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Synthesis of P,S,O-Ligands Incorporating a Planar Chiral Ferrocenyl Motif

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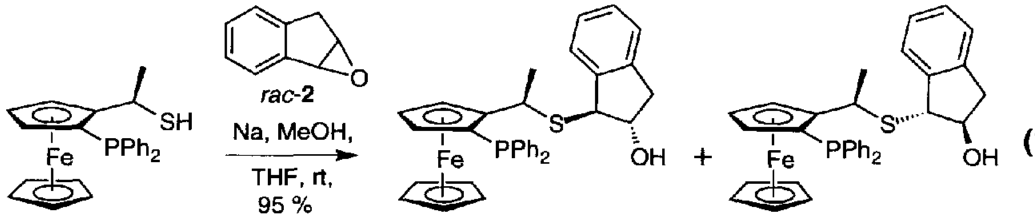
Abstract: The sodium salt of (*R*)-1-[(*S*)-(diphenylphosphino)ferrocenyl]ethyl mercaptan **1** reacted with racemic epoxide **2** to furnish the P,S,O system **3** as a separable mixture of diastereoisomers. The absolute configuration of (*R, S, S*)-(*S*)-**4a** and that of the palladium π-allyl complex **6a** were established by crystal structure determinations.

Our studies, directed towards new selective routes to ferro-[1] and ruthenocenyl[2] P,P and P,N systems, combined with the study of electronic effects in asymmetric catalysis, have resulted in the development of effective ligands which can impart good to very high enantioselectivities in a whole host of catalysed reactions.[3]

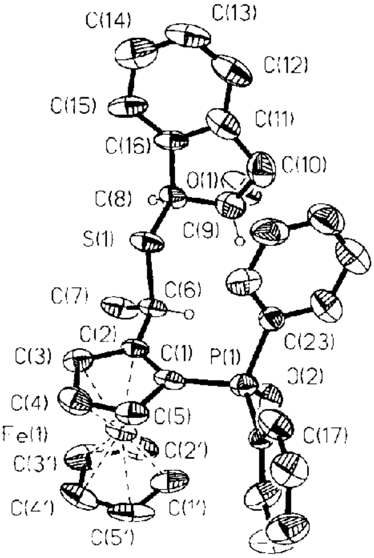
As a continuation of the use of the homochiral thiol **1** as a nucleophile for the preparation of multidentate ligands for asymmetric synthesis,[4] we were interested in preparing P,S,O ferrocenyl derivatives. The ring opening of epoxides was an interesting possibility, since it furthermore enables the incorporation of two new stereogenic centres in one synthetic step. Thus, treatment of the sodium salt of **1**, in a MeOH/THF mixture, followed by the addition of racemic *cis*-indene epoxide **2**[5] at rt, led to **3** as virtually a 1:1 mixture of diastereomers which were separated by the use of column chromatography (silica gel, hexane/ether; 2:1), and obtained as oils or yellow foam-like solids.[6]

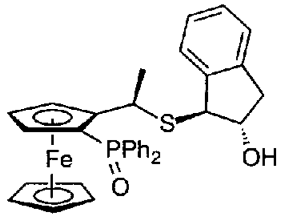


(1)

A single crystal X-ray diffraction study of the P-oxide derivative of **3a** (**4a**; a small amount of crystals of the oxidised ligand were obtained by evaporation of an hexane/ethyl acetate mixture) established its absolute configuration as being *(R, S, S)-(S)*. Moreover, the solid state structure (see Figure 1) shows some usual features[1a]; the sulphur atom is found to be in a pseudo axial position, with C(7) forced below the plane of the upper Cp ring, and the indenyl unit is positioned away from the ferrocene fragment, no doubt for steric reasons.

Figure 1; ORTEP plot of *(R, S, S)-(S)*-**4a**





4a

Selected bond lengths (Å)	
S(1)-C(6)	1.842(8)
S(1)-C(8)	1.829(8)
P(1)-O(2)	1.495(5)
Selected bond angles (°)	
S(1)-C(6)-C(2)	104.0(5)
C(2)-C(6)-C(7)	114.3(6)
C(1)-P(1)-C(17)	104.3(4)
C(1)-P(1)-C(23)	107.1(4)

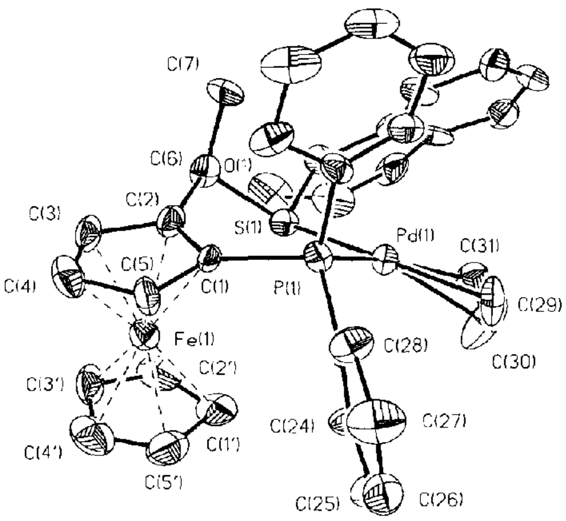
$C_{33}H_{31}FeO_2PS$. M=578.5.
Orthorhom., $P2_12_12_1$. a=9.491(12);
b=12.52(2); c= 23.64(2).
Final R (obs. data)=3.84 %; wR=5.21 %.

Our present goals are focused on the synthesis of transition metal complexes of **3** and of related P,S,O-ferrocenes, the study of their conformational aspects and bonding modes by both NMR spectroscopy and X-ray studies, and their exploitation in asymmetric catalysis. Preliminary results have shown that **3** give poor enantioselectivities for the Rh-catalysed hydroboration of styrene (e.e.'s of ca. 10%) and for the Pd-catalysed alkylation[7] of *rac*-1,3-diphenylprop-2-enyl acetate (**5**) with dimethyl malonate. Using 0.5 mol % $[Pd_2Cl_2(\eta^3\text{-}PhCH\text{-}CH\text{-}CHPh)_2]$ as a catalyst precursor and **3a**, the (*R*)-product was obtained with 37 % e.e. and 76 % conversion after 17 h, and with 55 % e.e. and 90 % conversion using **3b**. The latter results are in contrast to those obtained with related state-of-the-art ferrocenyl systems, which led to enantioselectivities for this reaction in excess of 90 %.[3a,8]

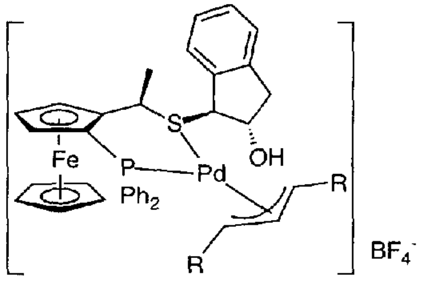
In order to have some insight into possible structural/conformational (albeit groundstate) reasons for such a poor catalytic performance, we have succeeded in the preparation of various Pd(II) derivatives of **3**,[6] and in particular the cationic palladium allyl complexes **6a** and **6b** (the actual intermediate in the alkylation reaction of substrate **5**). Only **6a** gave suitable crystals for an X-ray diffraction study, an ORTEP plot of which is shown in Figure 2. In **6a**, a drastic change in conformation of the ligand, in the solid state, as compared to **3a** is observed, with the methyl group (C(7)) being forced into a pseudo axial position due to coordination of the sulphur atom to palladium.[9] As a consequence, the *anti* O(1) is held away from palladium, whereas the PPh_2 unit adopts virtually the same configuration as in **3a**. The existence of both *exo* and *endo* π-allyl configurational isomers in solution, evidenced notably by two signals in the ^{31}P NMR for both **6a** and **6b**, coupled with the high conformational flexibility of the ligand may be contributing factors to the low selectivity acheived with **3**, these aspects having been discussed in some detail elsewhere.[3c]

We are currently working on the use of the pendant (deprotonated) hydroxyl function of **3** as a further anchoring function for a transition metal, and hence tridentate ligation of the ligand as a whole.

Figure 2; ORTEP plot of the cationic part of **6a**; 30% ellipsoids are shown



$C_{36}H_{36}BF_4FeOPPdS$. M=796.7.
Orthorhom.,$P2_12_12_1$. a=10.615(6);
b=14.509(8); c= 21.736(13).
Final R(obs. data)=4.43 %; wR=5.90 %.



6a (R = H); **6b** (R = Ph)

Selected bond lengths (Å)	
Pd(1)-S(1)	2.349(4)
Pd(1)-C(31)	2.228(17)
Pd(1)-C(30)	2.128(22)
Pd(1)-C(29)	2.111(16)
Pd(1)-P(1)	2.265(4)
Selected bond angles (°)	
S(1)-Pd(1)-P(1)	96.9(1)
S(1)-Pd(1)-C(29)	167.1(5)
P(1)-Pd(1)-C(31)	160.9(4)
Pd(1)-S(1)-C(6)	112.8(4)
Pd(1)-P(1)-C(1)	112.9(4)
S(1)-C(6)-C(2)	107.8(9)

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6) Sodium (80 mg, 3.5 mmol) was added to a THF: MeOH solution (50 mL: 50 mL) of (*R*)-(*S*)-**1** (1.51g, 3.5 mmol) at rt. After 0.25 h the epoxide **2** (460 mg, 3.5 mmol) was added, and the mixture stirred a further 3 h. Following solvent removal by evaporation, ether (50 mL) and water (20 mL) were added to the resulting brown paste. After separation of the organic layer, the aqueous layer was extracted with a further amount of ether (50 mL). The combined organic extracts were dried over $MgSO_4$. After removal of the latter by filtration, the orange filtrate was evaporated to afford a yellow crude solid. Separation of **3a** and **3b** was achieved using silica and a mixture of hexane and ether (2:1) as eluants. Typically, **3a** was obtained as the first fraction (720 mg, 37 %), followed by a mixed fraction **3a/3b** (150 mg, 15 %) then **3b** (840 mg, 43 %). **3a**; $[\alpha]_D$ = -387 ($CHCl_3$, c=0.38). ^1H NMR (250 MHz): δ 1.83 (t, J=7, 3H), 2.70 (dd, J=15, 8, 1H), 2.89 (dd, J=15, 7, 1H), 3.80 (s, 5H), 3.97 (m, 1H), 4.04 (m, 1H), 4.13 (br q, 1H), 4.34 (m, 1H), 4.47 (m, 1H), 4.54 (qd, J=7, 3, 1H)7.00-7.20 (m, 10H), 7.31-7.40 (m, 2H), 7.53-7.63 (m, 2H). ^{31}P NMR (101 MHz): δ -25.7. **3b**; $[\alpha]_D$ = -328 ($CHCl_3$, c=0.29). ^1H NMR (250 MHz): δ 1.77 (t, J=7, 3H), 2.61 (dd, J=15, 6, 1H), 3.05 (dd, J=15, 7, 1H), 3.83 (s, 5H), 3.91 (m, 1H), 4.03 (m, 1H), 4.20 (m, 1H), 4.36 (m, 2H), 4.42 (m, 1H), 6.74 (br d, 1H), 6.90-7.06 (m, 3H), 7.11-7.26 (m, 5H), 7.34 (m, 3H), 7.51-7.63 (m, 2H). ^{31}P NMR (101 MHz): δ -26.4. **6a**; $[\alpha]_D$ = -131 (CH_2Cl_2, c=0.16). ^{31}P NMR (101 MHz): δ 10.8, 11.4 (two diastereoisomers in ca. 1 to 1 ratio). **6b**; $[\alpha]_D$ = -137 (CH_2Cl_2, c=0.11). ^{31}P NMR (101 MHz): δ 11.6, 13.9 (two diastereoisomers in ca. 1 to 1 ratio). The ^1H NMR spectra are complex and under current investigation by 2D NMR methods. Satisfactory microanalyses for all compounds reported have been obtained.

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9) A similar conformation was found for thiolate **1** coordinated to Cu(I), see ref. 4a).

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