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1-Methyl-2-vinylpyrrole and 1-phenyl-3,4-dimethylphosphole: their coordination chemistries and reactivities in a chiral palladium complex promoted asymmetric Diels–Alder reaction

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Abstract

Coordinated 1-phenyl-3,4-dimethylphosphole in the chiral complex chloro{(*S*)-1-[1-(dimethylamino)ethyl]-naphthylC^2,*N*}[1-phenyl-3,4-dimethylphosphole-*P*]palladium behaves as an activated cyclic diene in the intermolecular Diels–Alder reaction with 1-methyl-2-vinylpyrrole to give a pair of diastereomeric P-chiral *endo*-cycloadducts. The diastereomeric palladium complexes could be separated by fractional crystallization and the enantiomerically pure phosphanorbornene ligands could be liberated individually from the complexes by treatment with potassium cyanide. In contrast, the [4+2] cycloaddition reaction did not occurred under similar conditions when the chloro ligand in the phosphole complex was replaced with a perchlorato ligand.

1. Introduction

Functionalized P-chiral phosphines have long been considered as powerful auxiliaries for homogeneous asymmetric catalysis.[1] In these catalyst systems, the P-chiral donors, which are the primary chirality inducers, are coordinated directly onto the catalytic metal centres while, simultaneously, a secondary control is in operation by selected functionalities. Synthetic approaches to the enantiomerically pure forms of such phosphines include asymmetric synthesis using some specific organic chirons and, more commonly, resolution by means of metal complexation. Recently, we found that P-chiral phosphines with functionalized phosphanorbornene skeletons can be prepared efficiently from the palladium complex promoted asymmetric Diels–Alder reaction, between 1-phenyl-3,4-dimethylphosphole (DMPP) and several selected dienophiles using (*R*)- and (*S*)-dimethyl[1-(2-naphthyl)ethyl]amine as the chiral auxiliaries.[2–5] Continuing our effort in the development of these useful auxiliaries, and to compare the

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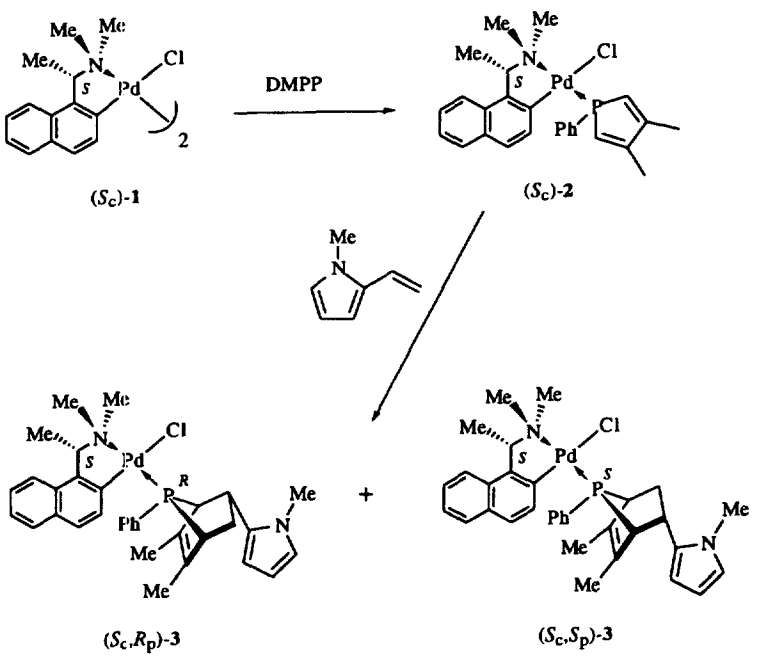
coordination chemistry and reactivity between phospholes and pyrroles, we now describe the asymmetric Diels–Alder reaction between DMPP and 1-methyl-2-vinylpyrrole. It is noted that, in contrast to its counterpart in the phosphole rings, the cyclic diene system in pyrrole rings rarely reacts with dienolphiles in Diels–Alder reactions.[6] Hence only the vinyl group in 1-methyl-2-vinylpyrrole may be involved as a simple dienophile in the [4+2] cycloaddition reaction. The aromatic pyrrole ring is expected to provide a desirable π–π directing interaction with the reacting substrates in a catalytic process.

2. Results and discussion

Coordination of DMPP to the chiral reaction promoter (S_c)-**1** destroys the aromaticity of the phosphole ring and hence activates the cyclic diene towards the [4+2] cycloaddition reaction (Scheme 1). Thus, treatment of (S_c)-**2** with excess 1-methyl-2-vinylpyrrole in 1,2-dichloroethane at 85°C for 5 days gave the [4+2] *endo*-cycloadducts (S_c,R_p)- and (S_c,S_p)-**3** as an approximately 1:1 diastereomeric mixture. Prior to purification, the ^{31}P NMR spectrum of the crude product in $CDCl_3$ exhibited two sharp singlets of approximately equal intensities at δ 118.2 and 120.2. The product mixture was purified by silica column chromatography and (S_c,S_p)-**3** was subsequently isolated in 56% as yellowish-brown needles by fractional crystallization from chloroform–hexane, with $[\alpha]_D$ −4.1 (*c* 1.0, dichloromethane), $[\alpha]_{436}$ −102.4 (*c* 1.0, dichloromethane). Attempts to isolate the diastereomeric complex (S_c,R_p)-**3** by fractional crystallization were unsuccessful.



Scheme 1.

The crystallized complex (S_c,S_p)-**3** behaves as a typical non-electrolyte in dichloromethane and in acetone. In $CDCl_3$, the ^{31}P NMR spectrum of this *endo*-cycloadduct exhibited a sharp singlet at δ 118.2. A single-crystal X-ray analysis of (S_c,S_p)-**3** reveals that the pyrrole ring is attached to the *endo* position at C(27) of the rigid biccyclic ring with the Ph–P group orientated in the *syn* orientation (Fig. 1). The absolute configuration of the four new stereogenic centres at P, C(22), C(25) and C(27) are *S*, *R*, *S* and *R*,

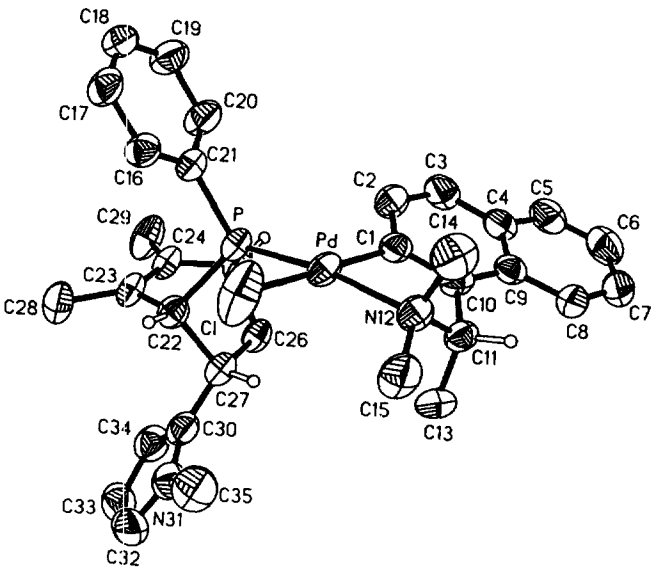
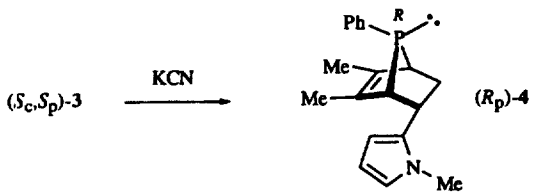


Fig. 1. Molecular structure and the absolute stereochemistry of (S_c,S_p)-**2**. Selected bond lengths (Å) and angles (deg): Pd–C(1), 2.004(3); Pd–N(12), 2.146(2); Pd–P(1), 2.233(1); Pd–Cl(2), 2.382(1); P–C(21), 1.814(3); P–C(22), 1.847(3); P–C(25), 1.856(3); C(23)–C(24), 1.337(4); C(26)–C(27), 1.551(4); C(27)–C(30), 1.480(4); C(30)–N(31), 1.375(4); C(30)–C(34), 1.378(5); N(31)–C(32), 1.372(5); C(32)–C(33), 1.359(7); C(33)–C(34), 1.404(6); N(31)–C(35), 1.462(6); C(1)–C(10), 1.389(4); C(10)–C(11), 1.505(4); C(11)–N(12), 1.513(4); C(11)–C(13), 1.535(4); N(12)–C(14), 1.474(5); N(12)–C(15), 1.480(4); C(1)–Pd–N(12), 81.5(1); C(1)–Pd–P, 97.1(1); C(1)–Pd–Cl, 173.7(1); P–Pd–N(12), 169.4(1); C(22)–P–C(25), 80.9(1); C(22)–C(23)–C(24), 110.8(3); C(23)–C(24)–C(25), 110.1(2); C(24)–C(25)–C(26), 106.6(2); C(25)–C(26)–C(27), 106.8(2); C(26)–C(27)–C(22), 111.5(2), C(27)–C(22)–C(23), 108.6(2); C(27)–C(22)–P, 98.3(2); C(23)–C(22)–P, 102.0(2); C(24)–C(25)–P, 100.7(2); C(26)–C(25)–P, 100.1(2)

respectively. The geometry of the phosphanorbornene skeleton is typical, with the angle at phosphorus acute [80.9(1)°]. The aromatic pyrrole ring is planar and is not coordinated to palladium.

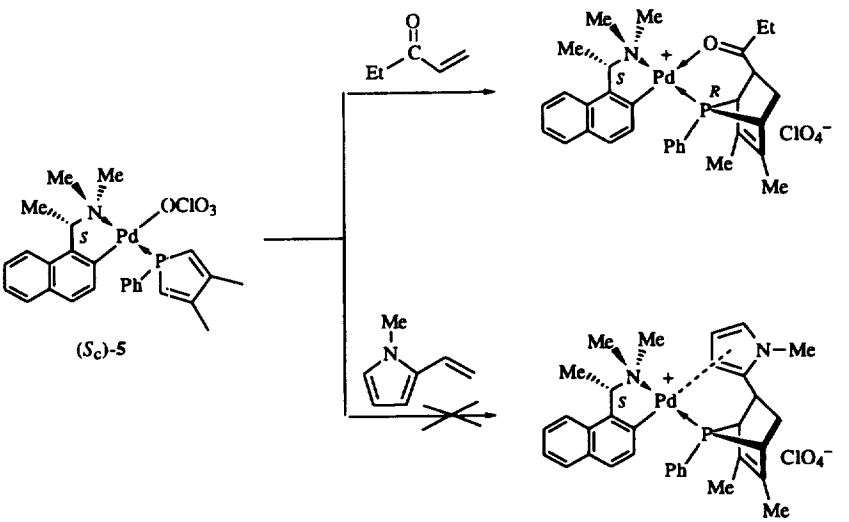
As illustrated in Scheme 2, the pyrrole-substituted phosphine ligand can be liberated from (S_c,S_p)-**3** stereospecifically by treating it with aqueous potassium cyanide to give (R_p)-**4** as a highly air-sensitive colourless solid in 80% yield, $[\alpha]_D$ −55.9 (*c* 0.5, dichloromethane). The ^{31}P NMR spectrum of the free phosphine in $CDCl_3$ exhibited a sharp singlet at δ 101.0. The low field NMR signal confirms that the *endo–syn* stereochemistry of the phosphanorbornene skeleton is retained.[7] It should be noted that the apparent inversion of configuration that takes place at the phosphorus stereogenic centre when the functionalized phosphine is liberated from the reaction promoter is merely a consequence of the Cahn–Ingold–Prelog (CIP) sequence rules.[8] Stereospecific displacement of the pyrrole-substituted phosphine was confirmed by the quantitative re-preparation of (S_c,S_p)-**3** from (S_c)-**1** and liberated (R_p)-**4**: the 202 MHz ^{31}P NMR spectrum of the crude product indicated the diastereomer (S_c,S_p)-**3** only. In a further test of enantiomeric purity, the soluble diastereomer (R_c,S_p)-**3** was prepared from (R_p)-**4** and the equally accessible (R_c)-**1**: only one sharp singlet was observed at δ 120.2. Partially resolved (S_p)-**4** was liberated similarly from (S_c,R_p)-**3** by the treatment with aqueous potassium cyanide. The free ligand was purified by re-coordination to (R_c)-**1** forming the highly crystalline complex (R_c,R_p)-**3** from which pure (S_p)-**4** was liberated.

It is noteworthy that no Diels–Alder reaction was observed between DMPP and 1-methyl-2-vinylpyrrole in the absence of the chiral reaction promoter. Furthermore, we have previously observed that when the chloro ligand in (S_c)-**2** was replaced with the extremely labile perchlorato ligand,[9] DMPP underwent the Diels–Alder reaction with dienophiles such as *N*,*N*-dimethylacrylamide,[2] vinylketones,[3]



Scheme 2.

vinylsulfoxides[4] and vinylsulfides[5] to give exclusively the thermodynamically less stable *exo*-substituted cycloadducts (Scheme 3). It was suggested that these dienophiles displaced the labile and weak Pd–$OClO_3$ bond in (S_c)-**5** so that the dienophiles and DMPP were coordinated simultaneously on the palladium template during the course of the cycloaddition reaction. Indeed, in all cases, the P–O and the P–S chelates were isolated in the cycloadducts. In contrast to this general reaction trend, no Diels–Alder reaction was observed when 1-methyl-2-vinylpyrrole was treated with (S_c)-**5** despite the fact that similar and even stronger reaction conditions have been utilized (Scheme 3).



Scheme 3.

From a mechanistic standpoint, the lack of reactivity between coordinated DMPP in (S_c)-**5** and 1-methyl-2-vinylpyrrole can be attributed to the incapability of the pyrrole ring to undergo metal complexation. Due to the aromaticity of the five-membered pyrrole ring, it has been well established that the nitrogen lone pair of *N*-alkyl pyrrole is not available for metal complexation.[10] In several instances, however, the pyrrole ring is able to coordinate to metal ions *via* the cyclic π-complexation mode.[10] Obviously this relatively uncommon bonding mode was not involved in Scheme 3. In contrast to the formation of the *endo*-cycloadducts that were isolated in Scheme 1, it is interesting to note that these inter-molecular cycloaddition adducts were not formed when (S_c)-**5** was used. The different chemical reactivities of coordinated DMPP in (S_c)-**2** and in (S_c)-**5** toward 1-methyl-2-vinylpyrrole must be due to a major electronic factor. Since Pd–$OClO_3$ bonds are extremely weak and labile, the anionic perchlorato ligand is readily displaced by solvent molecules at higher temperatures. Accordingly, under the reaction conditions of the cycloaddition reactions, DMPP in (S_c)-**5** may be considered to be attached to a pseudo cationic palladium complex. Owing to the electronic deficiency in this cyclic diene complex, DMPP is less activated in (S_c)-**5** than its counterpart in the stable and electronically neutral complex (S_c)-**2**. Hence, in (S_c)-**5**, DMPP may undergo the relatively flexible intra-molecular cycloaddition reactions provided

that the dienophiles are capable of coordinating to this cationic template. However, it fails to react with 1-methyl-2-vinylpyrrole in a strict inter-molecular mechanism.

Investigation into the catalytic properties of transition metal complexes containing this optically active functionalized phosphine is currently in progress.

3. Experimental

3.1. General

Reactions involving moisture-sensitive compounds were performed under a positive pressure of purified nitrogen. ^{1}H and ^{31}P NMR spectra were recorded at 25°C on a Brucker 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 341 polarimeter. Elemental analyses were determined on an analyser by the Microanalytical Laboratory staff of the Chemistry Department.

The compounds bis(μ-chloro)-bis{(*S*)-1-[1-(dimethylamino)ethyl]naphthyl-C^2,N}dipalladium(II) (S_c)-**1**,[11] chloro{(*R*)-1-[1-(dimethylamino)ethyl]naphthyl-C^2,N}[1-phenyl-3,4-dimethylphosphole-*P*]palladium(II) (S_c)-**2**,[3,4] and its perchlorato analogue (S_c)-**5**[2–5] were obtained according to procedures in literature.

3.2. Asymmetric Diels–Alder reaction: Isolation of [SP-4-4-[(1α,4α,5β,7R,(S)]]-chloro[1-[1-(dimethylamino)ethyl]-2-naphthalenyl-C,N][(S)-5-(1-methylpyrrolyl)-2,3-dimethy-7-phenyl-7-phosphabicyclo[2.2.1]hept-2-ene-O^5,P^7]palladium(II) ((S_c, S_p)-3)

A solution of the chloro monomeric compound (S_c)-**2** (1.00 g, 1.89 mmol) in 1,2-dichloroethane (20 mL) was refluxed with 1-methyl-2-vinylpyrrole (0.40 mL, 5.71 mmol) for 5 days. Removal of solvent left a dark brown solid. Prior to purification, $^{31}P\{^{1}H\}$ NMR spectrum of the crude product in $CDCl_3$ exhibited two individual singlets of approximately equal intensity at δ 118.2 and 120. The crude product was chromatographed on a silica column (silica gel-60, 50 g) using $CHCl_3$/hexane (3:2 v/v) as eluent and the first fraction collected (R_f=0.37) was crystallized from chloroform–hexane to give (S_c,S_p)-**3** as browish-yellow needles: 0.35 g, (56%); mp 224–225°C; $[\alpha]_D$ −4.1 (c 1.0, CH_2Cl_2), $[\alpha]_{436}$=−102.4 (c 1.0, CH_2Cl_2). Found: C, 62.2; H, 5.7; Cl, 5.2; N, 4.2; P, 4.6. $C_{33}H_{38}ClN_2PPd$ requires: C, 62.4; H, 6.0; Cl, 5.6; N, 4.4; P, 4.9. ^{1}H NMR ($CDCl_3$) δ 1.01 (s, 3H, C=C*Me*), 1.64 (dddd, 1H, $^{3}J_{PH}$=33.7 Hz, $^{2}J_{HH}$=12.5 Hz, $^{3}J_{HH}$=5.0 Hz, $^{3}J_{HH}$=1.6 Hz, H_{6endo}), 1.86 (s, 3H, C=C*Me*), 1.94 (d, 3H, $^{3}J_{HH}$=6.4 Hz, CH*Me*), 2.57 (d, 3H, $^{4}J_{PH}$=1.3 Hz, NMe_{ax}), 2.63–2.67 (m, 1H, H_{6exo}), 2.90 (d, 3H, $^{4}J_{PH}$=3.0 Hz, NMe_{eq}), 3.04 (s, 1H, H_4), 3.60 (s, 1H, H_1), 3.85 (s, 3H, N$Me_{pyrrole}$), 4.28 (qn, 1H, $^{3}J_{HH}$=$^{4}J_{PH}$=6.0 Hz, C*H*Me), 4.89–4.91 (m, 1H, H_5), 5.53 (dd, 1H, $^{3}J_{HH}$=3.4 Hz, $^{3}J_{HH'}$=1.6 Hz, NCH=C*H*), 5.95 (dd, 1H, $^{3}J_{HH}$=3.4 Hz, $^{4}J_{HH}$=2.8 Hz, NC(C)=C*H*), 6.56 (dd, 1H, $^{4}J_{HH}$=2.6 Hz, $^{3}J_{HH}$=1.8 Hz, NC*H*=CH), 7.12–7.97 (m, 11H, aromatics); $^{31}P\{^{1}H\}$ NMR ($CDCl_3$) δ 118.2 (s). The other diastereomer (S_c,S_p)-**3** collected as the second fraction (R_f=0.35) from the silica column could not be crystallized from a wide range of solvent systems tried.

3.3. Liberation of (1α,4α,5β,7R)-[5-(1-methylpyrrolyl)-2,3-dimethy-7-phenyl-7-phosphabicyclo-[2.2.1]hept-2-ene] ((R_p)-4)

A solution of (S_p, S_c)-**3** (0.5 g, 0.7 mmol) in degassed dichloromethane (100 ml) was treated with excess potassium cyanide (5.0 g, 100 equiv) in water (20 mL) for 2 h under vigorous stirring. The organic

layer was separated, washed throughly with water (2×100 ml), extracted with dilute H_2SO_4 (0.5 M) and dried over $MgSO_4$. Removal of solvent under partial pressure left a pale yellow solid: 0.17 g, (80%); $[\alpha]_D$ −55.9 (c 0.3, CH_2Cl_2); $^{31}P\{^1H\}$ NMR ($CDCl_3$) δ 101.0 (s). The highly air-sensitive and unstable free ligand was re-coordinated to (S_c)-**1** (0.2 g, 0.6 mmol) within 30 min. $^{31}P\{^1H\}$ NMR of the crude product indicated the formation of (S_c,S_p)-**3** only.

3.4. Crystal structural analysis

Crystal data for (S_c,S_p)-**3**: $C_{33}H_{38}ClN_2PPd$ M=635.47, monoclinic, space group $P2_1$, a=13.3434(2), b=8.6097(1), c=13.7607(2) Å, β=105.366(1)°, V=1524.35(4) Å^3, Z=2, D_c=1.384 g cm^{-3}, μ(Mo–K_α)=7.73 cm^{-1}, F(000)=656. A colorless block with dimensions 0.35×0.18×0.16 mm was selected and used for diffraction studies. 9897 [R=0.0171] Independent reflections were measured on a Siemens SMART CCD diffractometer with Mo–K_α 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=0.0296, wR_2=0.0730 for 6824 independent observed reflections [$|F_o|>4\sigma(|F_o|)$, $2\theta\leq58.20°$] and 344 parameters. The absolute stereochemistry was determined unambiguously by refining the Flack parameter [x=0.00(2)].

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