

Hydroxyferrocene as a prochiral analog of phenols: cyclopalladation of a mixed phosphite ester of hydroxyferrocene

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Abstract

Hydroxyferrocene (ferrocenol), a metallocene analog of phenol, has been converted into a phosphite ester with chiral (racemic) butane-1,3-diol which undergoes cyclopalladation similarly to hydroxyarene phosphites. In this case, a planar chirality emerges but no diastereoselectivity has been observed. The molecular structure of the cyclopalladated product as pyridine adduct has been established by the X-ray study of a single crystal. © 2002 Elsevier Science B.V. All rights reserved.

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1. Introduction

Cyclopalladation is one of the most studied organometallic reactions [1] whose exceptionally high regioselectivity is based on the formation of the chelated five- or six-membered metallocycles depending on some directing atom which becomes a ligand at the metal. The following atoms are known to usually serve as directing ones: nitrogen in amines or imines, phosphorus in tertiary phosphines and sulfur in sulfides.

Recently we have extended cyclopalladation as a preparative method on mixed phenol phosphites [2,3] using the ability of P(III) in these compounds to ligate transition metals, in part, palladium. Cyclopalladation was earlier known to occur with triarylphosphites [4,5], however, only one aryl group of three was available for metalation. In our approach, the complete usage of aryl groups has been ensured by starting with mixed monoaryldialkylphosphites that makes this approach applicable to the whole phenolic family including the important natural representatives like tyrosine and estrone [3].

It was interesting to try to extend the scope of this reaction outside the classical purely organic phenols for

their organometallic analogs built on π -complex frameworks in which the stereochemical aspect may be involved because in such systems planar chirality can arise.

2. Results and discussion

In this communication, we wish to report that a metallocenyl analog of phenol, hydroxyferrocene, or ferrocenol (**1**), first prepared [6] by Nesmeyanov et al. 40 years ago, can be involved in the same reaction as a mixed phosphite ester. Chemistry of readily oxidisable ferrocenol is little explored [7]. However, tris(ferrocenyl)phosphite was recently prepared by Herberhold et al. [8]. According to our approach, a dialkyl(ferrocenyl)phosphite was required.

Hydroxyferrocene **1** was reacted with chloro-*cyclo*-phosphite of 1,3-di(hydroxy)butane, or 2-chloro-4-methyl-1,3,2-dioxaphosphane (**2**), prepared in accordance with the general procedure derived by Arbuzov et al. [9], to give the phosphite ester **3**. Cyclophosphite **2** was chosen because of the presence of a chiral carbon that might allow to use the enantiomeric compound in future, if necessary. Mixed phosphite **3** is very prone to oxidation and, as obtained, without any purification, was reacted with $(\text{PhCN})_2\text{PdCl}_2$ in CH_2Cl_2

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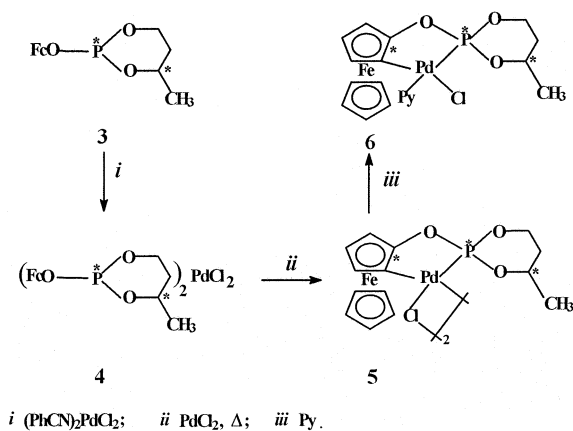


Fig. 1.

at room temperature to afford complex **4** which was cyclopalladated. It was not possible to get ³¹P-NMR spectrum of **3**, instead chemical shift was measured characteristic for the corresponding phosphate: –9.30 ppm which is similar to that observed by Herberhold et al. [8] for a related tris(ferrocenyl)phosphate: –14.1 ppm. Reaction sequence is shown on Fig. 1.

Alkoxy analogues of **3** are known [10] to exist in solution as *trans*-isomers with axial RO–P and equatorial Me group that was explained by anomeric effect. At the same time **3** may be considered as pure diastereomer with two chiral centres, phosphorus atom and carbon atom C(4). However, configuration of three-coordinated phosphorus is labile and can be changed during coordination with the metal.

In the course of cyclopalladation in the ferrocene series specifically [11,12] replacement of hydrogen atom next to the substituent in Cp ring by palladium occurs, so 1,2-disubstituted η⁵-cyclopentadienyl ligand is formed and, subsequently, planar chirality arises, in addition to chiral centres. In general, formation of four racemic diastereomers of a product is possible, but chiral carbon and phosphorus can induce the configuration of chiral planes in **5** and **6**.

NMR and single-crystal X-ray diffraction data obtained for **6** correspond completely to the structure expected. Compound **6** was crystallised in the form of orange plates. A view of the molecule **6** is shown in Fig. 2. The molecule occupies a general position in the crystal. Ferrocenyl groups form layers perpendicular to the *c*-axis. Intermolecular contacts have typical van der Waals lengths. Powder X-ray analysis at room temperature has shown that **6** is a single phase with unit cell parameters corresponding well to the single-crystal data, taking into account the thermal expansion (see Table 1). Structure was solved with direct methods and refined by least squares against *F*² using SHELXTL programs, *R*₁ = 0.056 (for 3772 reflections with *I* > 2σ(*I*), *wR*₂ = 0.167 (for all reflections). All ordered non-hydrogen atoms were refined anisotropically. Hydrogen

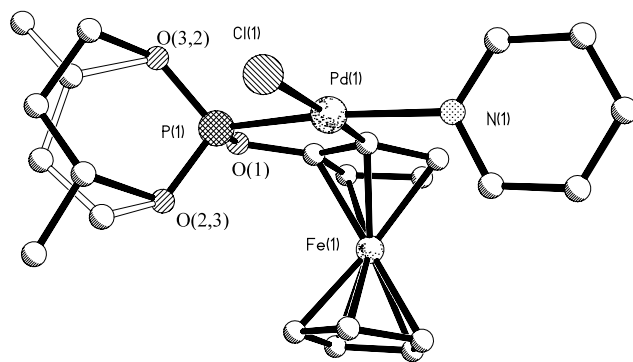


Fig. 2.

Table 1

Crystal data and structure refinement parameters for compound **6**

	Single crystal (110 K)	Powder (298 K)
Unit cell parameters		
<i>a</i> (Å)	7.332(1)	7.25(1)
<i>b</i> (Å)	10.483(2)	10.76(2)
<i>c</i> (Å)	26.316(6)	27.58(3)
α (°)	90	90
β (°)	93.261(5)	93.3(1)
γ (°)	90	90
Temperature (K)	110	
Crystal system	Monoclinic	
Space group	<i>P</i> 2 ₁ / <i>n</i>	
<i>V</i> (Å ³)	2019	2148
<i>Z</i>	4	
<i>D</i> _{calc} (g cm ^{–3})	1.778	
μ (mm ^{–1})	1.83	
X-ray device	Bruker SMART	
X-ray wavelength	Mo–K _α	
Reflections	16644	
Independent	5851	
Observed (<i>F</i> > 4σ)	3774	
Parameters refined	244	
<i>R</i> (<i>F</i> > 4σ)	0.056	

atoms were refined within the riding atom approximation. Dioxaphosphane cycle was refined as a superposition of two orientations with common P and O atoms. Powder XRD analysis was performed at room temperature on DRON-3 diffractometer in Bragg–Brentano geometry. The measured interval was 4–54° in 2θ. Unit cell parameters were refined with the PIRUM program.

The palladium atom has a planar square coordination environment with neighbouring atoms displaced from the mean plane for less than 0.03 Å. The pyridine ligand occupies a *trans* position in respect to the phosphorus atom. The bond lengths Pd–Cl, Pd–P, Pd–N, Pd–C have typical values. The ferrocenyl fragment attains eclipsed conformation with the usual Fe–C distances (see Fig. 2). The metallocycle Pd–P–O–C–C is planar within 0.03 Å; the P–Pd–C angle is diminished to 80.2°. The sum of the angles in the cycle (539.26°) is practically equal to the value for a flat pentagon (540°).

Correspondingly, the flip angle about the line Pd–O (that is the dihedral angle between planes PdCCO and PdPO) is as low as 7.2°. This is probably characteristic of this group of complexes since very close values (10.3 and 11.2°) were found for the first representative of this family, viz. cyclopalladated phosphite of estrone as dimeric chloride [3]. It is very similar to the molecular geometry of the cyclopalladated ferrocenylketimine [13] wherein the five-membered ring is almost flat, but contrasts sharply with the structure of the palladium chelate derived from $\text{FcCH}_2\text{NMe}_2$ in whose acetylacetonate complex the corresponding dihedral angle about the line Pd–C was found [14] to be 41 and 43°.

Two diastereomers can be recognised in ^{31}P - and ^1H -NMR spectra of **6**. In the latter, diastereomeric differences have been observed for the phosphite part of the molecule only, namely, in Me groups (δ 0.89 and 0.99 ppm), methine proton and one of methylene protons in CH_2O (δ 5.44 and 5.54 ppm). Basing on the molecular structure of **6**, the chemical shifts observed may be due to shielding of Cp protons by the neighbouring pyridine ring situated perpendicularly to the palladacycle, whereas the protons of CH_2O fragment are held in the deshielding zone of the molecule.

An X-ray study revealed the presence of the two diastereomers **6**. As was mentioned above the molecule contains three chiral elements, viz. the methyl-bearing carbon of the dioxaphosphane cycle, the phosphorus atom and the chiral plane of ferrocenyl fragment. The dioxaphosphane cycle is disordered between two orientations with almost equal occupancies, both in chair conformation. The ferrocenol oxygen atom and the methyl group are equatorial substituents in *cis* position to each other, while the Pd atom is in the axial position and in the *trans* position to them. In both orientations of the disordered group, the chiral plane has the same absolute configuration. However, the two orientations differ in the configuration of the chiral carbon and the phosphorus atoms, resulting in the molecular configurations $R_pR(P)R(C)$ and $R_pS(P)S(C)$. As the crystal is centrosymmetric, the enantiomorphs of both configurations are present too. Therefore, it may be concluded that crystal structure contains two diastereoisomers with the same configuration of chiral plane and opposite configurations of phosphite fragments. Because starting **3** was racemic this points to the non-diastereoselectivity of cyclopalladation. Hence the remote methyl group in the dioxaphosphane ring does not influence the stereochemistry of cyclopalladation.

3. Conclusions

It has been demonstrated that an organometallic analog of phenols, hydroxyferrocene (ferrocenol) **1** behaves like phenols in the cyclopalladation of the mixed

phosphite ester **3**. The cyclopalladated product **5** owes planar chirality but no diastereoselectivity was observed. The molecular structure of the cyclopalladated complex with pyridine ligand **6** has been determined using an X-ray method.

4. Experimental

All reactions were carried out under Ar. Hydroxyferrocene (**1**), very susceptible to oxidation, was prepared according to [6]. NMR spectra were registered with a Bruker AMX-400 instrument. 1% H_3PO_4 was used as external standard for ^{31}P -NMR.

4.1. Synthesis of 2-chloro-4-methyl-1,3,2-dioxaphosphane (**2**)

An ethereal solution (5 ml) of PCl_3 (4.44 g) was added dropwise at 0 °C on stirring to a mixture of 1,3-dihydroxybutane (2.9 g) and dimethylaniline (7.8 g) in 10 ml of abs. Et_2O . After 2 h, stirring was stopped and the reaction mixture was left overnight. After filtration and evaporation, distillation afforded 3.5 g (70%) of **2**, b.p. 73°/14 mmHg; ^{31}P { δ , CDCl_3 } 151.2 ppm.

4.2. Synthesis of the phosphite ester of hydroxyferrocene, 2-ferrocenyloxy-4-methyl-1,3,2-dioxaphosphane **3** and of its PdCl_2 complex **4**

In a flask supplied with magnetic stirring and Ar inlet suspension of **1** (0.328 g) in 30 ml of THF and 0.164 g of Et_3N were placed. Solution of **2** (0.275 g) in THF (15 ml) was added slowly at –78 °C under Ar. The reaction mixture was left overnight without cooling and after usual workup 0.424 g (81.7%) of crude **3** was obtained (^{31}P -NMR –9.30 ppm for the corresponding phosphate, cf. –14.1 ppm for tris(ferrocenyl)-phosphate [8]) which, without further purification, was reacted with $(\text{PhCN})_2\text{PdCl}_2$ in CH_2Cl_2 at room temperature (r.t.) for 15 min. Complex **4** was obtained in 84% yield. Anal. Found: C, 40.33; H, 4.42; P, 8.09. Calc. for $\text{C}_{28}\text{H}_{34}\text{Cl}_2\text{Fe}_2\text{O}_6\text{P}_2\text{Pd}$: C, 41.14; H, 4.19; P, 7.58%. ^{31}P -NMR (δ , CDCl_3 , ppm): 88.26.

4.3. Synthesis of cyclopalladated derivatives **5** and **6**

Cyclopalladation was carried out as follows. Compound **4** (0.240 g, 0.29 mM), PdCl_2 (0.055 g, 0.31 mM) and K_2CO_3 (0.08 g, 0.58 mM) were suspended in $\text{C}_6\text{H}_5\text{CH}_3$ or C_6H_6 (60 ml) and refluxed for 3 h under Ar. After filtration and evaporation 0.112 g (41.4%) of crude cyclopalladated dimeric chloride **5** was obtained. This crude product **5** in all cases was crystallised from a benzene to heptane mixture. Anal. Found: C, 41.06; H, 4.22. Calc. for $[\text{C}_{14}\text{H}_{16}\text{ClFeO}_3\text{PPd}]_2 \cdot \text{C}_6\text{H}_6$: C, 40.84; H, 3.83%. ^{31}P -NMR (δ , CDCl_3 , ppm): 129.41.

Metal chloride bridges in the dimer **5** were cleaved with pyridine in CH_2Cl_2 to give a monomeric pyridine complex **6** characterised by X-ray study.

Anal. Found: C, 42.37; H, 3.80; N, 2.44. Calc. for $\text{C}_{19}\text{H}_{21}\text{ClFeNO}_3\text{PPd}$: C, 42.31; H 3.93; N, 2.60%. ^{31}P -NMR (δ , C_6D_6 , ppm): 136.23 and 136.53. ^1H -NMR (δ , C_6D_6 , ppm): 0.89 and 0.99 (both d, 3H, $J = 5.0$ and 6.2 Hz, Me, **6** a,b); 1.4–1.6 (m, 2H, CH_2), 3.26, 3.65 and 4.29 (3m, 3H, C_5H_3); 3.74–3.84 and 3.84–3.95 (2m, CH, **6** a,b); 4.40 (c, 5H, Cp); 5.44 and 5.55 (2m, 1H, CH_2O , **6** a,b); 5.7–5.8 (m, 1H, CH_2O); 6.4 (dd, 2H, $J = 5.6$ and 7.1 Hz, Py); 6.70 (t, 1H, $J = 7.1$ Hz, Py); 8.77 (d, 2H, $J = 5.6$ Hz, Py).

5. Supplementary material

Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC no. 153560 for compound **6**. Copies of this information can be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: <http://www.ccdc.cam.ac.uk>).

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