Diphosphonites as highly efficient ligands for enantioselective rhodium-catalyzed hydrogenation

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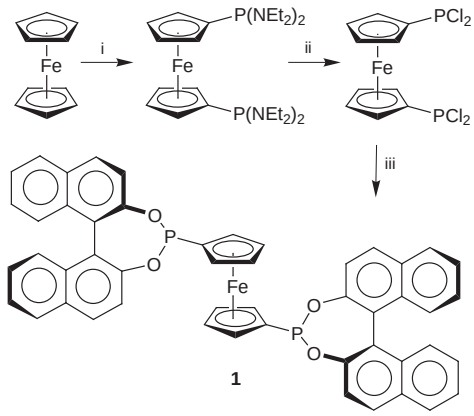
Chiral ligands with achiral backbones such as ethano- or ferroceno-bridges linking two phosphonites derived from chiral diols such as binaphthol (BINOL) have been prepared; the corresponding Rh complexes are excellent catalysts in the hydrogenation of prochiral olefins such as itaconic acid dimethyl ester or 2-acetamido methyl acrylate, the ee values being 90–99.5%.

Although a number of chiral diphosphanes and diphosphinites have been shown to be effective ligands in transition metal catalyzed asymmetric reactions,[1] the search for new types of chiral auxiliaries continues.[2] Surprisingly, very little is known concerning chiral diphosphonites as ligands in these reactions.[3] Perhaps this is due to the fact that in all cases reported so far the enantioselectivity is poor (ee = 0–32%).[3] We speculated that chelating diphosphonites derived from a proper combination of an achiral backbone and a chiral diol might constitute useful and easily accessible ligands.[4]

Using ferrocene and (*R*)- or (*S*)-BINOL as cheap building blocks,[5] the diphosphonite **1** was easily assembled in three steps (Scheme 1).[6] **1** is an orange–brown crystalline compound, which in the solid state‡ shows some interesting features (Fig. 1). In spite of their different environments, the two independent molecules in the unit cell have almost identical conformations [P1–Cp1–Cp2–P2 −9(1)°, P3–Cp3–Cp4–P4 −7(1)°; Cp, centroid], with the two P atoms in each molecule situated close to one another [P1···P2 3.506(3), P3···P4 3.428(3) Å].

The ethano-bridged analog **2** was also readily synthesized (Scheme 2).

In order to prepare hydrogenation catalysts, the ligands were treated with $Rh(cod)_2BF_4$ under standard conditions,[7] affording the corresponding complexes (*R*,*R*)-(**1**)Rh(cod)BF_4 or (*R*,*R*)-(**2**)Rh(cod)BF_4, which were characterized by NMR, ESI-MS and IR spectroscopy. Thus far it has not been possible to obtain crystals suitable for crystallographic investigations. Two different types of olefins were chosen as substrates for asymmetric



Scheme 1 *Reagents and conditions*: i (*a*) 2.2 equiv. BuLi–TMEDA, hexane, r.t., 12 h; (*b*) 2.2 equiv. $ClP(NEt_2)_2$, THF, −78 °C, 67%; ii, excess HCl, Et_2O, −78 °C, 95%; iii, 2 equiv. (*R*)-(+)-BINOL, toluene, heat, 36 h, 90%

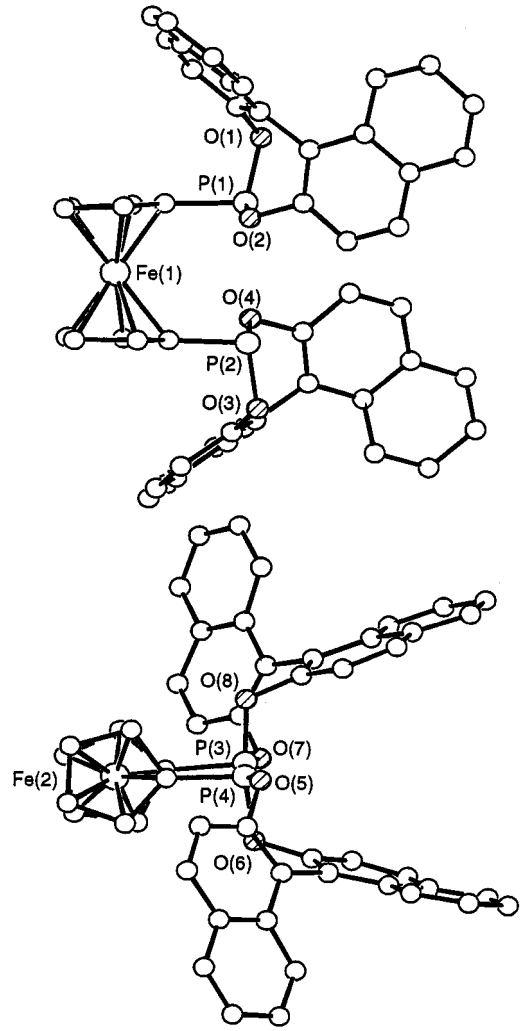
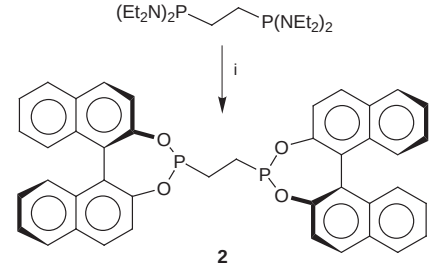
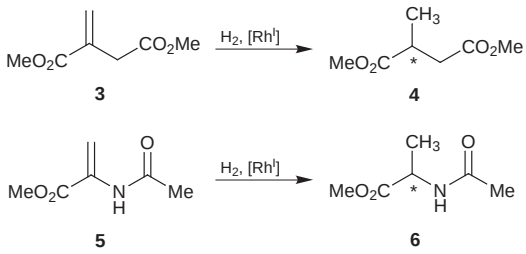


Fig. 1 Molecular structures of the two independent molecules of **1**. Side (upper structure, molecule 1) and top views (the toluene solvent of crystallization has been omitted for clarity).



Scheme 2 *Reagents and conditions*: i, 1.95 equiv. (*R*)-(+)-BINOL, THF, heat, 48 h, (70–85%)



hydrogenation, namely itaconic acid dimethyl ester **3** and 2-acetamido methyl acrylate **5**, leading to the products **4** and **6**, respectively. The results of the hydrogenation experiments with formation of the *R*-configurated products **4** and **6** are remarkable in several ways (Table 1).

Table 1 Enantioselective hydrogenation of dimethyl itaconate (**3**) and 2-acetamido methyl acrylate (**5**)[a]

Entry	Ligand	Substrate	S/C[d]	Yield (%)[e]	ee (%)[e]
1	**1**	**3**	1000	100	> 99.5
2	**1**	**3**	2000	100	> 99.5
3[b]	**1**	**3**	5380	100	> 99.5
4	**2**	**3**	1000	100	97–99
5	**2**	**3**	2000	100	97–99
6[c]	**1**	**5**	1000	100	99.5
7[c]	**2**	**5**	1000	100	90

[a] Hydrogenations were carried out under the following general conditions: 1.3 bar H_2, dichloromethane, r.t., 20 h, *c*(substrate) = 0.1 mol l^{-1}, catalysts prepared *in situ* with Lig/Rh = 1.1 (4 runs each). [b] Using preformed (*R*,*R*)-(**1**)Rh(cod)BF_4. [c] Lig/Rh = 1.0. [d] Substrate to catalyst ratio. [e] Determined by GC analysis.

In the case of substrate **3** both catalysts afford essentially enantiomerically pure product **4**. However, in the hydrogenation of **5** pronounced differences in enantioselectivity were observed (Table 1). Thus, the ferrocene-based catalyst (*R*,*R*)-(**1**)Rh(cod)BF_4 leads to complete enantioselectivity for both substrates (ee > 99.5%). Although experiments directed towards elucidating mechanistic and structural aspects need to be carried out, the present study shows that catalyst (*R*,*R*)-(**1**)Rh(cod)BF_4 is not only readily accessible, but also highly effective. It remains to be seen how well ligand **1** performs in other hydrogenation reactions and in C–C bond forming processes, metals other than rhodium constituting further possibilities.

Notes and References

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‡ *Crystal data for* **1**: $C_{50}H_{32}FeO_4P_2{\cdot}C_7H_8$, M_r = 906.7, orange–brown plate, crystal size 0.08 × 0.59 × 0.66 mm, a = 9.7235(3), b = 16.5610(4), c = 27.5239(7) Å, β = 97.765(1)°, U = 4391.6(2) Å^3, T = 100 K, monoclinic, space group $P2_1$ (no. 4), Z = 4, D_c = 1.37 g cm^{-3}, μ = 0.47 mm^{-1}. Siemens SMART diffractometer, Mo-Kα X-radiation, λ = 0.71073 Å. 39615 measured reflections, analytical absorption correction (T_{min} 0.7343, T_{max} 0.9626), 15179 unique, 11532 observed [$I > 2.0\sigma(F_o^2)$]. The structure was solved by direct methods (SHELXS-97) and refined by full-matrix least-squares (SHELXL-97) on F^2 for all data (C atoms of toluene solvate, isotropic) with Chebyshev weights to R = 0.089 (obs.), wR = 0.232 (all data), absolute stereochemistry determined [Flack parameter 0.00(3)], S = 1.17, H atoms riding, max. shift/error 0.001, residual ρ_{max} = 1.039 e Å^{-3}. CCDC 182/964.

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5 Enantiomerically pure (*R*)- and (*S*)-BINOL are commercially available from Kankyo Kagaku Center (Japan) at a price of about $1300 per kilo.
6 We thank A. Meiswinkel for performing some of the experiments.
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