Pergamon

Tetrahedron: Asymmetry, Vol. 8, No. 19, pp. 3185–3188, 1997

Printed in Great Britain
PII: S0957-4166(97)00380-7
0957-4166/97 $17.00 + 0.00

Novel P-chiral bidentate phosphine ligands: synthesis and use in asymmetric catalysis

Ulrike Nettekoven,[a] Michael Widhalm,[b] Paul C. J. Kamer[a] and Piet W. N. M. van Leeuwen[a,*]

[a] Department of Inorganic Chemistry and Homogeneous Catalysis, Universiteit van Amsterdam, Nieuwe Achtergracht 166, 1018 WV Amsterdam, The Netherlands
[b] Institut für Organische Chemie, Universität Wien, Währingerstraße 38, 1090 Vienna, Austria

Abstract: Two C_2-symmetrical P-chiral diphosphines, (R,R)-(−)-1,1′-bis[phenyl-(2-methoxyphenyl)phosphino]ferrocene (**BPAF**), and (R,R)-(−)-1,1′-bis(phenyl-1-naphthyl-phosphino)ferrocene (**BPNF**), were synthesized via a stereocontrolled nucleophilic substitution sequence. The catalytic performance of the new ligands was investigated in several allylic alkylation reactions; with BPNF asymmetric inductions up to 73% e.e. for dimethyl (1,3-diphenyl-2-propenyl)propanedioate were obtained. © 1997 Elsevier Science Ltd

Among the plenitude of chiral phosphines developed for application in asymmetric catalysis, examples of ligands possessing optically active phosphorus donors are rare.[1] Metal complexes of bidentate P-chiral compounds featuring marked asymmetry in utmost proximity to the catalytic center are considered to be excellent optical inducers, but an intensive exploitation of this class of molecules has been hampered due to elaborate multistep synthesis and/or resolution procedures.[2]

The synthetic approach employing ephedrine as a chiral auxiliary and consecutive stereoselective substitution reactions at borane protected phosphorus centers, however, offers a convenient access to a limited number of enantiomercially pure mono- and (after homocoupling) diphosphines.[3] Developed for the asymmetric synthesis of Monsanto's DIPAMP on an industrial scale,[4] this nucleophilic displacement route was found superior in comparison to other approaches described in the literature, since resolution steps or reduction of phosphine oxides leading to partly racemized products are avoided.[5] Only very recently attempts have been made to extend the scope of this route by introduction of sterically demanding groups at the stereogenic phosphorus atom.[6,7] In further consequence, direct (double) attachment of the enantiopure monophosphine precursor to a chosen backbone can be envisaged, thus leading to more rigid and compact ligand structures.

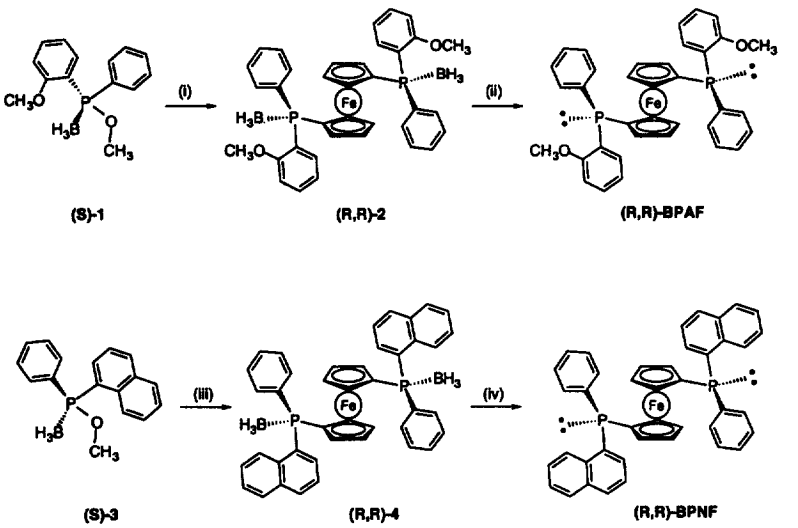
For the design of P-chiral ligands the choice of substituents at the stereogenic phosphorus centers will be crucial and has to be carefully adopted to reaction type, mechanism and substrate properties. A propeller-like arrangement of space-filling aromatic moieties at phosphorus creating an efficient chiral environment of the complexed transition metal seems to be most promising. Significant differences in the nature of the aromatic residues either with respect to their electronic or their steric properties, are therefore desired to generate a pronounced dissymmetric array.

In order to have a more universal route to P-chiral diphosphines available and, additionally, to test the efficiency of one set of substituents in different catalytic reactions, we chose to develop optically active bidentate phosphine ligands based on the versatile ferrocene unit as the backbone.[8]

Herein we wish to report on the synthesis of (R,R)-(−)-1,1′-bis[phenyl-(2-methoxyphenyl)-phosphino]-ferrocene (BPAF) and (R,R)-(−)-1,1′-bis(phenyl-1-naphthylphosphino)ferrocene (BPNF). These two new ligands[9] were accessible via the optically active monomethoxyphosphinite borane complexes **1** and **3**,[3] which could be attached stereoselectively to the ferrocene moiety (Scheme 1).

* Corresponding author. Email: pwnm@anorg.chem.uva.nl

Reaction conditions had to be adjusted carefully in order to ensure complete configurational inversion.[10] Decomplexation of intermediates **2**[11] and **4**, respectively, with diethylamine yielded after chromatographic purification air-stable crystals of BPAF and BPNF, which gave correct analytical data and were fully characterized by NMR spectroscopy.[12]



Scheme 1. Synthesis of BPAF and BPNF ligands.

Chiral HPLC analysis of the diphosphine diboranes **2** and **4** (Chiralcel OD, n-hexane:2-propanol:acetic acid=97:2.8:0.2; Chiralcel OJ, heptane:EtOH=85:15) gave no indications for the presence of other enantiomers or diastereoisomers.[13]

The catalytic performance of the two novel ligands was tested first in asymmetric allylic alkylation reactions.[14] Moderate to good enantioselectivities could be obtained with BPNF in the model reaction of 1,3-diphenyl-3-acetoxy-1-propene with dimethyl malonate (reaction 1), whereas the BPAF ligand gave rise to very low asymmetric induction (Table 1).

Table 1. Summary catalysis results[a]

entry	reaction	ligand L*	temperature [°C]	reaction time [h][b]	isolated yield [%]	%e.e.[c] (product configuration)
1	1	(–)-BPAF	25	4	85	0
2	1	(–)-BPAF	0	15	82	3 (S)
3	1	(–)-BPNF	25	3	88	68 (R)
4	1	(–)-BPNF	0	3	73	72 (R)
5	1	(–)-BPNF	-10	15	84	73 (R)
6	2	(–)-BPNF	25	24	47	4 (+)
7	2	(–)-BPNF	-10	24	76	9 (+)
8	3	(–)-BPNF	25	24	77	26 (R)

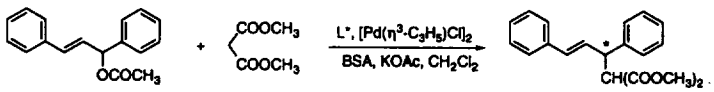
[a] Typical procedure: To a degassed solution of 0.005 mmol of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ and 0.01 mmol of ligand in 1 ml of CH_2Cl_2 were subsequently added 1 mmol of substrate, 3 mmol of dimethyl malonate, 3 mmol of N,O-bis(trimethylsilyl)acetamide (BSA) and a catalytic amount of KOAc. The reaction mixture was stirred at the given temperature and after workup the residue was purified by chromatography on silica gel.[15]

[b] Entries 1-5 were monitored by TLC and stopped after complete conversion, entries 6-8 were stopped after 24h.

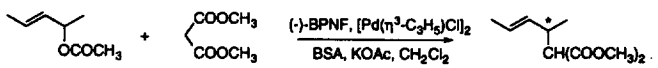
[c] Entries 1-5: Enantiomeric excesses were determined via chiral HPLC (Chiralcel OD-H, n-hexane:2-propanol = 99:1); entries 6-8: e.e. values were estimated on the basis of specific rotation values calculated for enantiomerically pure products: dimethyl (2-pent-3-enyl)propanedioate: $[\alpha]_D \pm 34$ (c=1.83, CH_2Cl_2)[16]; (S)-dimethyl cyclohex-2-enyl-propanedioate: $[\alpha]_D$ - 46.1 (c=2.86, $CHCl_3$).[17]

In the presence of BPNF, the use of other substrates such as (E)-pent-3-en-2-ylacetate or 3-acetoxycyclohex-1-ene (model reactions 2 and 3) resulted in considerably lower enantioselection, which may be partly ascribed to the absence of aromatic π-stacking interactions (Scheme 2).

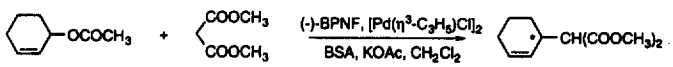
Reaction 1:



Reaction 2:



Reaction 3:



Scheme 2. Allylic alkylation — model reactions.

The e.e. values obtained employing BPNF in reaction 1 clearly demonstrate the potential applicability of these types of P-chiral diphosphines in enantioselective catalysis. The failure of the BPAF compound to accomplish effective stereodifferentiation supports our assumption that steric rather than electronic effects may play a dominant role in inducing asymmetry.

To summarize, we found an extension of the Jugé–Genêt nucleophilic displacement route to P-chiral phosphines which enabled us to synthesize bidentate ferrocene ligands bearing stereogenic phosphorus centers. Optimization experiments and testing of the new ligands in other catalytic reactions are currently under progress and results will be published in due course.

Acknowledgements

We are thankful to W. de Lange and Dr A. Werner (Universität Wien) for technical advice and to the IOP-Katalyse program (project IKA94081) for financial support. Furthermore we are indebted to Dr A. Mezzetti (ETH, Zürich) for sending us his manuscript dealing with the synthesis of (S,S)-C,C′-tetramethylsilanebis(α-naphthylphenylphosphine) prior to publication.[18]

References

1. H. Brunner, W. Zettlmeier, Eds., *Handbook of Enantioselective Catalysis*, VCH, Weinheim, **1993**.
2. For recent reviews see: (a) T. Imamoto, *Pure Appl. Chem.*, **1993**, *65*, 655; (b) K. M. Pietrusiewicz, M. Zablocka, *Chem. Rev.*, **1994**, *94*, 1375.
3. (a) S. Jugé, J. P. Genêt, *Tetrahedron Lett.*, **1989**, *30*, 2783; (b) S. Jugé, M. Stephan, J. A. Laffitte, J. P. Genêt, *Tetrahedron Lett.*, **1990**, *31*, 6357.
4. (a) S. Jugé, M. Stephan, S. Achi, J. P. Genêt, *Phosphorus Sulfur Silicon*, **1990**, *49*, 267; US Patent 5 043 465 (1991); (b) S. Jugé, M. Stephan, J. P. Genêt, S. Halut-Desportes, S. Jeannin, *Acta Crystallogr., C46*, **1990**, 1869; French Patent 91 01674 (1991).
5. J. A. Ramsden, J. M. Brown, M. B. Hursthouse, A. I. Karalulov, *Tetrahedron: Asymmetry*, **1994**, *5*, 2033.
6. J. M. Brown, J. C. P. Laing, *J. Organomet. Chem.*, **1997**, *529*, 435.
7. E. B. Kaloun, R. Merdès, J. P. Genêt, J. Uziel, S. Jugé, *J. Organomet. Chem.*, **1997**, *529*, 455.
8. A. Togni, T. Hayashi, (Eds.), *Ferrocenes*, VCH, Weinheim, **1995**.
9. Simultaneously with our work, R. M. Stoop, F. Maienza, T. Y. H. Wong, F. Spindler and A. Mezzetti presented the synthesis of the BPAF ligand and its application in asymmetric hydrogenation

reactions as a poster contribution at the OMCOS 9 symposium in Göttingen, Germany, in July 1997.

10. Assignments of absolute configurations are based on literature findings: S. Jugé, M. Stephan, R. Merdès, J. P. Genêt, *J. Chem. Soc., Chem. Comm.*, **1993**, 531 and Ref. 6.
11. The diborane complex **2** has been isolated as a byproduct by J. M. Brown and J. C. P. Laing.[6]
12. 1,1′-bis[phenyl-(2-methoxyphenyl)phosphino]ferrocene (BPAF): yellow crystals; m.p. 153°C (CH_2Cl_2/EtOH); $[\alpha]_D^{20}=-198.9$; $[\alpha]_{578}^{20}=-208.5$ (c=0.27, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$): δ 3.61 (m, 2H); 3.68 (s, 6H); 4.26 (m, 2H); 4.32 (m, 2H); 4.42 (m, 2H); 6.77–6.89 (m, 6H); 7.22–7.32 (m, 8H); 7.34–7.42 (m, 4H) ppm. ^{13}C-NMR (75.42 MHz, CD_2Cl_2): δ 56.27; 73.03; 73.36; 75.91; 76.26; 77.38 (d, J_{PC}=8.2 Hz); 111.14; 121.35; 128.59 (d, J_{PC}=7.5 Hz); 129.02 (d, J_{PC}=14.3 Hz); 129.21; 130.63; 134.12; 134.40; 138.70 (d, J_{PC}=9 Hz); 161.44 (d, J_{PC}=15.8 Hz) ppm. ^{31}P-NMR (121.44 MHz, $CDCl_3$): δ −29.19 (s) ppm. Anal. Calc. for $C_{36}H_{32}FeO_2P_2$: C, 70.37; H, 5.25. Found: C, 70.63; H, 5.60. 1,1′-Bis(phenyl-1-naphthylphosphino)ferrocene (BPNF): orange crystals; m.p. 176°C (CH_2Cl_2/hexane); $[\alpha]_D^{20}=-197.2$; $[\alpha]_{578}^{20}=-205.9$ (c=0.25, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$): δ 3.68 (m, 2H); 4.26 (m, 2H); 4.34 (m, 2H); 4.38 (m, 2H); 7.11–7.16 (m, 2H); 7.20–7.45 (m, 16H); 7.76–7.83 (m, 4H); 8.31–8.37 (m, 2H) ppm. ^{13}C-NMR (75.42 MHz, $CDCl_3$): δ 72.48; 73.02 (br); 75.09; 75.44; 76.47 (d, J_{PC}=6.1 Hz); 125.23; 125.85 (br); 126.19; 128.14 (d, J_{PC}=7.5 Hz); 128.50; 128.82; 129.09; 131.41; 133.33 (d, J_{PC}=4.5 Hz); 133.71; 133.98; 134.69 (d, J_{PC}=21 Hz); 136.70 (d, J_{PC}=14.3 Hz); 137.07 (d, J_{PC}=8.2 Hz) ppm. ^{31}P-NMR (121.44 MHz, $CDCl_3$): δ −25.99 (s) ppm. Anal. Calc. for $C_{42}H_{32}FeP_2$: C, 77.07; H, 4.93. Found: C, 76.98; H, 5.02.
13. The deboronation step is reported to proceed without significant loss of enantiomeric purity: (a) Ref. 3; (b) T. Imamoto, T. Oshiki, T. Onozawa, T. Kusumoto, K. Sato, *J. Am. Chem. Soc.*, **1990**, *112*, 5244.
14. B. M. Trost, D. L. van Vranken, *Chem. Rev.*, **1996**, *96*, 395.
15. M. Widhalm, P. Wimmer, G. Klintschar, *J. Organomet. Chem.*, **1996**, *523*, 167.
16. B. M. Trost, A. C. Krueger, R. C. Bunt, J. Zambrano, *J. Am. Chem. Soc.*, **1996**, *118*, 6520.
17. P. Sennhenn, B. Gabler, G. Helmchen, *Tetrahedron Lett.*, **1994**, *35*, 8595.
18. R. M. Stoop, F. Spindler, A. Mezzetti, submitted to *Organometallics*.

(Received in UK 30 July 1997)