

# Synthesis and first application of a new family of monophosphine ferrocene ligands (MOPF)

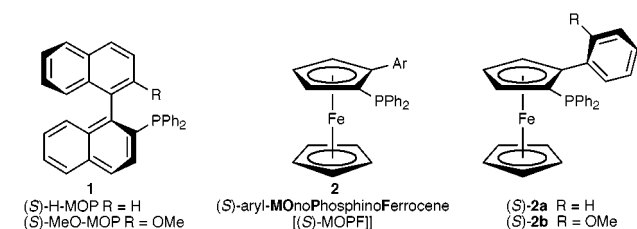
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A new family of monophosphine ferrocene ligands (MOPF) has been synthesised in two steps from an optically pure ferrocenyl sulfoxide and the first preliminary studies employing these ligands in asymmetric hydrosilylation of styrene are presented.

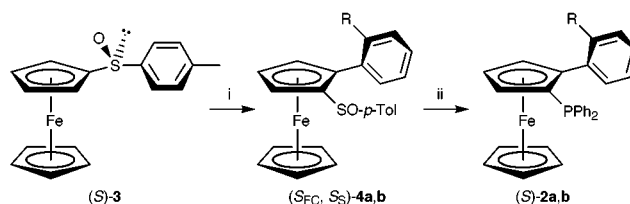
During the last decades only very few efficient chiral monophosphine ligands have been developed, in which the only Lewis base is the phosphorus atom. The fact that bisphosphine ligands form more rigid and stable complexes with metals, as compared to those with monophosphines, has probably stimulated the more abundant research in the former type. However, recently it has become increasingly clear that there is a need for efficient chiral monophosphine ligands for use in those reactions where the usual  $C_2$ -symmetric bisphosphines (e.g. BINAP) fail.<sup>1</sup>



One of the few efficient types of monophosphine ligands discovered to date is Hayashi's MOP ligands **1**.<sup>1a,2</sup> Here we disclose a new family of arylMOPF ligands **2** (hereafter abbreviated MOPF), which show some resemblance to the MOP ligands, but are simpler to modify in a rational manner.<sup>3</sup>

We also present the first catalytic reactions employing these new ligands. In terms of enantioselectivity, the results are very encouraging and we believe that they can be further improved by simple variation of the aryl unit.

During the initial phase of this project we searched for a simple procedure to obtain a suitable building block for this new family of ligands. Recently, great progress has been achieved within the field of Directed *ortho*-Metallation (DoM) of ferrocenes.<sup>4</sup> However, the enantioselective *ortho*-lithiation of e.g. diphenylphosphinoferrrocene, which in principle would allow us to synthesise these ligands in a single step, has met with only limited success.<sup>5</sup> On the other hand, Kagan *et al.*<sup>4a,6</sup> and Robinson *et al.*<sup>4b</sup> have recently described highly selective *ortho*-lithiation procedures of optically pure ferrocenyl sulfoxides. As the sulfoxide can be removed from the ferrocene by treatment with Bu<sup>t</sup>Li we chose this compound as a starting material for the synthesis of the MOPF ligands. The synthesis of the first two members of the MOPF family is shown in Scheme 1. After diastereoselective *ortho*-lithiation of the sulfoxide (S)-**3**<sup>4a</sup> and lithium–zinc exchange, the aryl scaffold is introduced by a Negishi coupling giving **4**. The selective removal of the sulfoxide is accomplished with Bu<sup>t</sup>Li and the lithiated ferrocene is then captured with ClPPh<sub>2</sub> giving the ligands (S)-**2a,b**.



**Scheme 1** Reagents and conditions: i, LDA (1.2 equiv.), THF,  $-78\text{ }^{\circ}\text{C}$ , 20 min, then ZnCl<sub>2</sub> (1 equiv.)  $-78\text{ }^{\circ}\text{C}$ , 1 h, then Pd<sub>2</sub>dba<sub>3</sub> (2 mol%), P(fur)<sub>3</sub> (8 mol%), aryl iodide, (1.5 equiv.), (R = H) room temp., 96 h, 67%, (R = OMe) reflux, 72 h, 54%; ii, (2 equiv.) Bu<sup>t</sup>Li, THF,  $-78\text{ }^{\circ}\text{C}$ , 5 min; then ClPPh<sub>2</sub>, (3.5 equiv.) room temp., 3 h, (R = H) 67%, (R = OMe) 76%.

The potential and efficiency of the MOPF ligands is exemplified in the asymmetric hydrosilylation of styrene.<sup>7</sup> This transformation belongs to the class of reactions where e.g. BINAP gives only poor results.<sup>1a</sup> However, using the most simple phenyl-MOPF ligand **2a** the reaction proceeds nicely with up to 70% ee (Table 1, entries 1 and 2). Introducing a simple methoxy substituent on the aryl group interferes slightly with the selectivity of the reaction and it is observed that the addition of benzene as solvent improves the enantioselectivity from 60 to 64% (entries 3 and 4). Currently, we have no information on the catalytically active species in this reaction, but it is noteworthy that a similar but more pronounced behaviour has been observed in the hydrosilylation of styrene using H-MOP (91% ee) and MeO-MOP (14% ee) as ligands.<sup>8</sup> Moreover the sense of induction in the reactions using the (S)-MOPF or the (S)-H-MOP ligands is the same. The rationalisation of these observations, however, must await further study.

In summary, a short and efficient synthesis of two members of a novel family of monodentate phosphine ferrocene ligands (MOPF) has been carried out. The simple procedure developed paves the way for the preparation of an array of structurally varied aryl-MOPF ligands. The preliminary catalytic reactions employing these ligands have given encouraging results and we

**Table 1** Enantioselective hydrosilylation of styrene using MOPF ligands **2a,b**.<sup>9</sup>

Entry	Ligand	t/h	T/°C	Yield of <b>5</b> (%) <sup>a</sup>	Ee of <b>6</b> (%) <sup>b,c</sup>
1	<b>2a</b>	24	room temp.	66	70 (S)
2	<b>2a</b>	36	room temp.	73	70 (S)
3	<b>2b</b>	36	room temp.	49	60 (S)
4	<b>2b</b>	72	room temp.	41 <sup>d</sup>	64 (S) <sup>e</sup>

<sup>a</sup> Isolated yield after distillation or flash chromatography. <sup>b</sup> Ee determined by HPLC on a DAICEL OD-H column. <sup>c</sup> Absolute configuration determined by optical rotation [see ref. 2(b)]. <sup>d</sup> Yield of **6** based on styrene. <sup>e</sup> Benzene added as solvent.

are pursuing the synthesis of a range of new aryl-MOPF as well as alkyl-MOPF family members in order to find even better ligands.<sup>10</sup>

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## Notes and references

- 1 For some examples where monophosphine ligands or ligands with a phosphine and a hemilabile coordinating group are superior to the usual bisphosphines, see *e.g.*: (a) Asymmetric hydrosilylation: Y. Uozumi and T. Hayashi, *J. Am. Chem. Soc.*, 1991, **113**, 9887; (b) Asymmetric hydrovinylation: T. V. RajanBabu, N. Nomura, J. Jin, B. Radetich, H. Park and M. Nandi, *Chem. Eur. J.*, 1999, **5**, 1963; (c) Asymmetric Grignard cross-coupling: T. Hayashi, K. Hayashizaki, T. Kiyoi and Y. Ito, *J. Am. Chem. Soc.*, 1988, **110**, 8153.
- 2 For the synthesis and application of MOP and other monophosphine ligands see *e.g.*: (a) Y. Uozumi, A. Tanahashi, S.-Y. Lee and T. Hayashi, *J. Org. Chem.*, 1993, **58**, 1945; (b) K. Kitayama, Y. Uozumi and T. Hayashi, *J. Chem. Soc., Chem. Commun.*, 1995, 1533; (c) H. Tye, D. Smyth, C. Eldred and M. Wills, *Chem. Commun.*, 1997, 1053; (d) C. D. Graf, C. Malan, K. Harms and P. Knochel, *J. Org. Chem.*, 1999, **64**, 5581; (e) G. Zhu, Z. Chen, Q. Jiang, D. Xiao, P. Cao and X. Zhang, *J. Am. Chem. Soc.*, 1997, **119**, 3836; (f) B. L. Feringa, M. Pineschi, L. A. Arnold, R. Imbos and A. H. M. de Vries, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 2620; (g) B. Bartels and G. Helmchen, *Chem. Commun.*, 1999, 741.
- 3 The MOPF ligands are structurally different from known ferrocene monophosphines which have a methylene spacer group next to the phosphine. See *e.g.* T. Hayashi, in *Ferrocenes*, ed. A. Togni and T. Hayashi, VCH, Weinheim, 1995, p. 118.
- 4 (a) O. Riant, G. Argourch, D. Guillaneux, O. Samuel and H. B. Kagan, *J. Org. Chem.*, 1998, **63**, 3511; (b) D. H. Hua, N. M. Lagneau, Y. Chen, P. M. Robben, G. Clapham and P. D. Robinson, *J. Org. Chem.*, 1996, **61**, 4508; (c) M. Tsukazaki, M. Tinkl, A. Roglans, B. J. Chapell, N. J. Taylor and V. Snieckus, *J. Am. Chem. Soc.*, 1996, **118**, 685; (d) For references prior to 1996 see: A. Togni, *Angew. Chem.*, 1996, **108**, 1581.
- 5 D. Price and N. S. Simpkins, *Tetrahedron Lett.*, 1995, **36**, 6135.
- 6 F. Rebière, O. Riant, L. Richard and H. B. Kagan, *Angew. Chem.*, 1993, **105**, 644.
- 7 For other asymmetric hydrosilylation reactions of styrene see *e.g.*: G. Bringmann, A. Wuzik, M. Breuning, P. Henschel, K. Peters and E.-M. Peters, *Tetrahedron: Asymmetry*, 1999, **10**, 3025; G. Pioda and A. Togni, *Tetrahedron: Asymmetry*, 1999, **9**, 3903; T. Okada, T. Morimoto and K. Achiwa, *Chem. Lett.*, 1990, 999.
- 8 This selectivity has been shown to be substrate dependent. MeO-MOP generally gave better results than H-MOP using non-styrene-type substrates such as *e.g.* oct-1-ene (up to 96% ee) [ref. 2(b)]. We are currently investigating the MOPF ligands to see whether they display similar behaviour.
- 9 *A representative hydrosilylation-oxidation procedure*: To a flame dried Schlenk tube was added [CIPd(C<sub>3</sub>H<sub>5</sub>)<sub>2</sub>] (6.2 mg, 0.017 mmol) and **2b** (30 mg, 0.067 mmol) under N<sub>2</sub>. The solids were dried on the vacuum line for 1 h before styrene (0.378 ml, 3.3 mmol) and 2 ml of benzene were added *via* syringe. After another 30 min the silane (0.404 ml, 4 mmol) was added *via* syringe and the solution was left with stirring for 72 h. An aliquot of the reaction was used for NMR and it showed that the reaction was completed. The crude reaction mixture was slowly added to a suspension of KF (3.9 g, 67 mmol) in 30 ml of MeOH and the resulting solution was stirred for 30 min. The solvent was evaporated *in vacuo* and the resulting solid was suspended in 40 ml of DMF. Finally 4 ml H<sub>2</sub>O<sub>2</sub> (35%) was added at room temperature and the reaction was heated to 60 °C for 1 h before quenching with 30 ml saturated Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> (aq). After aqueous workup and extraction the product was purified by flash column chromatography (15% EtOAc in pentane) giving **6** as a colorless oil in 41% yield (167 mg) and 64% ee detected by HPLC using a Chiralcel OD-H column (10% Pr<sup>+</sup>OH-90% hexane, 0.5 ml min<sup>-1</sup>). [ $\alpha$ ]<sub>D</sub><sup>25</sup> -36 (c 1.065, CHCl<sub>3</sub>). Spectroscopic data were in accordance with those from a commercial sample.
- 10 During the course of our investigation we became aware of a paper from another group synthesising related benzene chromium tricarbonyl complexes. This prompted us to report our findings at this early stage. See: S. C. Nelson and M. A. Hilfiker, *Org. Lett.*, 1999, **1**, 1379.

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