Chiral (iminophosphoranyl)ferrocenes: highly efficient ligands for rhodium- and iridium-catalyzed enantioselective hydrogenation of unfunctionalized olefins

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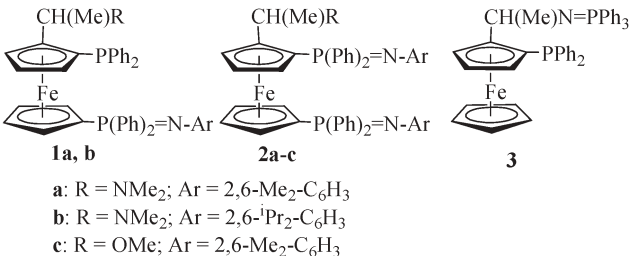
A series of chiral (iminophosphoranyl)ferrocenes (1–3) are highly efficient ligands for Rh- and Ir-catalyzed hydrogenation of a number of unfunctionalized olefins; almost perfect enantiomeric excesses (up to 99% ee) have been achieved under mild reaction conditions.

Homogeneous asymmmetric catalytic hydrogenation is one of the most widely studied class of organometallic reactions.[1] In particular, hydrogenation of chelating olefins with chiral ruthenium or rhodium catalysts has been most thoroughly examined, and thus has reached a very high level of development.[1c–e,2] Nevertheless, there still remain a great body of olefin substrates that resist high enantioselection by conventional Ru- and Rh-phosphine type catalysts.[3] Unfunctionalized olefins belong to this class of substrates. Recently, however, a breakthrough has been made by Pfaltz and co-workers who have demonstrated that iridium complexes of oxazoline-based ligands can catalyze a variety of unfunctionalized olefins with very high enantioselectivities (up to 99% ee).[4] Buchwald and co-workers had earlier reported the use of Brintzinger's chiral titanocene complexes as catalysts for the hydrogenation of unfunctionalized tri- and tetrasubstituted olefins with high % ees, yet with low activity as well as a high catalyst loading.[5] The work of Pfaltz has spurred renewed interest in the hydrogenation of largely unfunctionalized alkenes including dienes.[6]

We have recently reported the synthesis of chiral ferrocene-based iminophosphoranes (**1–3**, Chart 1) and demonstrated that they can serve as a new class of practical ligands for Pd-catalyzed allylic alkylation of allyl acetates and Rh-catalyzed hydrogenation of olefins.[7] In particular, these new ligands exhibit exceptionally high enantioselectivity (up to 99% ee) and catalytic activity in the Rh-catalyzed hydrogenation of functionalized olefins such as (*E*)-methylcinnamic acid, (*Z*)-2-acetamidocinnamate and (*Z*)-2-acetamidoacrylate. Encouraged by these observations and motivated by our continuing effort in the design and application of new ferrocene-based ligands for use in asymmetric catalysis,[8] we have prepared cationic Rh(I)- and Ir(I)-complexes of the type $[M(L)(COD)]BF_4$ (L = **2**, **3**; M = Rh, Ir) (Chart 2) to employ as catalysts in the hydrogenation of various unfunctionalized olefins (eqn (1)).



1a, b **2a-c** **3**

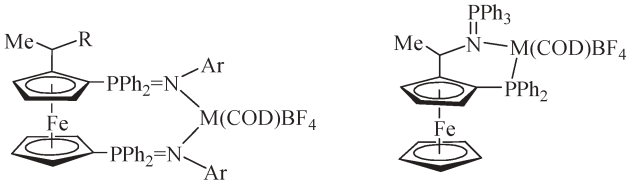
a: R = NMe_2; Ar = 2,6-Me_2-C_6H_3
b: R = NMe_2; Ar = 2,6-$^{i}Pr_2$-C_6H_3
c: R = OMe; Ar = 2,6-Me_2-C_6H_3

Chart 1

$$\text{Alkene} \xrightarrow[\text{L = 2-3}]{\text{[M(L)(COD)]BF}_4\text{ (2 mol \%)}}{\text{H}_2,\ \text{CH}_2\text{Cl}_2\text{ or MeOH, 24 h}} \text{Alkane} \quad (1)$$

We anticipated that these compounds should act as tightly binding chelates and thus would be capable of stabilizing metal centers involved in catalytic cycles, even in rather low oxidation states.[9,10] Furthermore, as sterically demanding and robust chelates, they are supposed to accomplish higher asymmetric induction.

In the first set of experiments to benchmark the potential of our ligands, we performed Ir- and Rh-catalyzed hydrogenation of trisubstituted alkenes such as *trans*-α-methylstilbene (**4**), ethyl *trans*-β-methylcinnamate (**5**), *trans*-2-methyl-3-phenyl-2-propen-1-ol (**6**) and 6-methoxy-1-methyl-3,4-dihydronaphthalene (**7**). Hydrogenation was conducted at ambient temperature under a H_2 pressure of 10 bar in the presence of 2 mol% of catalysts.† Indeed the results are remarkable in that exceptionally high enantioselectivities (up to 99% ee) are achieved regardless of the types of ligands or metals (Table 1). The most characteristic feature of Table 1 is the demonstration that it is for the first time for the Rh-catalyzed hydrogenation of unfunctionalized trisubstituted olefins to accomplish such high enantioselectivities under such very mild reaction conditions. These results may well be compared with those obtained with Pfaltz's Ir-systems.[6] In our hands, as far as chemical yields are concerned, rhodium complexes serve better than the iridium analogues (Table 1). Of two ligands **2** and **3**, the former works better both in terms of enantioselectivity and the



M = Rh, Ir

Chart 2

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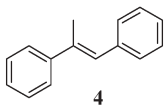
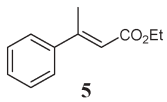
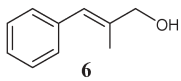
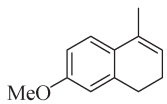
Table 1 Asymmetric hydrogenation of trisubstituted olefins[a]

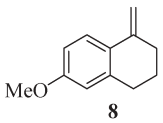
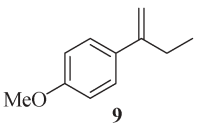
			Ir		Rh	
Entry	Substrate	Ligand	Yield[b] (%)	ee[c] (%)	Yield[b] (%)	ee[c] (%)
1	 **4**	(*S*,*R*)-**2a**	71	91	100	69
2		(*S*,*R*)-**2b**	69	82	100	58
3		(*S*,*R*)-**2c**	100	70	100	49
4		(*S*,*R*)-**3**	100	74	98	46
5	 **5**	(*S*,*R*)-**2a**	98	91	100	86
6		(*S*,*R*)-**2b**	68	89	**100**	**99**
7		(*S*,*R*)-**2c**	74	79	100	86
8		(*S*,*R*)-**3**	52	88	90	56
9	 **6**	(*S*,*R*)-**2a**	99	96	99	91
10		(*S*,*R*)-**2b**	50	91	100	95
11		(*S*,*R*)-**2c**	73	90	99	86
12		(*S*,*R*)-**3**	88	92	100	59
13	 **7**	(*S*,*R*)-**2a**	**90**	**97**	92	76
14		(*S*,*R*)-**2b**	49	92	100	97
15		(*S*,*R*)-**2c**	91	76	100	55

[a] *Reaction conditions*: Catalyst precursor = $[M(COD)_2]BF_4$; $P(H_2)$ = 10 bar; at room temperature; reaction time = 24 h; solvent = CH_2Cl_2 (Ir); MeOH (Rh). [b] GC yield. [c] Determined by chiral capillary GC on a Chiralsil-Val column (25 m) and the product configuration by comparison with the literature values; *R* in all cases.

chemical yield. A generalized trend is not clearly observed among the same series **2a–c**, although **2c** seems to be the least effective in both Rh- and Ir-catalyses. The steric bulkiness of the arylimine (=N–Ar) also seems to play a minor role on yields and % ees as deduced from Table 1. Finally, decrease in the temperature below room temperature drastically reduces overall chemical yields although enantioselectivities rise a little in most cases.

Encouraged by the results shown in Table 1, we further pursued the asymmetric hydrogenation of 1,1-disubstituted alkenes such as 6-methoxy-1-methylene-1,2,3,4-tetrahydronaphthalene (**8**) and 2-(4-methoxyphenyl)-1-butene (**9**). Although one might expect facile conversion with this class of substrates as compared with sterically more hindered tri- or tetrasubstituted analogues, high asymmetric induction can hardly be anticipated due in part to the conformational freedom in the metal–olefin complex intermediates. The results in Table 2 seem to be consonant at least partially with this statement. Under the standard set of reaction conditions, the conversions are quantitative with Ir-catalysts with the degree of enantioselectivity depending on the nature of substrates or the ligands. Of four ligands employed, **2b** is the most powerful, giving 88 and 90% ee for the hydrogenation of **8** and **9**, respectively (entries 2 and 6). These results also compare well with the highest optical yield of 97% ee obtained with substrate **9**.[6c] Even more impressive are the very high % ees with Rh-catalysis reaching as high as 97% ee, although chemical yields are a little low in some cases (entries 2, 3 and 7). Yet the results are significant enough, in

Table 2 Asymmetric hydrogenation of disubstituted olefins[a]

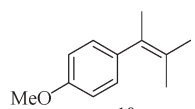
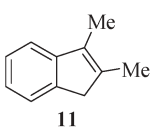
			Ir		Rh	
Entry	Substrate	Ligand	Yield[b] (%)	ee[c] (%)	Yield[b] (%)	ee[c] (%)
1	 **8**	(*S*,*R*)-**2a**	99	72	61	93
2		(*S*,*R*)-**2b**	99	88	7	94
3		(*S*,*R*)-**2c**	100	17	10	33
4		(*S*,*R*)-**3**	99	48	78	50
5	 **9**	(*S*,*R*)-**2a**	100	78	99	95
6		(*S*,*R*)-**2b**	**99**	**90**	**39**	**97**
7		(*S*,*R*)-**2c**	100	52	—	—
8		(*S*,*R*)-**3**	100	80	99	69

[a] Same reaction conditions as in Table 1. [b] GC yield. [c] Determined by chiral capillary GC on a Chiralsil-Val column (25 m) and the product configuration by comparison with the literature values; *R* in all cases.

that there are only a limited numbers of reports dealing with the Rh-catalyzed hydrogenation of disubstituted olefins, with enantioselectivity of 82% at best.[11]

We have further extended our investigation to the hydrogenation of tetrasubstituted olefins. They constitute an intriguing class of substrates in that they can potentially generate two adjacent chiral centers in one step.[6a] At the same time, they are generally the least reactive class of olefins in hydrogenation reactions; steric bulk hinders their ability to bind to most transition metal complexes. Understandably, there have appeared only two reports dealing with this class of olefins.[4a,5] Table 3 shows the results of asymmetric hydrogenations of 2-(4′-methoxyphenyl)-3-methylbut-2-ene (**10**) and 2,3-dimethyl-1*H*-indene (**11**). Expectedly chemical yields are rather lower than those obtained with other classes of substrates with the highest reaching 87% in the hydrogenation of **11** with **3a** (entry 7). The highest enantioselectivity of 88% ee is achieved with **2b** in the hydrogenation of **10**, yet with a low yield of 21% (entry 2). Again, an attempt to increase ee%'s by lowering the reaction temperature to RT was frustrated in that conversion is very slow. It is reported that an

Table 3 Asymmetric hydrogenation of tetrasubstituted olefins[a]

Entry	Substrate	Ligand	Yield[b] (%)	ee[c] (%)
1	 **10**	(*S*,*R*)-**2a**	54	52
2		(*S*,*R*)-**2b**	**21**	**88**
3		(*S*,*R*)-**2c**	56	76
4		(*S*,*R*)-**3**	41	64
5	 **11**	(*S*,*R*)-**2a**	72	53
6		(*S*,*R*)-**2b**	64	83
7		(*S*,*R*)-**3**	87	59

[a] *Reaction conditions*: Catalyst precursor = $[Ir(COD)_2]BF_4$; $P(H_2)$ = 10 bar; solvent = MeOH; at 45 °C; reaction time = 24 h. [b] GC yield. [c] Determined by chiral capillary GC on a Chiralsil-Val column (25 m).

Ir-phosphanodihydrooxazole catalyst gives 81% ee (>99% yield) from the hydrogenation of **10**,[4a] and that the (EBTHI)$ZrMe_2$ system gives 93% ee (86% yield).[5] All-in-all our ligands do not show any promise for practical applications to the tetrasubstituted olefins.

In summary, we have demonstrated that both cationic Ir- and Rh-complexes of chiral (iminophosphoranyl)ferrocenes are very powerful catalysts for asymmetric hydrogenation of a series of unfunctionalized di- and trisubstituted olefins. Also notable is that in some cases rhodium complexes may serve as even better practical catalysts than their iridium counterparts.

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Notes and references

† Typical procedure for asymmetric hydrogenation is as follows:[7] A solution of 0.5 mmol substrate and 2 mol% of pre-catalyst in 5 mL of CH_2Cl_2 (for Ir-catalysis) or MeOH (for Rh-catalysis) was stirred in an autoclave under 10 bar of hydrogen pressure for 24 h at RT. Work-up consisted of releasing the gas, evaporating the solvent, followed by extraction of the hydrogenated product with 3 mL of heptane (HPLC quality). The solution was applied directly to GC or HPLC for chemical and optical yield measurements.

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