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The first tridentate phosphine ligand combining planar, phosphorus and carbon chirality†

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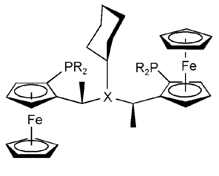
Two new diastereomerically pure tridentate phosphine ligands combining planar, phosphorus and carbon chirality have been conveniently synthesized *via* resolution of their phosphineoxide–diborane adducts and structurally characterized by X-ray analyses.

Tridentate phosphines are recognized as one of the most important classes of auxiliaries in homogeneous catalysis by transition metal complexes.[1] Triphosphine ligands are able to stabilize metal ions in a variety of oxidation states and coordination geometries that can provide strong steric control and, ultimately, fostering reactions that would otherwise be inaccessible. In comparison with stereohomogeneous chelating diphosphines,[2] however, chiral triphosphines have been scarcely investigated for the inherent difficulty in their preparation, yet their potential in asymmetric catalysis remains very high.[3]

In recent papers, we reported the synthesis of a series of bis-ferrocenyl triphosphine ligands (Scheme 1) and described their use in Ru(II), Ni(II) and Rh(III)-catalyzed enantioselective reactions.[4] This project was motivated by perspective of combining optically pure 1,2-disubstituted ferrocenyl units, that are excellent carriers of chiral information in asymmetric catalysis,[5] with a backbone containing three phosphorus atoms. A most important feature of ferrocenyl ligands is their synthetic versatility, allowing a great variety of derivatives to be assembled into a single common fragment.[6] Herein we report the preparation, characterization and crystal structure of the two new tridentate phosphine ligands P3Chir (Fig. 1) in which the planar chirality of the ferrocenyl moiety is combined with phosphorus and carbon stereocenters in an unprecedented molecular assembly.‡ The reaction of (*R*)-(*S*)-PPFA with racemic $C_6H_5P(H)CH_2CH_2P(O)(C_6H_5)_2$ in acetic acid gave a 1:1 mixture of diastereomers **1** having opposite absolute configuration at phosphorus (Fig. 1, step c).[7] Treatment of this mixture with borane dimethyl sulfide, followed by column flash chromatography afforded the pure phosphine oxide–diborane adducts $(R)_C$-$(S)_{Fe}$-$(S)_P$-**2** and $(R)_C$-$(S)_{Fe}$-$(R)_P$-**2** in good yields, respectively. All products could be easily identified by $^{31}P\{^1H\}$ and ^1H NMR spectroscopy (Table 1 and ESI†). The absolute configurations were determined by single-crystal X-ray diffraction analysis (Fig. 2).§ One-pot reduction ($CeCl_3$, $NaBH_4$, $LiAlH_4$)[8]/deboronation reactions of the two stereoisomers gave pure **3** and **4**, respectively (Fig. 1, step f and g).[9]

The X-ray crystal structure of **3** proved the reduction step to proceed with retention of configuration at all stereocenters (Fig. 3).§ Most importantly, the synthetic procedure illustrated in



(*S*)-(*R*)-Pigiphos

X = P; R = 3,5-$(CF_3)_2$-Ph, 3-CF_3-Ph, Ph, 3,5-$(CH_3)_2$-Ph
X = S, R = Ph

Scheme 1

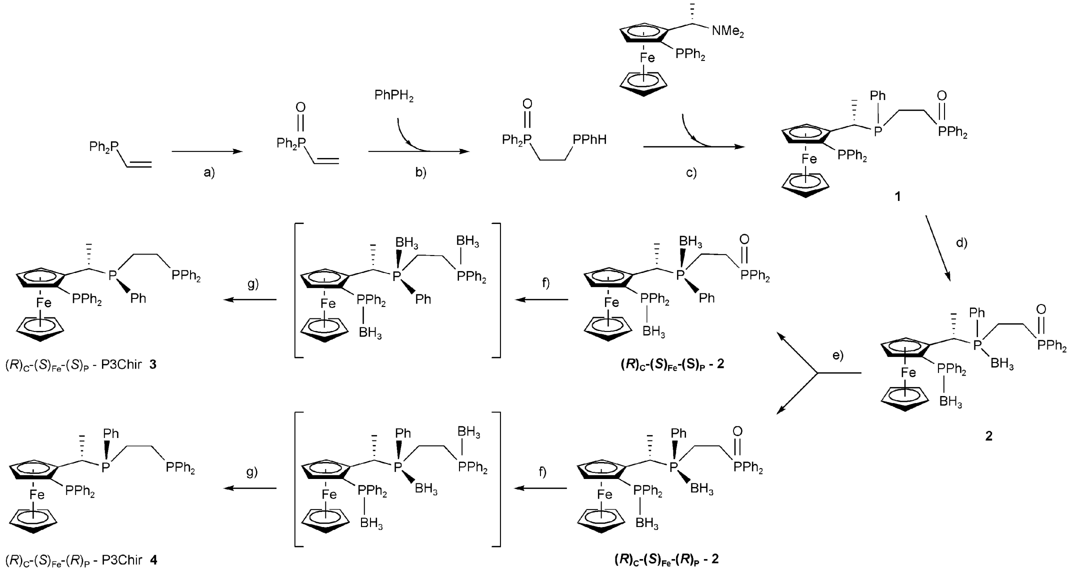


Fig. 1 Reaction scheme for the synthesis of $(R)_C$-$(S)_{Fe}$-$(S)_P$-P3Chir (**3**) and $(R)_C$-$(S)_{Fe}$-$(R)_P$-P3Chir (**4**). *Reagents and conditions*: a) H_2O_2, $CHCl_3$; b) tBuO$^-$K$^+$, THF, reflux; c) AcOH, 75 °C; d) $BH_3{\cdot}(CH_3)_2S$, THF; e) flash chromatography; f) $CeCl_3$, $NaBH_4$, $LiAlH_4$, THF; g) morpholine, 70 °C.

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† Electronic supplementary information (ESI) available: experimental section. See http://www.rsc.org/suppdata/cc/b2/b208384a/

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Table 1 ^{31}P{^{1}H} NMR data for the ligands

	Entry	δ P(1)	δ P(2)	δ P(3)	$^{4}J_{\mathrm{P1P2}}$/ Hz	$^{3}J_{\mathrm{P2P3}}$/ Hz
1	*epi-A*	−24.50 (d)	−0.16 (dd)	33.42 (d)	18.3	50.2
1	*epi-B*	−25.57 (d)	−1.24 (dd)	33.37 (d)	37.7	52.0
2	$(R)_{\mathrm{C}}$-$(S)_{\mathrm{Fe}}$-$(S)_{\mathrm{P}}$	11.7 (br s)	32.0 (br s)	33.2 (d)		43.8
2	$(R)_{\mathrm{C}}$-$(S)_{\mathrm{Fe}}$-$(R)_{\mathrm{P}}$	11.8 (br s)	32.8 (br s)	32.8 (br s)		
3	$(R)_{\mathrm{C}}$-$(S)_{\mathrm{Fe}}$-$(S)_{\mathrm{P}}$	−25.89 (d)	−2.02 (t)	−12.07 (d)	36.0	32.7
4	$(R)_{\mathrm{C}}$-$(S)_{\mathrm{Fe}}$-$(R)_{\mathrm{P}}$	−25.70 (d)	−0.27 (dd)	−13.32 (d)	12.9	35.3

In $CDCl_3$, 161.98 MHz, 294 K. Chemical shifts in ppm, *J* in Hz.

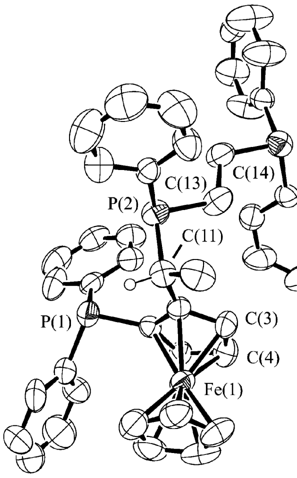

Fig. 2 ORTEP drawing of $(R)_{\mathrm{C}}$-$(S)_{\mathrm{Fe}}$-$(R)_{\mathrm{P}}$-**2**. Selected bond lengths (Å) and angles (°): P(1)–B(1) 1.923(12), P(2)–B(2) 1.910(11), P(3)–O(1) 1.470(6), P(2)–C(11) 1.848(9); C(2)–C(11)–P(2)–C(13) 40.36(2), C(3)–C(2)–C(11)–P(2) 45.79(2).

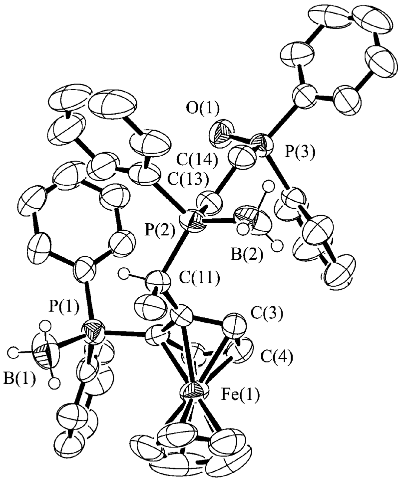

Fig. 3 ORTEP drawing of **3**. Selected bond lengths (Å) and angles (°): P(2)–C(11) 1.873(10); C(2)–C(11)–P(2)–C(13) −63.82(2), C(3)–C(2)–C(11)–P(2) 101.87(2).

Fig. 1 enables the large-scale preparation of the P3Chir ligands in excellent overall yields using cheap and commercially available reagents through simple manipulations. It is anticipated that as many as four stereoisomers can be prepared starting from either (*R*)-(*S*)-PPFA (as described here) or (*S*)-(*R*)-PPFA hence allowing a fine tuning of stereochemical control. It is also worth noting that the P3Chir ligands can form metal complexes displaying both five- and six-membered chelate rings. Chelation to a metal is expected to significantly reduce the number of available competing conformations, resulting in a quite rigid ligand framework. Preliminary results confirm the excellent ligand properties of the P3Chir molecules. The Ni(II) complexes $[((R)_{\mathrm{C}}$-$(S)_{\mathrm{Fe}}$-$(S)_{\mathrm{P}}$-P3Chir)Ni(CH_3CN)]BF_4 (**5**) and $[((R)_{\mathrm{C}}$-$(S)_{\mathrm{Fe}}$-$(R)_{\mathrm{P}}$-P3Chir)Ni(CH_3CN)]BF_4 (**6**) were readily isolated in the solid state and characterized in solution by NMR spectroscopy. Sharp resonances were observed in both ^{31}P{^{1}H} and ^{1}H NMR spectra. The ^{31}P{^{1}H} NMR parameters indicate the complexes to adopt a square-planar arrangement with *trans* P(1) and P(3) phosphorus atoms.¶ The use of P3Chir complexes with Ni(II), Rh(I), Ru(II) and Ir(I) metal ions in enantioselective reactions is currently under way in our laboratories.

In conclusion, we have shown that triphosphine ligands combining ferrocenyl, carbon and phosphorus chirality can be obtained in very good yield by resolution of diborane protected-phosphineoxide precursors, followed by stereoconservative reduction.

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Notes and references

‡ $(R)_{\mathrm{C}}$-$(S)_{\mathrm{Fe}}$-$(S)_{\mathrm{P}}$-P3Chir = (*R*)-1-[(*S*)-2-diphenylphosphino)ferrocenyl]ethyl-(*S*)-[phenylphosphin-2-(diphenylphosphino)ethane].

§ *Crystal data* for $(R)_{\mathrm{C}}$-$(S)_{\mathrm{Fe}}$-$(R)_{\mathrm{P}}$-**2**: single crystals of $(R)_{\mathrm{C}}$-$(S)_{\mathrm{Fe}}$-$(R)_{\mathrm{P}}$-**2** were obtained by recrystallization from CH_2Cl_2–CH_3OH. $C_{44}H_{47}FeB_2OP_3$, $M = 762.24$, orthorhombic, space group $P2_12_12_1$ (no. 19), $a = 11.436(15)$, $b = 31.504(5)$, $c = 11.270(3)$ Å, $V = 4060(5)$ Å^3, $T = 293(2)$ K, $Z = 4$, μ(Mo-Kα) = 0.522 mm^{-1}, 3202 measured reflections, 3202 independent reflections, *R* indices (all data) $R = 0.1055$ and $wR = 0.1368$, Flack parameter = −0.04(5).

Crystal data for **3**: single crystals of **3** were obtained by recrystallization from CH_3OH. $C_{44}H_{41}FeP_3$, $M = 718.53$, orthorhombic, space group $P2_12_12_1$ (no. 19), $a = 12.117(2)$, $b = 15.381(9)$, $c = 19.922(5)$ Å, $V = 3713(2)$ Å^3, $T = 293(2)$ K, $Z = 4$, μ(Mo-Kα) = 0.566 mm^{-1}, 2729 measured reflections, 2729 independent reflections, *R* indices (all data) $R = 0.1179$ and $wR = 0.1423$, Flack parameter = 0.01(5).

CCDC 184405 and 184406. See http://www.rsc.org/suppdata/cc/b2/b208384a/ for crystallographic data in CIF or other electronic format.

¶ ^{31}P{^{1}H} NMR data (CD_3CN, 161.98 MHz, 294 K). **5**: δ 6.68 (dd, P(1)), 84.20 (dd, P(2)), 65.68 (dd, P(3)), $^{2}J_{\mathrm{P1P2}}$ 80.2, $^{2}J_{\mathrm{P1P3}}$ 212.5, $^{2}J_{\mathrm{P2P3}}$ 46.7 Hz. **6**: δ 12.50 (dd, P(1)), 74.12 (dd, P(2)), 62.40 (dd, P(3)), $^{2}J_{\mathrm{P1P2}}$ 82.9, $^{2}J_{\mathrm{P1P3}}$ 213.0, $^{2}J_{\mathrm{P2P3}}$ 44.0 Hz.

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