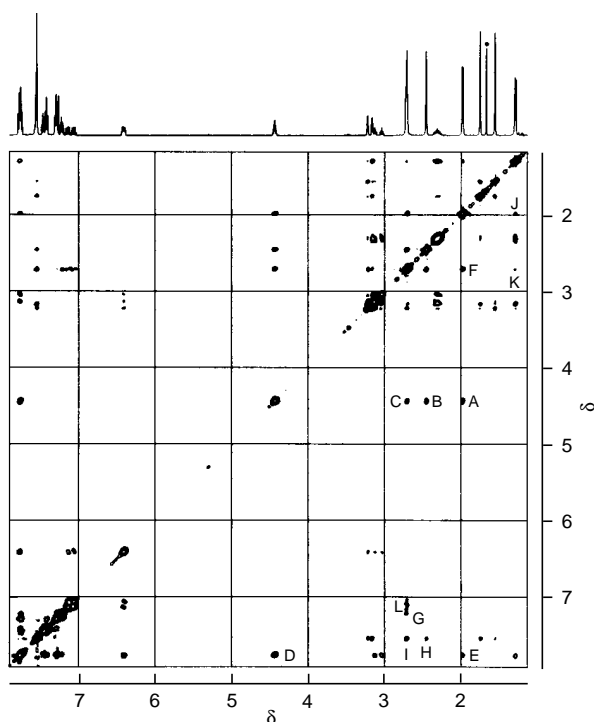


Fig. 2 Two-dimensional ^1H ROESY NMR spectrum at 500 MHz of (+)-**3** in CDCl_3 at 296 K. Selected NOE contacts: A, H(11)–Me(27); B, H(11)–Me(28); C, H(11)–Me(29); D, H(11)–H(8); E, Me(27)–H(8); F, Me(27)–Me(29); G, H(2)–Me(23); H, Me(28)–Ph(13); I, Me(29)–Ph(13); J, Me(24)–Me(27); K, Me(24)–Me(29); L, H(22)–Me(23). ●, H_2O signal.

Footnotes

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† All the new isolated complexes analysed satisfactorily. ^{31}P NMR (202 MHz, CDCl_3): (+)-**2**, δ –6.33; (+)-**3**, δ 13.50 [d, P(20) J 40.4 Hz], 112.78 [d, P(13), J 40.4 Hz]. Selected ^1H NMR for (+)-**3** (500 MHz, CDCl_3): δ 1.29 [d, Me(24), J 7.3 Hz], 1.56 [s, Me(25)], 1.75 [d, Me(26), J 1.2 Hz], 1.98 [d, Me(27), J 6.3 Hz], 2.31 [m, H(18)], 2.45 [d, Me(28), J 1.8 Hz], 2.70 [s, Me(29)], 2.71 [m, Me(23)], 3.08 [m, H(19)], 3.16 [m, H(17)], 3.22 [m, H(14)], 4.44 [m, H(11)], 6.41 [m, H(21)], 7.09 [m, H(22)], 7.21 [m, H(2)], 7.54 [m, Ph(13)], 7.70 [m, *o*-Ph(20)]. ^{31}P NMR for (+)-**4**: [202 MHz, $(\text{CD}_3)_2\text{SO}$], δ 5.54 (d, J 9.6 Hz), 121.90 (d, J 9.6 Hz).

‡ Crystal data for (+)-**3**: $\text{C}_{38}\text{H}_{45}\text{ClNO}_4\text{P}_2\text{Pd}$, $M = 783.54$, monoclinic, space group $P2_12_12_1$; $a = 8.931(3)$, $b = 19.337(6)$, $c = 21.428(8)$ Å, $U = 3701(2)$ Å³, $Z = 4$, $D_c = 1.406$ g cm^{–3}, $\mu = 7.00$ cm^{–1}. A clear prism of dimensions 0.10 × 0.25 × 0.30 mm was used. A total of 4779 independent reflections [$F > 3\sigma(F)$] were measured on a Siemens R3m/V four-circle diffractometer using graphite-monochromated Mo- $\text{K}\alpha$ radiation ($\lambda = 0.71073$ Å). Semiempirical absorption corrections were applied. The structure was solved by direct methods. All non-hydrogen atoms were refined anisotropically using full-matrix least squares based on F^2 to give $R = 0.036$, $R_w = 0.071$ and $S = 0.86$. The absolute configuration was determined unambiguously by use of the Flack parameter [$\chi^+ = 0.01$]. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Information for Authors, Issue No. 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 182/397.

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