Asymmetric synthesis of two diastereomeric P-chiral diphosphine ligands containing a pair of dissimilar asymmetric phosphorus donor atoms

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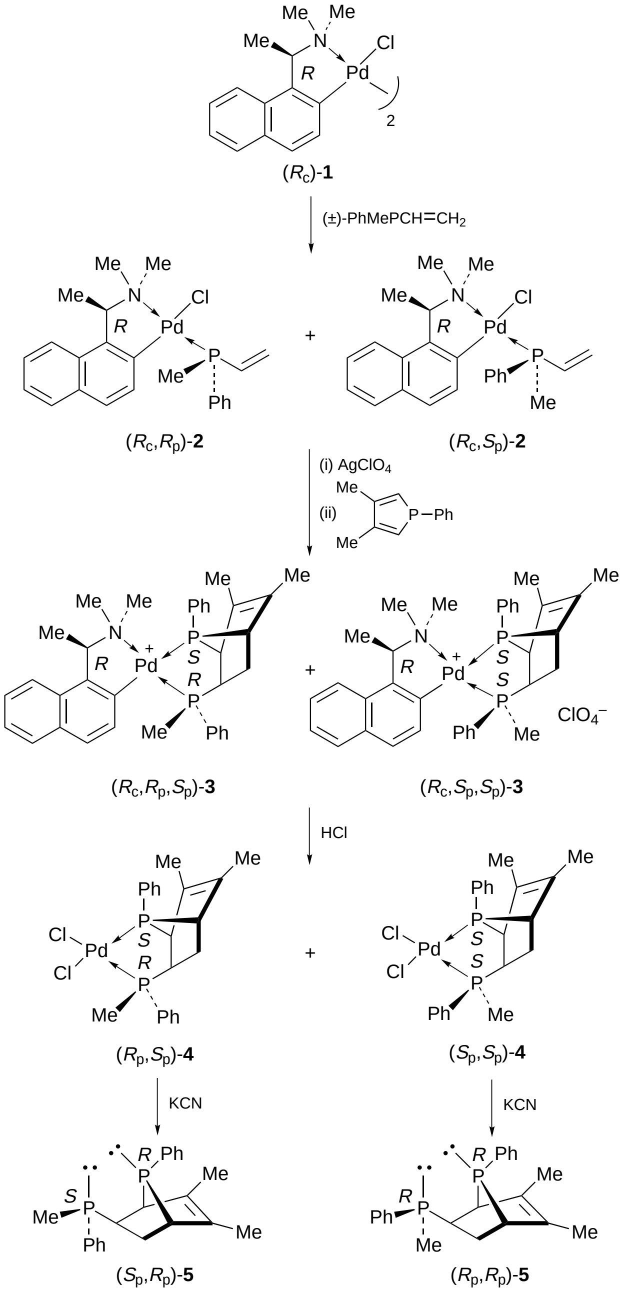
Two diastereoisomeric P-chiral diphosphine ligands, each containing a pair of dissimilar phosphorus donor atoms, have been prepared efficiently in their optically pure forms from a chiral organopalladium complex-promoted asymmetric Diels–Alder reaction between 1-phenyl-3,4-dimethylphosphole and methylphenylvinylphosphine.

Enantiomerically pure P-chiral diphosphines are critically important as chiral auxiliaries in asymmetric catalysis.[1] To date, these chiral ligands are readily available from asymmetric synthesis[2] or from classic optical resolution.[1,3] However, no asymmetric synthesis of diphosphines containing a pair of dissimilar asymmetric phosphorus donor atoms have been reported hitherto. The sole example of optical resolution of a related ligand, 1-(methylphenylarsino)-2-(methylphenylphosphino)benzene, required the somewhat difficult separation of the (*R**,*R**) and (*R**,*S**) diastereoisomers prior to the individual resolution of the two racemic diastereoisomers.[3] We believe that the development of a more efficient asymmetric synthesis to all possible diastereoisomers of dissimilar P-chiral diphosphines may present a unique opportunity to probe in detail the subtle stereochemical interactions between diphosphine auxiliaries and the incoming reaction substrates in the important field of homogeneous asymmetric catalysis. We now delineate the first asymmetric synthesis of two diastereoisomeric P-chiral diphosphines without the prerequisite diastereoisomer separation which can be rather tedious.

As illustrated in Scheme 1, the racemic form of methylphenylvinylphosphine split the chlorine bridges in (R_c)-**1** regiospecifically[4] to give a pair of diastereoisomeric complexes (R_c,R_p)- and (R_c,S_p)-**2**. The neutral complexes could not be separated by fractional crystallization and were crystallized quantitatively as a 1 : 1 diastereoisomeric mixture from CH_2Cl_2–Et_2O. The 202 MHz ^{31}P NMR spectrum of the crystallized product in $CDCl_3$ exhibited two sharp singlets of equal intensity at δ 17.1 and 17.2. Treatment of this diastereoisomeric chloro complex mixture with silver perchlorate gave the corresponding perchlorato analogues.[5] These reactive intermediates were not isolated and were treated directly with stoichiometric quantities of 1-phenyl-3,4-dimethylphosphole in CH_2Cl_2 at room temperature for 4 h. Thus a 1 : 1 mixture of the diastereoisomeric complexes (R_c,R_p,S_p)-**3** and (R_c,S_p,S_p)-**3** was formed quantitively. The ^{31}P NMR spectrum of the crude reaction mixture in $CDCl_3$ exhibited only four doublets of identical coupling constants (41.9 Hz) and similar intensities. Two of these doublets were recorded at δ 116.2 and 116.7. These typical low-field ^{31}P NMR chemical shifts are consistent with the formation of two stereochemically distinct bridgehead phosphorus atoms with the *exo-syn* stereochemistry in the two diastereoisomers. The other two non-bridgehead phosphorus atoms exhibited doublet resonances at δ 38.4 and 44.2. The diastereoisomeric template complexes, however, could not be induced to crystallize. Treatment of the complex mixture with conc. HCl removed the naphthylamine auxiliary chemoselectively to give the dichloro complexes (R_p,S_p)-**4** and (S_p,S_p)-**4**. These diastereoisomeric complexes exhibited very different solubilities in organic solvents. Hence, upon crystallization from CH_2Cl_2–Et_2O, the less soluble (S_p,S_p) isomer was obtained as pale yellow prisms (90%), mp > 230 °C (decomp.), $[\alpha]_D$ +11.2 (*c* 0.5, CH_2Cl_2). The more soluble (R_p,S_p) isomer was subsequently obtained from $CHCl_3$–Et_2O as beige prisms (70%), mp > 230 °C (decomp.), $[\alpha]_D$ +97.6 (*c* 0.5, CH_2Cl_2). The molecular structure and the absolute stereochemistry of both diastereoisomers were determined by X-ray structural analyses (Figs. 1 and 2).† The studies reveal that the absolute



Scheme 1

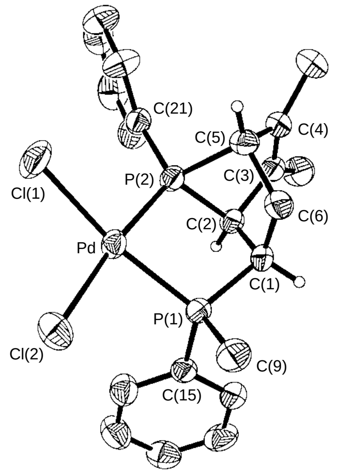


Fig. 1 Molecular structure and absolute stereochemistry of (R_p,S_p)-**4**. Selected bond lengths (Å) and angles (°); Pd–P(1) 2.238(1), Pd–P(2) 2.219(1), Pd–Cl(1) 2.359(1), Pd–Cl(2) 2.365(1), P(1)–C(1) 1.836(3), P(1)–C(9) 1.815(3), P(1)–C(15) 1.809(3), P(2)–C(2) 1.847(3), P(2)–C(5) 1.850(3), P(2)–C(21) 1.804(3), C(1)–C(6) 1.570(4), C(3)–C(4) 1.341(5), P(1)–Pd–P(2) 83.0(1), P(1)–Pd–Cl(1) 170.4(1), P(1)–Pd–Cl(2) 90.1(1), P(2)–Pd–Cl(1) 91.6(1), P(2)–Pd–Cl(2) 172.8(1), Cl(1)–Pd–Cl(2) 95.5(1), C(2)–P(2)–C(5) 81.6(1).

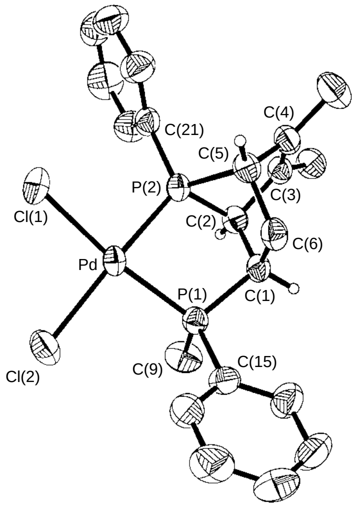


Fig. 2 Molecular structure and absolute stereochemistry of (S_p,S_p)-**4**. Selected bond lengths (Å) and angles (°); Pd–P(1) 2.246(1), Pd–P(2) 2.223(1), Pd–Cl(1) 2.351(1), Pd–Cl(2) 2.380(1), P(1)–C(1) 1.825(3), P(1)–C(9) 1.801(3), P(1)–C(15) 1.806(3), P(2)–C(2) 1.833(3), P(2)–C(5) 1.837(3), P(2)–C(21) 1.801(3), C(1)–C(6) 1.561(4), C(3)–C(4) 1.325(4), P(1)–Pd–P(2) 82.8(1), P(1)–Pd–Cl(1) 172.7(1), P(1)–Pd–Cl(2) 93.0(1), P(2)–Pd–Cl(1) 90.4(1), P(2)–Pd–Cl(2) 170.4(1), Cl(1)–Pd–Cl(2) 94.1(1), C(2)–P(2)–C(5) 82.1(1).

configurations at P(2), C(1), C(2) and C(5) in both molecules are *S*, *R*, *S* and *S*, respectively, and the two isomers are diastereoisomeric at P(1) only.

Treatment of a CH_2Cl_2 solution of (S_p,S_p)-**4** with aqueous cyanide liberated the optically pure diphosphine (R_p,R_p)-**5** quantitatively as an air-sensitive oil with $[\alpha]_D$ −22.6 (*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 91.2 and −22.6 (J_{PP} 70.2 Hz). The low field ^{31}P resonance indicates that the *exo–syn* stereochemistry is retained. It is noteworthy that the apparent inversion of configuration that takes place at both phosphorus stereogenic centres during the liberation reaction is merely a consequence of the Cahn–Ingold–Prelog (CIP) rules.[6] The optical purity of (R_p,R_p)-**5** was further confirmed by the quantitative repreparation of (R_c,S_p,S_p)-**3** from the liberated ligand and (R_c)-**1**: the 202 MHz ^{31}P NMR spectrum of the crude product exhibited a pair of doublets at δ 116.7 and 38.4 only. Similarly, free diphosphine (S_p,R_p)-**5** was liberated from (R_p,S_p)-**4** as an air-sensitive oil with $[\alpha]_D$ +42.4 (*c* 0.5, CH_2Cl_2). The ^{31}P NMR spectrum of (S_p,R_p)-**5** in $CDCl_3$ exhibited the two doublet resonances at δ 91.4 and −22.8 (J_{PP} 66.6 Hz).

Finally, it should be noted that the enantiomeric forms of (R_p,R_p)- and (S_p,R_p)-**5** can be prepared similarly from methylphenylvinylphosphine and 1-phenyl-3,4-dimethylphosphole using (S_c)-**1** as the chiral reaction promoter. Investigations on the catalytic properties of transition metal complexes containing these optically active diastereoisomeric diphosphines are currently in progress.

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Footnotes and References

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† *Crystal data* for (R_p,S_p)-**4**: [$C_{21}H_{24}Cl_2P_2Pd$], M = 515.64, orthorombic, space group $P2_12_12_1$, a = 8.949(1), b = 10.300(1), c = 23.606(2) Å, V = 2175.9(4) Å^3, Z = 4, D_c = 1.574 g cm^{-3}, μ(Mo-Kα) = 12.49 cm^{-1}, F(000) = 1040. A beige prism with dimensions 0.25 × 0.20 × 0.13 mm was used for diffraction studies. A total of 11 788 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. In the full-matrix least-squares based on F^2 with absorption corrected data to give R_1 = 0.0214, wR_2 = 0.0533. The absolute stereochemistry was determined unambiguously by refining the Flack parameter [x = 0.00(2)].

Crystal data for (S_p,S_p)-**4**: [$C_{21}H_{24}Cl_2P_2Pd$), M = 515.64, monoclinic, space group $P2_1$, a = 11.090(2), b = 8.875(1), c = 12.060(3) Å, β = 107.27(2), V = 1095.2(4) Å^3, Z = 2, D_c = 1.564 g cm^{-3}, μ(Mo-Kα) = 12.40 cm^{-1}, F(000) = 520. A pale yellow prism with dimensions 0.43 × 0.35 × 0.13 mm was used for diffraction studies. A total of 6418 independent reflections were measured on the above Siemens SMART CCD diffractometer using ω-scans. All the non-hydrogen atoms were refined anisotropically. In the full-matrix least-squares based on F^2 with absorption corrected data to give R_1 = 0.0194, wR_2 = 0.0475. The absolute stereochemistry was determined unambiguously by refining the Flack parameter [x = 0.001(1)]. CCDC 182/662.

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