Synthesis of 1,1'-Bis(phosphetano)ferrocenes, a New Class of Chiral Ligands for Asymmetric Catalysis

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Abstract: The C_2-symmetric, chiral 1,1'-bis(phosphetano)ferrocenes **1** have been prepared from the cyclic sulfates of optically pure, 1,3-diols. They have been tested in the rhodium catalysed hydrogenation of unsaturated substrates.

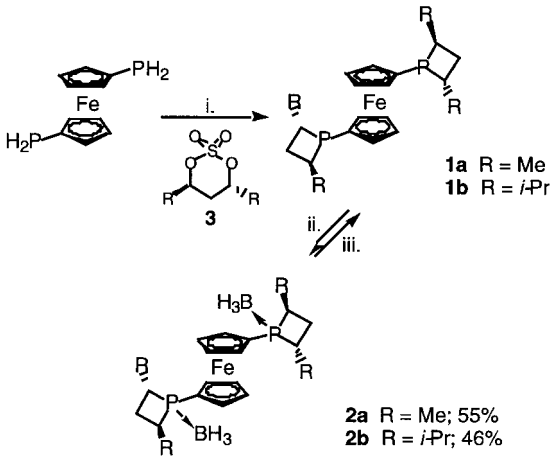
Key words: chiral phosphetanes, ferrocene, rhodium, hydrogenation

Nowadays, many successful chiral ligand designs, and especially design of chiral phosphines, take advantage from the peculiar properties of the ferrocenyl moiety:[1] the significant sterical hindrance of the ferrocenyl group operates in planar-chiral species, while large bite angles and restricted flexibility modulate the reactivity of the transition metal complexes of 1,1'-bis(phosphino)ferrocenes. In C_2 symmetric 1,1'-bis(phosphino)ferrocenes, chirality is brought about by either disymmetric disubstitution of both cyclopentadienyl rings (planar chirality)[2] or by chiral phosphorus substituents.[3] The 1,1'-bis(phosphetano)ferrocenes **1** described hereafter, belong to this last class of compounds, insofar as their chirality is afforded by optically pure, 2,4-disubstituted phosphetane units. They represent a new class of chiral phosphines and complement our previous work on phosphetane based ligands. [4]

Previous work from our group has shown that chiral 2,4-disubstituted phosphetane rings are easily accessible from optically pure *anti*-1,3-diol derivatives by reaction with primary phosphines.[4a,c] The same approach has been applied here to the synthesis of the bis(phosphetanes) **1a** and **1b** from 1,1'-bis(phosphino)ferrocene. [5]

1,1'-Bis(phosphino)ferrocene has been prepared from ferrocene, through a two-steps procedure, which requires the synthesis and subsequent reduction of tetraethyl 1,1'-(ferrocenyl)bisphosphonite.[5] In our hands this method afforded 1,1'-bis(phosphino)ferrocene, contaminated with small amounts of the starting ferrocene and of the monophosphino substituted ferrocene. The phosphetane syntheses were performed on the crude mixture. An alternative procedure includes purification of the intermediate tetraethyl 1,1'-(ferrocenyl)bisphosphonite by column chromatography, after complexation of the phosphorus atoms with BH_3.[7]

Deprotonation of 1,1'-bis(phosphino)ferrocene with 2.2 equivalents of *n*-BuLi afforded the corresponding dianion which was then treated with the cyclic sulfate of (*R*,*R*)-2,4-pentanediol (or (*R*,*R*)-2,6-dimethyl-3,5-heptanediol).



Reagents and conditions: **i**. (a) *n*-BuLi (2.2 eq.), THF, -78 °C / 25 °C; (b) cyclic sulfate **3** (2 eq.), -78 °C / 25 °C, 1h; (c) *s*-BuLi (2.2 eq.), -78 °C / 25 °C, 1h. **ii**. BH_3. SMe_2, 25 °C, 10 min. **iii**. DABCO, 40 °C, 3h, benzene.

Scheme

Addition of 2.2 equivalents of *s*-BuLi led to deprotonation of the remaining PH functions and final formation of the ring-closure product **1a** (or **1b**). Complexation of the phosphorus atoms with BH_3 prevented air oxidation during the purification steps and the protecting group was easily removed. The phosphetane-borane complexes **2**[8] were separated from the side products, including the 1-(phosphetano)ferrocene-BH_3 complexes, by chromatography on alumina column, with a cyclohexane-dichloromethane 1:1 mixture as eluent (Yield 50% on a 0.1 g scale). After quantitative decomplexation of **1** by a phosphine–amine exchange reaction (excess DABCO, 40 °C, 3h, benzene), the excess amine was removed from the crude reaction mixture by washing with aqueous HCl. Phosphetanes **1a** and **1b**[9] were crystallised from pentane. The new chiral bis(phosphetanes) proved to be relatively air stable, thus the above borane complexation could be likely avoided. The experimental procedure is not fully optimised to date.

Preparations of **la** and **1b** are representative examples of a general synthetic approach which could be extended to many other bis(phosphetano)ferrocenes with different R substituents, starting from the corresponding optically

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pure 1,3-diols. For instance, the pure cyclic sulfates **3** with R = Et, *t*-Bu, cyclohexyl, CH_2Ph have already been prepared and applied to phosphetane syntheses.[4c,d] Further developments are in progress.

In order to get insight into the potential of ligands **1** in asymmetric catalysis, we considered a few rhodium promoted hydrogenation reactions. Our first concern was in fact to compare these phosphetane-based ligands with the analogous 1,1'-bis(phospholano)ferrocenes described in ref. 5, which showed high catalytic activity and moderate enantioselectivities in the hydrogenation of selected olefins and carbonyl groups. Thus, we performed the hydrogenation of the same substrates under analogous conditions, by using a rhodium catalyst formed in situ from $(COD)_2RhOTf$ and the chiral ligands **1a** or **1b**. The results are given in Table 1.

Table 1 Rhodium catalysed hydrogenations with ligands **1a,b**.

Entry	Substrate[a]	Ligand	e.e.
1	$H_2C=C(CO_2Me)CH_2CO_2Me$	**1a**	91 (*R*)
2		**1b**	66 (*S*)
3	$H_2C=C(CO_2Me)NHAc$	**1a**	69 (*S*)
4		**1b**	94 (*R*)
5	$MeCOCH_2CO_2Me$	**1a**	13 (*S*)
6		**1b**	57 (*S*)
7	(*Z*)-$PhCH=C(CO_2Me)NHAc$	**1a**	90 (*S*)
8		**1b**	83 (*R*)

[a] Conditions: catalyst 0.5 mol%, MeOH, 4 bars H_2, room temperature, 18h. 100% conversion.

Concerning the catalytic activity of these phosphetane-rhodium catalysts, we have not yet any reliable information, because quite long reaction times have been applied to ensure total conversion.

As shown in Table 1, the enantioselectivity levels are highly dependent on the nature of the R-substituent on the phosphetane rings, however they are at least comparable (entry 6) and sometimes higher (entries 1 and 4) than those obtained with the phospholane analogues. [5] Thus, it appears that in the series of 1,1'-disubstituted ferrocenes, chiral phosphetane moieties can perform better than the corresponding phospholanes in the enantioselective rhodium-catalysed hydrogenations. On the whole, the preliminary results reported in Table 1 are very promising, when considering that they were obtained under non-optimised conditions.

Moreover, it must be emphasized that many, variously substituted phosphetanes **1** should be accessible. Thus, it is likely that a "matching ligand" could be found for each substrate, which would optimise both the catalytic activity and stereoselectivity in the hydrogenation reactions. As there are no guidelines to predict the efficiency of these and analogous chiral ligands as a function of the R substituent, a large number of tests is still required to establish the potential of phosphetanes **1**.

More detailed studies are in progress. Investigations will be extended also to other fields of organometallic catalysis, where the specific properties of the ferrocene backbone should emerge.

In summary, the first members of a new class of optically pure phosphetanes have been prepared, characterised and successfully tested in the enantioselective rhodium-catalysed hydrogenations of model substrates.[10] Studies are under way to optimise the synthetic approach and to find significant catalytic applications.

References and Notes

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(6) (*R,R*)-2,4-pentanediol and (*R,R*)-2,6-dimethyl-3,5-heptanediol were conveniently prepared by ruthenium-BINAP catalysed hydrogenations (see ref. 4c and references therein).

(7) Tetraethyl 1,1'-(ferrocenyl)bisphosphonite bis-borane complex: ^1H NMR ($CDCl_3$): δ 1.30 (t, J_{H-H} = 7.1 Hz, Me), 3.9-4.2 (m, CH_2), 4.62 (CH), 4.63 (CH) ppm.

(8) The experimental procedure previously applied to the preparation of other phosphetane-borane complexes[4c,d] has been used here for the synthesis of **2**. **(*S,S*)-2a**, ^1H NMR ($CDCl_3$): δ 1.00 (dd, J_{H-P} = 15.8 Hz, J_{H-H} = 7.4 Hz, Me), 1.46 (dd, J_{H-P} = 18.8 Hz, J_{H-H} = 7.4 Hz, Me), 2.2-2.4 (m, 4H), 2.6-2.7 (m, 2H), 2.7-2.9 (m, 2H), 4.5 (m, 2H, Cp), 4.6 (m, 2H, Cp), 4.7 (m, 4H, Cp); ^{13}C NMR ($CDCl_3$): δ 15.8 (Me), 15.9 (Me), 28.0 ($^1J_{C-P}$ = 42.3 Hz, PCH), 29.2 ($^1J_{C-P}$ = 41.0 Hz, PCH), 35.9 ($^2J_{C-P}$ = 16.1 Hz, CH_2), 67.7 (J_{C-P} = 38.3 Hz, PC), 72.0 (J_{C-P} = 3.2 Hz, CH), 74.0 (J_{C-P} = 5.5 Hz, CH), 74.7 (J_{C-P} = 7.5 Hz, CH), 75.8 (J_{C-P} = 13.3 Hz, CH); ^{31}P NMR ($CDCl_3$): δ 49 ppm. MS (DCI/NH_3) m/e 432 (M+NH_4). $[\alpha]_D$ = -35 (c = 0.5, CH_2Cl_2). Anal. Calcd. For $C_{20}H_{34}B_2P_2Fe$: C, 58.04; H, 8.28. Found: C, 58.02; H, 8.29. **(*S,S*)-2b**, ^1H NMR (C_6D_6): δ 0.51 (dd, J_{H-H} = 6.6 Hz, J_{H-P} = 0.7 Hz, Me), 0.72 (d, J = 6.5 Hz, Me), 0.90 (dd, J_{H-H} = 6.6 Hz, J_{H-P} = 0.5 Hz, Me), 1.1 (m, 2H), 1.32

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(d, J = 6.4 Hz, Me), 1.9-2.1 (m, 10H), 4.3 (m, 2H, Cp), 4.5 (m, 2H, Cp), 4.7 (m, 2H, Cp), 4.8 (m, 2H, Cp); ^{13}C NMR (C_6D_6): δ 19.8 ($^3J_{C-P}$ = 12.2 Hz, Me), 21.0, 21.1, 21.2, 21.3 (2 Me), 23.0 ($^3J_{C-P}$ = 4.7 Hz, Me), 29.5 ($^2J_{C-P}$ = 2.7 Hz, CH), 30.7 ($^2J_{C-P}$ = 4.7 Hz, CH), 31.4 ($^2J_{C-P}$ = 16.9 Hz, CH_2), 40.4 ($^1J_{C-P}$ = 38.5 Hz, PCH), 42.2 ($^1J_{C-P}$ = 39.8 Hz, PCH), 68.9 ($^1J_{C-P}$ = 40.5 Hz, PC), 71.0 (CH), 74.4 (J_{C-P} = 5.4 Hz, CH), 74.9 (J_{C-P} = 7.4 Hz, CH), 76.3 (J_{C-P} = 14.2 Hz, CH); ^{31}P NMR (C_6D_6): δ 50 ppm. Anal. Calcd. For $C_{28}H_{50}B_2P_2Fe$: C, 63.92; H, 9.58. Found: C, 62.96; H, 9.62.

(9) Decomplexation procedure: The phosphetane-borane complex **2** (1mmol) was heated with DABCO (4 mmol) in benzene (2 mL), under argon, at 40 °C for 3 h. ^{31}P NMR analysis of the crude reaction mixture showed quantitative formation of **1**. The benzene solution was washed twice with degassed aqueous HCl (5%), dried over $MgSO_4$, filtered and concentrated. The residue was crystallised from pentane to afford pure **1** in 80% yield. **(*S,S*)-1a**, ^{1}H NMR (C_6D_6): δ 0.83 (dd, J = 8.5 and 7.0 Hz, Me), 1.47 (dd, J_{H-P} = 17.7 Hz, J_{H-H} = 7.2 Hz, Me), 2.2-2.3 (m, 6H), 2.4-2.5 (m, 2H), 4.2 (m, 6H, Cp), 4.3 (m, 2H, Cp); ^{13}C NMR (C_6D_6) (« m » indicates a complex pattern due to the virtual coupling of the two phosphorus atoms): δ 15.8 (t, J_{C-P} = 1.5 Hz, Me), 19.3 (m, Me), 22.0 (dd, J_{C-P} = 5.3 and 2.3 Hz, PCH), 22.8 (dd, J_{C-P} = 9.2 and 3.0 Hz, PCH), 38.6 (CH_2), 69.9 (t, J_{C-P} = 2.3 Hz, CH), 70.1 (CH), 71.0 (t, J_{C-P} = 3.8 Hz, CH), 74.4 (m, CP), 75.5 (m, CH); ^{31}P NMR (C_6D_6): δ 19 ppm. MS (DCI/NH_3) m/e 387 (M+1). **(*S,S*)-1b**, ^{1}H NMR (C_6D_6): δ 0.66 (d, J = 6.5 Hz, Me), 0.76 (d, J = 6.4 Hz, Me), 1.08 (d, J = 6.4 Hz, Me), 1.30 (d, J = 6.4 Hz, Me), 1.4 (m, 2H), 1.7-1.9 (m, 6H), 2.5-2.7 (m, 4H), 4.34 (m, 6H, Cp), 4.45 (m, 2H, Cp); ^{13}C NMR (C_6D_6) δ 15.5 (Me), 19.4 (Me), 21.1 (J_{C-P} = 9.9 Hz, Me), 21.7 (J_{C-P} = 13.6 Hz, Me), 31.4 (CH), 31.6 (J_{C-P} = 19.3 CH), 35.1 (CH_2), 35.9 (J_{C-P} = 9.9 Hz, CH), 37.3 (J_{C-P} = 7.8 Hz, CH), 70.9, 71.6, 72.7 (CH), 75.6 (J_{C-P} = 32.5 Hz, PC), 78.0 (J_{C-P} = 33.4 Hz, CH); ^{31}P NMR (C_6D_6): δ 13 ppm.

(10) Preliminary communication of this work has been made at the *10th IUPAC Symposium on Organometallic Chemistry Directed Towards Organic Synthesis* (OMCOS 10), Versailles (France), 18-22 July **1999**.

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