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Synthesis and reactivity of cationic iridium(I) complexes of cycloocta-1,5-diene and chiral dithioether ligands. Application as catalyst precursors in asymmetric hydrogenation †

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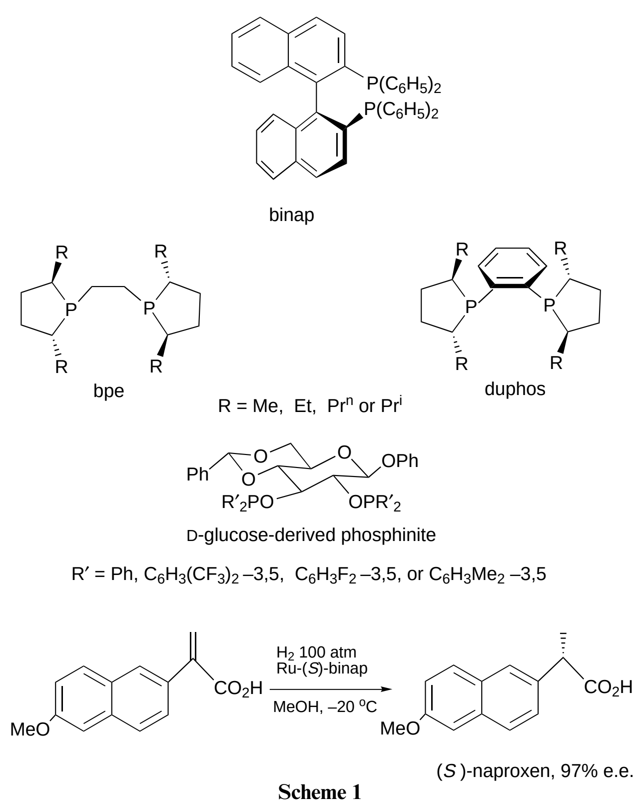
New chiral dithioether compounds (−)-2,2-dimethyl-4,5-bis(isopropylsulfanylmethyl)-1,3-dioxolane (−)-diospr and (+)-2,2-dimethyl-4,5-bis(phenylsulfanylmethyl)-1,3-dioxolane (+)-diosph were prepared from diethyl (+)-L-tartrate. An alternative synthetic method for preparing the previously described bis(methylsulfanylmethyl) dithioether (−)-diosme was devised. By co-ordinating of the dithioethers to different (cycloocta-1,5-diene)iridium(I) compounds chiral cationic complexes [Ir(cod){(−)-diosme}]BF_4 **1**, [Ir(cod){(−)-diospr}]$BF_4{\cdot}CH_2Cl_2$ **2** and [Ir(cod){(+)-diosph}]BF_4 **3** were synthesized and then studied by ^1H, ^{13}C NMR and FAB mass spectrometry. The complexes reacted with CO to give the corresponding binuclear tetracarbonyls [$Ir_2(\mu\text{-}L)_2(CO)_4$][$BF]_2$ **4-6**. The dithioether ligands were replaced by PPh_3 in **1**–**3** providing [Ir(cod)$(PPh_3)_2$]BF_4. The addition of H_2 to complexes **1** and **2** at −70 °C gave *cis*-dihydridoiridium(III) complexes [IrH_2(cod){(−)-L}]BF_4 **7** and **8** which are in equilibrium in solution with the parent complexes, depending on the temperature. Two possible diastereomers were distinguished for **8** at low temperatures. Complexes **1**–**3** were active precursors in the asymmetric hydrogenation of different prochiral dehydroamino acid derivatives and itaconic acid, at room temperature under an atmospheric pressure of H_2, and the highest enantiomeric excess obtained was 47%.

Iridium(I) complexes of cycloocta-1,5-diene (cod) are of interest because co-ordinated cod is readily replaced with other ligands. It can also be hydrogenated with H_2 to provide vacant co-ordination sites around iridium and increase the catalytic activities of the complexes.[1] Phosphorus ligands are mainly used, but several reports describe results obtained with sulfur compounds as ligands in homogeneous catalysis of reactions like hydrogenation[2–5] or hydroformylation[2,6] of olefins. In the last few years we have been studying the synthesis of new chiral dithioethers so that they can be applied to the asymmetric hydroformylation[6d,g] and hydrogenation of prochiral olefins. To the best of our knowledge, dithioether chiral ligands have only been used in the asymmetric hydrogenation of ketones with palladium complexes.[7]

Homogeneous asymmetric catalytic hydrogenation is one of the most important applications of enantioselective catalytic technologies[8–11] and there are considerable economic and ecological reasons for this.[12] Recently great progress has been made in this field and very high enatiomeric excess (e.e.) values have been achieved. Since the beginning of the 90's, Burk *et al.*[13] have been exploring novel electron-rich phospholane ligands (bpe and duphos derivatives) and RajanBabu *et al.*[14] have explored electron-rich phosphinite D-glucose-derived ligands that give powerful rhodium catalysts for the enantioselective hydrogenation of dehydroamino acids. They provide the most impressive results to date as far as intrinsic reactivity and enantioselectivity are concerned. Nevertheless, Ru–binap [binap = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl] complexes have been shown to be more versatile asymmetric hydrogenation catalysts than rhodium complexes for a series of unsaturated substrates.[9a,c] It should be noted that in the synthesis of (*S*)-naproxen using Ru–binap complexes both a low reaction temperature and a high hydrogen pressure are necessary to obtain a high enantiomeric excess,[9c,15] Scheme 1. For the synthesis to be applied in industry it would be desirable for the conditions to be smoother and the ligands more accessible. Iridium systems have been used less in asymmetric hydrogenation of prochiral olefins.[16]



Scheme 1

By taking the diop [4,5-bis(diphenylphosphinomethyl)-2,2-dimethyl-1,3-dioxolane] chiral structure as a model[17] and by modifying the known chiral dithiol diosh,[18] almost twenty years ago James and McMillan[3] prepared the methyl dithioether derivative (−)-diosme. Here, we report an alternative synthetic method to prepare (−)-diosme, the synthesis of new more

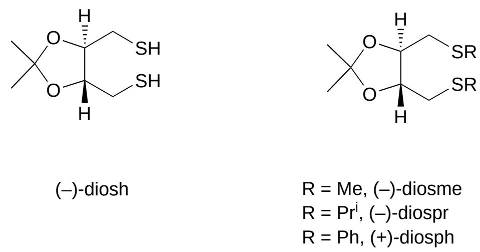
† *Non-SI unit employed*: atm = 101 325 Pa.

hindered chiral dithioethers (−)-diospr and (+)-diosph, and the preparation of cationic iridium(I) complexes with all three of these compounds, and their reactivity. We also examine the asymmetric hydrogenation of prochiral olefinic substrates by using the complexes as catalyst precursors at room temperature and atmospheric pressure of hydrogen.

Results and Discussion

Synthesis of the dithioethers

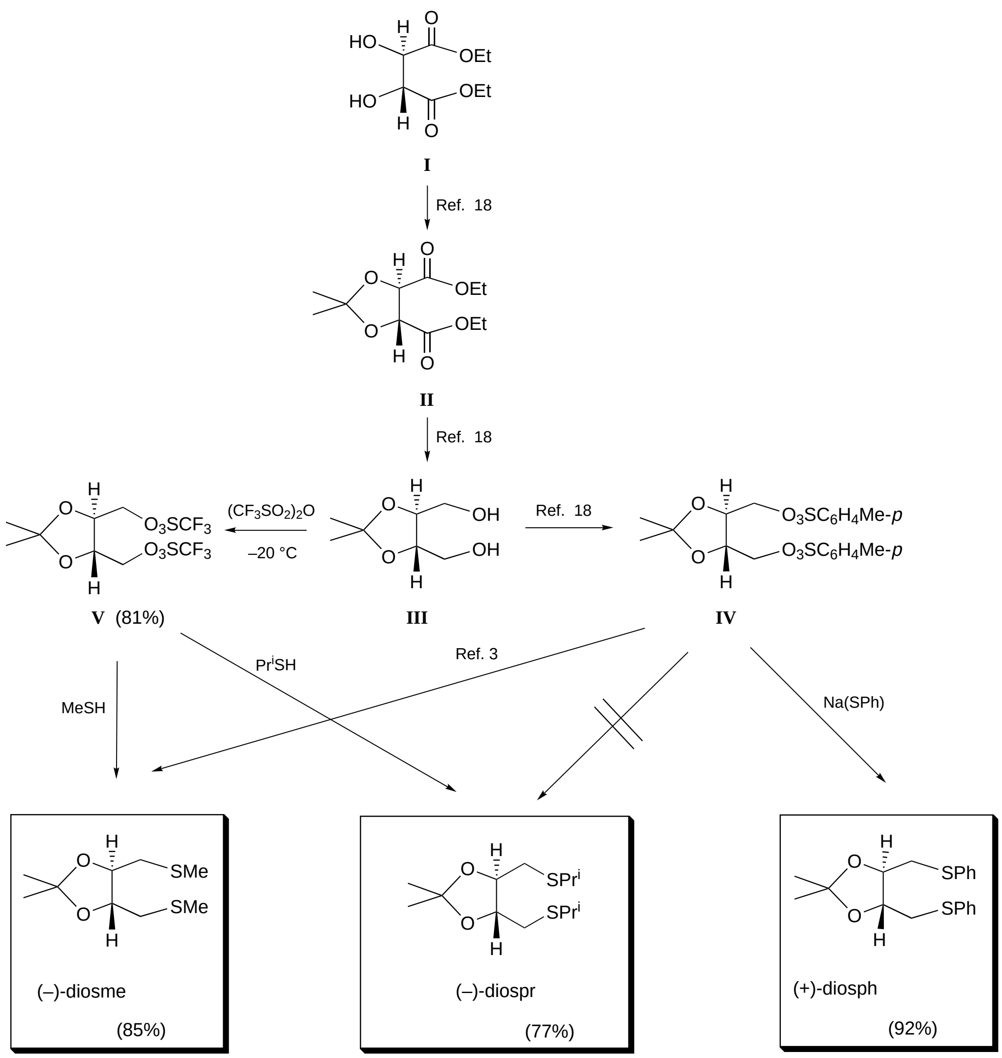
The new compounds (−)-diospr and (+)-diosph were prepared from diethyl (+)-L-tartrate, **I** (Scheme 2). The route to compounds **III** and **IV** follows previously described procedures.[18] For the preparation of (−)-diospr the diol **III** is converted into the ditriflate **V** by adding pyridine and triflic anhydride to a dichloromethane solution of **III**. The ditriflate was isolated as a white solid and characterised by elemental analyses and ^{1}H and ^{13}C NMR spectroscopy. The ^{13}C NMR spectrum shows a quadruplet at δ 118.6 ($^1J_{CF}$ = 320.2 Hz) which confirms the presence of a triflate group. The compound is stable for a few hours in air.



Treatment of compound **V** with NaH and propane-2-thiol in tetrahydrofuran (thf) affords (−)-diospr which was isolated as a colourless liquid. It is not stable in air at room temperature but at low temperature is stable for several days. It was not possible to prepare this dithioether from the ditosyl compound **IV** previously described.[18] Ditriflate **V** with a better leaving group, had to be prepared.

The dithioether diosph was prepared from the ditosyl compound **IV**. A dimethylformamide solution of **IV** was treated with benzenethiol in aqueous NaOH under reflux, to give diosph as a white solid in high yield. It is stable in the solid state. The dithioethers diospr and diosph were characterised by elemental analyses and ^{1}H and ^{13}C NMR spectroscopy.

The ^{1}H NMR spectra in $CDCl_3$ of (−)-diospr and (+)-diosph show a singlet due to the methyl protons at δ 1.41 and 1.40 respectively. The four methylenic protons CH_2S appear as an ABX system showing a multiplet at δ 2.80 and 3.20 and the two methinic protons CH also appear in an ABX system as a multiplet signal at δ 3.90 and 4.05 respectively. The ^{13}C NMR spectra also show only one signal for the tertiary and secondary carbon atoms for both compounds, in agreement with a C_2 symmetry. The ^{1}H NMR spectrum of (−)-diospr also shows a septuplet at δ 3.05 (J = 6.7 Hz) corresponding to the methinic protons of the isopropyl group and two doublets at δ 1.28 (J = 6.7) and 1.31 (J = 6.7 Hz) corresponding to the diastereotopic methyl protons of the isopropyl group. In the case of (+)-diosph the ^{1}H and ^{13}C NMR spectra also show signals from

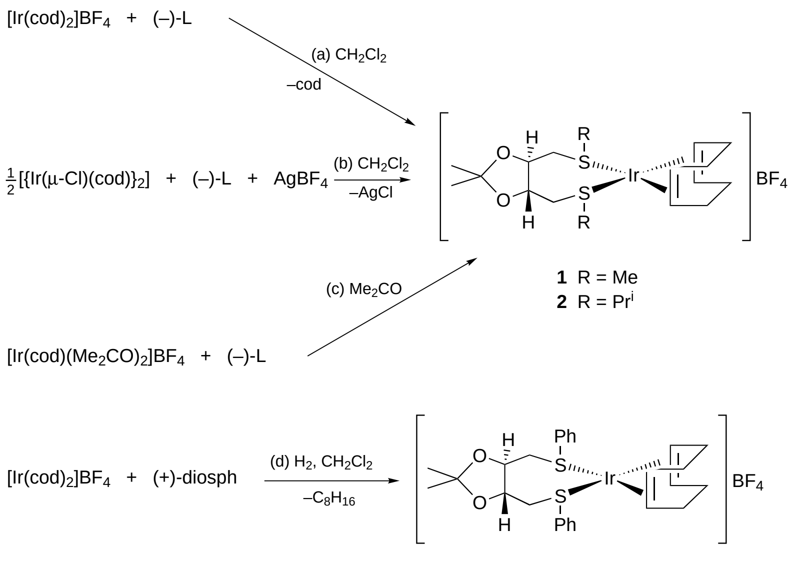


Scheme 2 Synthetic procedures for the preparation of (−)-diosme, (−)-diospr and (+)-diosph

Table 1 The NMR spectroscopic data for the dithioethers[a]

Compound	C*Me*	CH	CH_2	SCH	Me	SMe	Ph	*C*Me
^{1}H								
(−)-diosme	1.45(s)	4.05(m)	2.80(m)	—	—	2.20(s)	—	—
(−)-diospr	1.41(s)	3.90(m)	2.80(m)	3.05(sep)[b]	1.28(d)[c] 1.31(d)[d]	—	—	—
(+)-diosph	1.40(s)	4.05(m)	3.20(m)	—	—	—	7.15–7.35(m)	—
^{13}C								
(−)-diosme	27.2	79.6	36.8	—	—	16.5	—	109.0
(−)-diospr	27.1	79.9	33.2	35.3	23.2	—	—	108.9
(+)-diosph	27.3	79.0	37.0	—	—	—	126.3, 129.0 129.4, 135.6	109.7

[a] In $CDCl_3$ solvent. Chemical shifts in ppm with $SiMe_4$ as internal standard, coupling constants in Hz; room temperature. Abbreviations: s, singlet; m, multiplet; d, doublet; sep, septuplet. [b] $^{3}J_{HH}$ = 6.7 Hz. [c] $^{3}J_{HH}$ = 6.7 Hz. [d] $^{3}J_{HH}$ = 6.7 Hz.



Scheme 3 L = Chiral dithioether

the phenyl groups. The NMR signals for diospr and diosph were assigned using correlation spectroscopy (COSY) and heteronuclear correlation spectroscopy (HETCOR). The chemical shifts and coupling constants as well as those of diosme are listed in Table 1.

In this work, the methyl dithioether (−)-diosme was prepared using an alternative route to that described by James and McMillan.[3] This consisted of treating the ditriflate **V** with NaH and methanethiol (Scheme 2) and there was no need to prepare the dithiol derivative (−)-diosh, thus involving fewer steps and a greater yield.

Synthesis of the dithioether complexes

Olefinic complexes. [Ir(cod){(−)-diosme}]BF_4 **1**, [Ir(cod)-{(−)-diospr}]BF_4·CH_2Cl_2 **2** and [Ir(cod){(+)-diosph}]BF_4 **3**. In order to obtain chiral complexes, the chiral dithioethers were co-ordinated to $[Ir(cod)]^+$ fragments. Compounds **1** and **2** were obtained by the reactions (a)–(c) in Scheme 3 from different starting materials. It was only possible to obtain **3** by bubbling H_2 through a dichloromethane solution of $[Ir(cod)_2]BF_4$ and adding a stoichiometric amount of chiral diosph according to (d) in Scheme 3. The presence of cyclooctane formed from the hydrogenation of cycloocta-1,5-diene was observed in solution by ^{1}H NMR spectroscopy.

Complexes **1**–**3** were isolated by adding diethyl ether as yellow, orange and red-brown powders respectively. The elemental analysis matches the stoichiometry $[\{Ir(cod)L\}_n][BF_4]_n$ for **1** and **3** and $[\{Ir(cod)L\}_n][BF_4]_n \cdot nCH_2Cl_2$ for **2**. The FAB mass spectra show the heaviest ions at *m*/*z* 523 **1**, 579 **2** and 647 **3** which correspond to the loss of the BF_4^- anion from the molecular species. For complex **2** CH_2Cl_2 is also lost. This suggests that **1**–**3** are mononuclear complexes. The conductivity of their acetone solutions at different concentrations gives **A** values around 326 in Onsager's equation ($\Lambda_e = \Lambda_0 - Ac^{\frac{1}{2}}$) showing the mononuclear nature of the complexes (1 : 1 electrolytes) in acetone solution.[19]

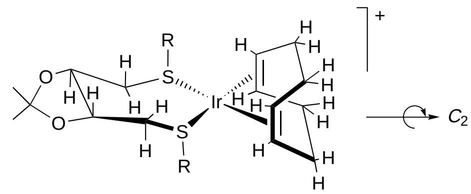


Fig. 1 Molecular symmetry of the cationic complexes $[Ir(cod)L]^+$

Complexes **1**–**3** exist in solution as cations with a C_2 molecular symmetry and with the two alkyl or aryl groups in *anti* position respectively as shown in Fig. 1. This follows from the analysis of NMR data (see Table 2), assigned using COSY and distortionless enhancement of polarisation transfer (DEPT) spectra in combination with a ^{13}C–^{1}H correlation (HETCOR). In particular for the signals from the dithioether ligands we can see that: (*i*) the two CH–O groups are equivalent, one signal being observed in the ^{1}H and ^{13}C NMR spectra in all cases; (*ii*) there is only one signal in ^{13}C NMR spectra for the two secondary carbons in the three complexes; for **1** and **2**, in the ^{1}H NMR spectra the diastereotopic methylenic protons appear as two double doublets which correspond to H_{ax} (J_{gem} *ca.* 12.3, $J_{ax\text{-}ax}$ *ca.* 10.3) and H_{eq} (J_{gem} *ca.* 12.3 and $J_{eq\text{-}ax}$ = 3.5 Hz) respectively; for **3** these methylenic protons appear as a multiplet at δ 3.5 which

Table 2 The NMR spectroscopic data for complexes **1**–**3**[a]

	cod		Dithioether							
Complex	CH_2	CH=CH	C*Me*	CH	CH_2	SCH	Me	SMe	Ph	C*Me*
^1H										
1[b]	1.85(m) 2.00(m) 2.35(m)	4.45(m)[c]	1.45(s)	4.30(m)	3.20(dd) H_{ax}[d] 3.35(dd) H_{eq}[e]	—	—	2.55 (s)	—	—
2[f]	1.75(m) 2.20(m) 2.40(m)	4.15(m) 4.60(m)	1.41(s)	4.68(m)	3.11(dd) H_{ax}[g] 3.45(dd) H_{eq}[j]	3.80(sep)[h]	1.31(d)[i] 1.55(d)[i]	—	—	—
3	1.70(m) 2.30(m)	3.90(m) 4.05(m)	1.35(s)	4.20(m)	3.50(m)	—	—	—	7.30–7.55 (m)	—
^{13}C										
1[b]	32.2 32.3	79.4 80.0	26.8	78.4	43.0	—	—	17.0	—	110.2
2	29.5 33.6	76.0 80.8	26.7	78.1	39.9	36.1	21.0 22.7	—	—	110.1
3[b]	31.1 31.2	79.4 79.6	26.8	78.1	40.3	—	—	—	128.2, 130.3 130.8, 131.1	111.0

[a] Chemical shifts in ppm with $SiMe_4$ as internal standard, coupling constant in Hz; room temperature; ^1H and ^{13}C NMR in $CDCl_3$. [b] In CD_2Cl_2 solvent. [c] $T = -40$ °C; δ 4.35(m) and 4.45(m). [d] $^2J_{gem} = 12.0$, $^3J_{ax\text{-}ax} = 10.0$ Hz. [e] $^2J_{gem} = 12.0$, $^3J_{eq\text{-}ax} = 3.5$ Hz. [f] δ 5.3 (CH_2Cl_2). [g] $^2J_{gem} = 12.6$, $^3J_{ax\text{-}ax} = 10.7$ Hz. [h] $^3J_{HH} = 6.5$ Hz. [i] $^3J_{HH} = 6.4$ Hz. [j] $^2J_{gem} = 12.6$, $^3J_{eq\text{-}ax} = 3.5$ Hz.

cannot be resolved by changing the temperature; (*iii*) the two MeS, Pr^{i}S and PhS groups are equivalent; thus, in the ^{13}C NMR spectra there is only one signal for the MeS groups, three for the Pr^i groups and four for the PhS groups.

The ^1H NMR spectra show the olefinic proton signals of the co-ordinated cyclooctadiene ligand as one multiplet for complex **1** and two multiplets for **2** and **3**. When the temperature is decreased to −40 °C, the olefinic protons for **1** also appear as two multiplets at δ 4.35 and 4.45 as expected for C_2 symmetry. For the *endo*- and *exo*-methylenic protons of cyclooctadiene four signals were expected but only three multiplets were observed for complexes **1** and **2** and two for **3**. The ^{13}C NMR spectra reveal two different olefinic and methylenic resonances for the three complexes which correspond to a C_2 symmetry.

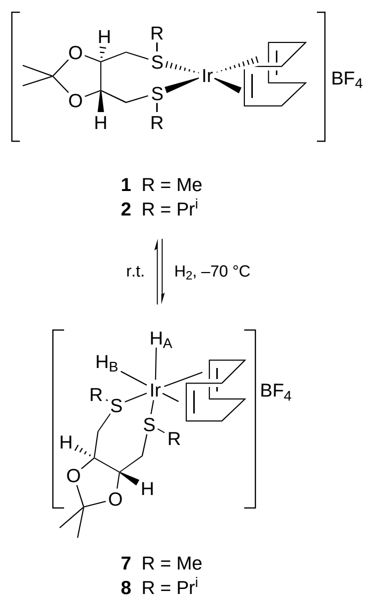
All the NMR data indicate that only one of two possible *anti* diastereomers can be distinguished for complexes **1**–**3**. When the temperature was changed from −60 to 40 °C no other diastereomers were observed in the ^{1} NMR spectra.

The C_2-related equivalencies within the dithioether ligands and the diolefin are consistent with the formulation of these complexes as square-planar four-co-ordinate cations, similar to related complexes containing chiral diphosphines, [Ir(cod){(−)-chiraphos}]$^+$ [(−)-chiraphos = (2*S*,3*S*)-2,3-bis(diphenylphosphino)butane] and [Ir(cod){(−)-norphos}]$^+$ {(−)-norphos = 2,3-bis(diphenylphosphino)bicyclo[2.2.1]heptane}.[20]

Reactivity of olefinic complexes

With carbon monoxide. Bubbling carbon monoxide through dichloromethane solutions of the diene complexes **1**–**3** yields carbonyl complexes $[\{IrL(CO)_2\}_n][BF_4]_n$ (R = Me **4**, Pr^i **5** or Ph **6**) which are formed by displacing the diene. The elemental analyses for **4** and **5** match the stoichiometry proposed. Complex **6** could not be isolated.

The nuclearity of complexes **4** and **5** was established by measuring their equivalent conductivity in acetone solutions at different concentrations. Plots of the Onsager equation gave *A* values around 890 which are characteristic of 2:1 electrolytes.[19] The Fourier-transform-IR spectra of the dichloromethane solutions of these tetracarbonyl complexes show three stretching frequencies υ(CO) in the 2100–1960 cm^{-1} region which are characteristic of dinuclear tetracarbonyl complexes of Ir^I and Rh^I.[19c,21] The ^1H NMR spectra of solutions of the complexes prepared '*in situ*' show signals which correspond to the co-ordinated dithioether ligands and the non-co-ordinated cyclooctadiene.

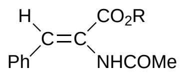


Scheme 4 r.t. = Room temperature

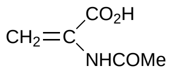
With PPh_3. The reaction of the diene complexes **1**–**3** with PPh_3 in a complex:PPh_3 molar ratio of 1:2 displaces the dithioether ligands and provides the previously prepared complex $[Ir(cod)(PPh_3)_2]BF_4$.[22]

With H_2. Hydridoiridium diolefin complexes are intermediates in the homogeneous hydrogenation of olefins.[16a] For this reason we believe that it is interesting to study the reactivity of the olefinic dithioether complexes synthesized with H_2.

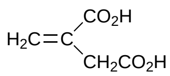
When H_2 is bubbled for 30 mins at −70 °C and at atmospheric pressure through CD_2Cl_2 solutions of olefinic iridium complexes **1** and **2**, dihydrido olefin complexes **7** and **8** are formed in solution, Scheme 4. In the high-field region of the ^1H NMR spectrum of the CD_2Cl_2 solution of **7** at −70 °C two metal hydride resonances at δ −12.88 and −13.18 which each integrate for one proton can be distinguished; one of the resonances is due to H_A and the other to H_B *cis* to each other and *trans* to the cyclooctadiene and thioether. Two close metal hydride signals can also be seen at very similar δ for the related complex *cis*-$[IrH_2(cod)(tht)_2]ClO_4$[23] (tht = tetrahydrothiophene). This may be due to the fact that the cod and thioether



VI R = H
VII R = Me



VIII



IX

ligands *trans* with respect to H_A and H_B have similar σ-donor and π-acceptor properties.[24]

In a CD_2Cl_2 solution of complex **8** at −70 °C four signals of two different intensities can be observed (relation 2:1) at δ −13.13, −14.78 and −13.29 and −15.00 which may be from two diastereomeric dihydridoiridium complexes. Two minor signals of not identified products are also observed. The related complex [Ir(cod)(diop)]PF_6 also adds hydrogen easily to give a *cis*-dihydrido olefin complex cation [IrH_2(cod)(diop)]PF_6[25] but the possible diastereomers were not distinguished, just as they were not for complex **7**. In the low-field region of the ^1H NMR spectra for CD_2Cl_2 solutions of **7** and **8**, there are signals corresponding to cyclooctadiene and dithioether ligands co-ordinated in the hydridoiridium(III) complexes, together with a small amount of starting material. When both complexes **7** and **8** are warmed hydrogen is partly lost and there is an increase in the amount of parent complexes. These complexes can be recovered in high yield by adding diethyl ether at room temperature. This indicates that the dihydridoiridium complexes in solution are in equilibrium with the parent complexes depending on the temperature, Scheme 4. The related olefinic dihydrido complexes [Ir(cod)L_2]PF_6 (L = $PMePh_2$, PPh_3, $\frac{1}{2}Ph_2PCH_2$-CH_2PPh_2, PBu^n_3 or $\frac{1}{2}$diop) also have similar behaviour.[25]

The nature of these hydrido ligands was confirmed by measuring T_1 using ^1H relaxation rates.[26a] The hydride resonances have T_1 values of 211 and 288 ms for complex **7** and 180 and 200 and 178 and 227 ms for the major and minor diastereoisomers of **8** respectively, in CD_2Cl_2 at −70 °C and 300 MHz. These values are consistent with classical hydride.[26]

When diethyl ether is added to CD_2Cl_2 solutions of *cis*-[IrH_2(cod){(−)-diosme}]BF_4 **7** at −70 °C a yellow powder is obtained. The elemental analysis matches this stoichiometry. The Fourier-transform-IR spectrum in KBr and Nujol mull shows a broad signal at 2013 cm^{-1} which may include the two asymmetric absorption bands, ν(Ir–H), expected for a *cis*-dihydridoiridium(III) compound.[27] The situation is similar for the related complex *cis*-[IrH_2(cod)(dth)]ClO_4 (dth = 2,6-dithiaheptane).[23]

As far as the reactivity of [Ir(cod){(+)-diosph}]BF_4 **3** with H_2 is concerned, when this gas is bubbled through a CD_2Cl_2 solution for 30 min at −70 °C broad signals appear between δ −12.5 and −16.5 in the high-field region of the ^1H NMR spectrum. When the temperature is gradually increased from −70 to 15 °C the signal at δ −15.9 disappears and the other resonances resolve into four narrower signals which may correspond to different diastereomers of *cis*-[IrH_2(cod){(+)-diosph}]BF_4 which are not rigid on the proton NMR time-scale. Likewise, when it is warmed to 28 °C, hydrogen is partly lost, as it is for complexes **7** and **8**. The hydride resonances at −70, −40, 0 and 15 °C have T_1 values in CD_2Cl_2 of around 300 ms at 300 Hz, consistent with classical hydride.[26]

Catalytic activity

Asymmetric hydrogenation of prochiral olefins. To explore how the iridium dithioether complexes **1**–**3** behave as catalyst precursors, we initially studied the asymmetric hydrogenation of prochiral olefins *Z*-α-(acetamido)cinnamic acid **VI**, methyl α-(acetamido)cinnamate **VII**, α-(acetamido)acrylic acid **VIII** and itaconic acid (methylenebutanedioic acid) **IX** at room temperature under atmospheric pressure of H_2. The three iridium complexes **1**–**3** lead to active systems for the asymmetric hydrogenation of prochiral olefins **VI**–**IX**. The best results are shown in Table 3.

Table 3 Hydrogenation results with catalytic systems **1**–**3**[a]

Entry	Precursor	Substrate	*t*/h	Conversion (%)	e.e. (%)
1	**2**	**VI**	16	96	37(*R*)
2	**3**	**VI**	16	99	16(*R*)
3	**3**	**VII**	48	50	13(*R*)[b]
4	**2**	**VIII**	16	91	11(*S*)
5	**3**	**VIII**	12	100	10(*S*)
6	**1**	**IX**	24	100	22(*S*)[b]
7	**2**	**IX**	6	91	47(*S*)[b]
8	**3**	**IX**	4	100	6(*S*)[b]

[a] At 20 °C and 1 atm H_2. Solvent 6 cm^3 CH_2Cl_2. Substrate : precursor = 40 : 1. [b] Determined by polarimetry.

For the hydrogenation of compound **VI** the most active systems are **2** and **3** (entries 1, 2) which have similar activity, but the e.e. is higher (37% *R*) for precursor **1**. All the systems lead to the (*R*) enantiomer of *N*-acetylphenylalanine, as does the rhodium–(*R*,*R*)-diop system.[17] It is well known that polar solvents can considerably affect the activity observed in the asymmetric hydrogenation of prochiral olefins. However, for the hydrogenation of **VI** using the catalytic system **1**, experiments in CH_2Cl_2 (99% conversion in 24 h) and MeOH (6% conversion in 48 h) reveal that the activity in CH_2Cl_2 is higher.

The hydrogenation of compound **VII** with the catalytic systems **1**–**3**, proceeds very slowly achieving conversions between 6 and 50% in 48 h with low enantioselectivity [11% (*R*) with **1** and 13% (*R*) with **3**, entry 3]. The steric bulk of the methyl group probably makes the co-ordination of the prochiral olefin somewhat difficult. When **2** is used as the catalytic system the very low activity could be attributed to the methyl group in the olefin together with the isopropyl group in the catalytic system. The previously described iridium system [Ir(cod)(nmdpp)-(PhCN)]$^+$ [nmdpp = (−)-neomenthyldiphenylphosphine] also gives very low activity when hydrogenating **VII**.[16b,c]

Compound **VIII** was hydrogenated with catalytic systems **2** and **3** (entries 4, 5) at a comparable rate to **VI** but the enantioselectivity is lower. Compound **IX** is reduced with catalytic systems **2** and **3** (entries 7, 8) considerably faster than the other unsaturated compounds. For complex **2** a conversion of 91% is achieved in 6 h together with an e.e. of 47% (*S*), which is the highest e.e. obtained.

In general, although hydrogenation with complexes **1**–**3** takes place under ambient conditions of pressure and temperature the e.e. are low. The e.e. obtained with catalytic system **2** is higher than those with **1** and **3**, perhaps due to the greater hindrance and rigidity of the Pr^i group. These catalytic systems are more active but less enantioselective than related rhodium–chiral thiolate systems previously reported[5c–e] for the asymmetric hydrogenation of the prochiral olefins cited. However **1**–**3** are more active, and **2** is also more enantioselective, than related ruthenium–chiral sulfoxide systems for the hydrogenation of itaconic acid.[3]

As is well known, hydrogen pressure can have a considerable effect on the stereoselectivity of the asymmetric hydrogenation of prochiral olefins.[28] Studies at higher pressures are in progress.

Experimental

Elemental analyses were carried out with a Carlo-Erba microanalyzer. Infrared spectra were recorded on a Midac Grams/386 spectrophotometer, ^1H and ^{13}C NMR spectra on a Varian Gemini 300 MHz spectrometer. Proton T_1 studies were performed using the standard inversion recovery 180°–τ–90° pulse sequence.[26a] Fast atom bombardment mass spectrometry was performed on a VG autospect in a 3-nitrobenzyl alcohol matrix. Conductivities were measured in acetone solutions at several concentrations in the range 10^{-3}–10^{-5} M, with a Philips PW9509 conductimeter. Gas chromatography analyses were performed with a Hewlett-Packard 5890A instrument (fused-silica capillary column 25 m × 0.25 mm permabond L-Chirasil-Val). Optical rotations were determined with a Perkin-Elmer 241 MC polarimeter at the indicated temperature. The specific rotation is given in deg cm^3 g^{-1} dm^{-1} units. All synthesis of iridium complexes and dithioethers were carried out under nitrogen using standard Schlenk techniques. Solvents were distilled and deoxygenated before use. The indium compounds [{Ir(μ-Cl)(cod)}$_2$],[29] [Ir(cod)$_2$]BF_4[22] and [{Ir(μ-OMe)(cod)}$_2$][30] were prepared by the general procedures described.

Syntheses

diosme. A suspension of NaH (2.30 g, 95 mmol) in paraffin, cleaned twice in hexane, in thf (14 cm^3) was cooled to −78 °C and methanethiol (2 cm^3, 36 mmol) at −78 °C was added. The resulting solution was stirred and the temperature increased to 0 °C. After 5 min the solution was cooled and a solution of compound **V** (1 g, 2 mmol) in thf (9 cm^3) added. After 45 min the solvent was evaporated and water (100 cm^3) was added to the residue which was extracted with dichloromethane (3 × 50 cm^3). The extract was then dried and concentrated. The residue was purified by column chromatography (hexane–ethyl acetate 5:1) and the required compound was obtained (0.44 g, 85%) as a colourless liquid: $[\alpha]_D^{23} = -6.06$ (*c* 3.2 in $CHCl_3$) (Found: C, 49.00; H, 8.06; S, 2.91. Calc. for $C_9H_{18}O_2S_2$: C, 48.60; H, 8.16; S, 2.88%).

diospr. A solution of propane-2-thiol (0.2 cm^3, 2.30 mmol) in thf (2 cm^3) was added to a suspension of NaH (78 mg, 3.25 mmol) in paraffin, cleaned twice in hexane, in thf (1 cm^3). The resulting solution was stirred for 20 min. Then a solution of compound **V** (330 mg, 0.77 mmol) in thf (3 cm^3) was added. After 45 min the solvent was evaporated and water (50 cm^3) was added to the residue which was extracted with dichloromethane (3 × 50 cm^3). The extract was then dried and concentrated. The residue was purified by column chromatography (hexane–ethyl acetate 20:1) and the required compound was obtained (162 mg, 77%) as a colourless liquid: $[\alpha]_D^{23} = -7.58$ (*c* 3.2 in $CHCl_3$) (Found: C, 55.51; H, 9.9; S, 22.49. Calc. for $C_{13}H_{26}O_2S_2$: C, 56.07; H, 9.4; S, 23.02%).

diosph. Benzenethiol (3.3 cm^3, 32.3 mmol) was added to a solution of NaOH (1.27 g, 32 mmol) in water (12 cm^3). The resulting solution was stirred for 2 h. Then a solution of compound **IV** (5 g, 10.63 mmol) in dimethylformamide was added. The resulting solution was stirred under reflux for 24 h. The solvent was evaporated and water (100 cm^3) was added to the residue which was extracted with diethyl ether (3 × 50 cm^3). The extract was then dried and concentrated. The residue was purified by column chromatography (hexane–ethyl acetate 20:1) and the required compound was obtained (3.4 g, 92%) as a white solid: $[\alpha]_D^{23} = +45$ (*c* 3.2 in $CHCl_3$) (Found: C, 65.39; H, 6.44; S, 18.00. Calc. for $C_{19}H_{22}O_2S_2$: C, 65.86; H, 6.39; S, 18.50%).

Compound V. Pyridine (0.76 cm^3, 9.5 mmol) was added to a solution of compound **III** (0.57 g, 3.5 mmol) in dichloromethane (21 cm^3). The resulting solution was stirred for 10 min. Then it was cooled to −20 °C and triflic anhydride $(CF_3SO_2)_2O$ (1.4 cm^3, 8.3 mmol) was slowly added. After 25 min TLC (hexane–ethyl acetate 3:2) showed that the reaction was complete. The solvents were evaporated under vacuum and the residue was purified by column chromatography (hexane–ethyl acetate 5:1) and the required compound was obtained (1.68 g, 81%) as a white solid: $[\alpha]_D^{23} = -8.13$ (*c* 3.2 in $CHCl_3$) (Found: C, 24.86; H, 2.91; S, 15.53. Calc. for $C_9H_{12}F_6O_8S_2$: C, 25.36; H, 2.84; S, 15.04%); δ_H(300 MHz, $CDCl_3$, $SiMe_4$) 1.46 (6 H, s, CMe_2), 4.23 (2 H, m, CH) and 4.55 (4 H, m, CH_2); δ_C(74.5 MHz, $CDCl_3$) 26.2 (C*Me*$_2$), 73.5 (CH_2), 74.1 (CH), 111.9 (*C*Me_2) and 118.6 (q, CF_3, $J_{CF} = 320.2$ Hz).

[Ir(cod){(−)-diosme}]BF$_4$ 1. The compound was prepared by the following three routes.

(*i*) Addition of an excess of (−)-diosme (23 mg, 0.11 mmol) to a dichloromethane solution (3 cm^3) of [Ir(cod)$_2$]BF_4 (40 mg, 0.08 mmol) produced an immediate colour change. Subsequent addition of ether precipitated the desired complex, which was filtered off, washed with cold ether and vacuum dried (34.3 mg, 70%).

(*ii*) Adding an excess of (−)-diosme (40 mg, 0.18 mmol) and the stoichiometric amount of $AgBF_4$ (23 mg, 0.12 mmol) to a dichloromethane solution (3 cm^3) of [{Ir(μ-Cl)(cod)}$_2$] (40 mg, 0.05 mmol) produced a white precipitate of silver chloride, which was filtered off through Kieselguhr. Addition of ether to the filtrate precipitated the required complex, which was filtered off, washed with cold ether and vacuum dried (38.0 mg, 50%).

(*iii*) An acetone solution (10 cm^3) of [Ir(cod)(Me_2CO)$_2$]BF_4 was prepared by treating [{Ir(μ-OMe)(cod)}$_2$] (66 mg, 0.10 mmol) with a solution of tetrafluorobic acid (54%) in diethyl ether (60 cm^3, 0.20 mmol). The resulting solution was stirred for 30 min and was added to a solution of (−)-diosme (44 mg, 0.22 mmol) in acetone (5 cm^3). The orange solution formed was stirred for 30 min. The desired complex was precipitated by adding ether and then filtered off, washed with cold ether and vacuum dried, (79.0 mg, 81%) (Found: C, 32.98; H, 4.98; S, 10.35. Calc. for $C_{17}H_{30}BF_4IrO_2S_2$: C, 33.49; H, 4.96; S, 10.52%); *m*/*z* 523 (M^+).

[Ir(cod){(−)-diospr}]BF$_4$·CH$_2$Cl$_2$ 2. The compound was prepared by the following two routes.

(*i*) Addition of an excess of (−)-diospr (33 mg, 0.12 mmol) to a dichloromethane solution (3 cm^3) of [Ir(cod)$_2$]BF_4 (40 mg, 0.08 mmol) produced an immediate colour change. Subsequent addition of ether precipitated the desired complex, which was filtered off, washed with cold ether and vacuum dried (42.0 mg, 79%).

(*ii*) Addition of an excess of (−)-diospr (54 mg, 0.19 mmol) and the stoichiometric amount of $AgBF_4$ (23 mg, 0.12 mmol) to a dichloromethane solution (3 cm^3) of [{Ir(μ-Cl)(cod)}$_2$] (40 mg, 0.05 mmol) produced a white precipitate of silver chloride, which was filtered off through Kieselguhr. Addition of ether to the filtrate precipitated the required complex which was filtered off, washed with cold ether and vacuum dried (43.0 mg, 54%) (Found: C, 35.46; H, 5.25; S, 8.65. Calc. for $C_{21}H_{38}BF_4IrO_2S_2$: C, 35.69; H, 5.44; S, 8.66%); *m*/*z* 579 (M^+).

[Ir(cod){(+)-diosph}]BF$_4$ 3. An excess of (+)-diosph (41 mg, 0.12 mmol) was added to a dichloromethane solution (3 cm^3) of [Ir(cod)$_2$]BF_4 (40 mg, 0.08 mmol). Then hydrogen was bubbled through for 15 min producing a change in colour. Subsequent addition of ether precipitated the desired complex, which was filtered off, washed with cold ether and vacuum dried (40.0 mg, 67%) (Found: C, 32.98; H, 4.98; S, 10.35. Calc. for $C_{27}H_{34}BF_4IrO_2S_2$: C, 33.49; H, 4.96; S, 10.52%); *m*/*z* 647 (M^+).

[Ir$_2${μ-(−)-diosme}$_2$(CO)$_4$][BF$_4$]$_2$ 4. Carbon monoxide was bubbled through a dichloromethane solution (6 cm^3) of the complex [Ir(cod){(−)-diosme}]BF_4 (40 mg, 0.065 mmol). After 5 min the starting solution lightened. Cold ether was added to give the desired compound, which was filtered off, washed with cold ether and vacuum dried (13.7 mg, 60%) (Found: C, 24.20; H, 3.40; S, 10.70. Calc. for $C_{11}H_{18}BF_4IrO_4S_2$: C, 23.70; H, 3.25; S, 11.50%); ν_{max}/cm^{-1} (CO) 2067s, 2021s and 1997s.

[Ir$_2${μ-(−)-diospr}$_2$(CO)$_4$][BF$_4$]$_2$ 5. Carbon monoxide was bubbled through a dichloromethane solution (6 cm^3) of the complex [Ir(cod){(−)-diospr}]BF_4 (40 mg, 0.060 mmol). After 5 min the starting solution lightened. Addition of cold ether gave the desired compound, which was filtered off, washed with cold ether and vacuum dried (28.1 mg, 61%) (Found: C, 26.02; H, 3.69; S, 8.96. Calc. for $C_{15}H_{26}BF_4IrO_4S_2\cdot 0.5CH_2Cl_2$: C, 25.79; H, 3.75; S, 9.18%); ν_{max}/cm^{-1} (CO) 2079s, 2021s and 1996s.

[Ir_2{μ-(+)-diosph}$_2(CO)_4$][BF_4]$_2$ 6. Carbon monoxide was bubbled through a dichloromethane solution (6 cm^3) of the complex [Ir(cod){(+)-diosph}]BF_4 (40 mg, 0.055 mmol). After 5 min the starting solution lightened. The final compound could not be isolated. ν_{max}/cm^{-1} (CO) 2054m, 2020s and 1994s.

[IrH_2(cod){(−)-diosme}]BF_4 7. Hydrogen was bubbled through a brown-orange solution of [Ir(cod){(−)-diosme}]BF_4 (40 mg, 0.065 mmol) in CD_2Cl_2 (0.4 cm^3) at −70 °C for 30 min. Addition of diethyl ether at −70 °C gave a yellow powder (Found: C, 33.38; H, 5.26; S, 10.26. Calc. for $C_{17}H_{32}BF_4IrO_2S_2$: C, 33.39; H, 5.27; S, 10.48%); δ_H(300 MHz, CD_2Cl_2, −70 °C) −12.88 (1 H, s) and −13.18 (1 H, s); ν_{max}/cm^{-1} (Ir–H) 2013 (br).

[IrH_2(cod){(−)-diospr}]BF_4 8. Hydrogen was bubbled through a brown-orange solution of [Ir(cod){(−)-diospr}]BF_4 (40 mg, 0.060 mmol) in CD_2Cl_2 (0.4 cm^3) at −70 °C for 30 min. The solution was then transferred to an NMR spectrometer tube and the ^1H NMR spectrum was recorded (see text for ^1H NMR data and characterisation).

Catalytic hydrogenations

The reactions under 1 atm of H_2 were performed in a previously described hydrogen-vacuum line.[31] In a typical run, substrate (100 mg) and catalyst precursor, dissolved in dichloromethane (6 cm^3), were shaken under H_2 (1 atm) at 293 K. After the required time the solvent was removed. The extent of conversion was measured by ^1H NMR spectroscopy.

Work-up of the hydrogenation product. The following procedures was used to isolate the hydrogenation product. A; for *N*-acetylalanine, the residue was dissolved in water and separated from the insoluble catalyst by filtration. Evaporation to dryness afforded the product. B; for methylsuccinic acid, *N*-acetylphenylalanine and *N*-acetylphenylalanine methyl ester, the residue was dissolved in 0.5 M NaOH and separated from the insoluble catalyst by filtration. The filtrate was acidified with dilute HCl, extracted with ether, and washed with a little water. The ether phase was dried over sodium sulfate and evaporated to dryness. C; for *N*-acetylphenylalanine, *N*-acetylphenylanine methyl ester and *N*-acetylalanine, gas chromatography analyses were performed with a Hewlett-Packard 5890A instrument (fused-silica capillary column 25 m × 0.25 mm, permabond L-Chirasil-Val) before treating the sample as described.[32] A 0.5 g amount of the residue was heated for 1 h at 100 °C with 6 M HCl (10 cm^3). Then the solvent was evaporated and Pr^iOH (10 cm^3) in 6% HCl was added. The resulting solution was stirred at 90 °C during 1.5 h. The reagent was evaporated and the residue dissolved in dichloromethane (2.5 cm^3) and pentafluoropropionic anhydride (0.3 cm^3). This solution was stirred for 1 h at room temperature. Then the solvent was evaporated and the residue dissolved in acetone (0.3 cm^3) and analysed by gas chromatography.

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References

1 C. S. Chin and B. Lee, *J. Chem. Soc., Dalton Trans.*, 1991, 1323 and refs. therein.
2 C. Claver and A. M. Masdeu, *Trends Organomet. Chem.*, 1994, **1**, 549 and refs. therein.
3 B. R. James and R. S. McMillan, *Can. J. Chem.*, 1977, **55**, 3927.
4 J. Solé, C. Bo, C. Claver and A. Ruiz, *J. Mol. Catal.*, 1990, **61**, 163; C. K. Lai, A. A. Naiini and C. H. Brubaker, jun., *Inorg. Chim. Acta*, 1989, **164**, 205; A. A. Naiini, H. M. Ali and C. H. Brubaker, jun., *J. Mol. Catal.*, 1991, **67**, 47 and refs. therein.
5 (*a*) Ph. Kalck, R. Poilblanc, R. P. Martin, A. Rovera and A. Gaset, *J. Organomet. Chem.*, 1980, **195**, C9; (*b*) H. Schumann, H. Hemling, N. Goren and J. Blum, *J. Organomet. Chem.*, 1995, **485**, 209; (*c*) M. Eisen, P. Weitz, S. Shtelzer, J. Blum, H. Schumann, B. Gorella and F. H. Görlitz, *Inorg. Chim. Acta*, 1991, **188**, 167; (*d*) H. Schumann, B. Gorella, M. Eisen and J. Blum, *J. Organomet. Chem.*, 1991, **412**, 251; (*e*) M. Eisen, J. Blum, H. Schumann and B. Gorella, *J. Mol. Catal.*, 1989, **56**, 329.
6 (*a*) Ph. Kalck, in *Organometallics in Organic Synthesis*, eds. A. de Meijere and H. tom Dieck, Springer, Heidelberg, 1987, pp. 297–320; (*b*) S. Gladiali, J. C. Bayón and C. Claver, *Tetrahedron Asymmetry*, 1995, **6**, 1453 and refs. therein; (*c*) F. Agbossou, J. F. Carpentier and A. Mortreux, *Chem. Rev.*, 1995, **85**, 2485; (*d*) C. Claver, S. Castillón, N. Ruiz, G. Delogu, D. Fabbri and S. Gladiali, *J. Chem. Soc., Chem. Commun.*, 1993, 1833; (*e*) A. M. Masdeu, A. Orejón, A. Ruiz, S. Castillón and C. Claver, *J. Mol. Catal.*, 1994, **94**, 149; (*f*) A. Castellanos-Paéz, S. Castillón and C. Claver, *J. Organomet. Chem.*, 1997, **539**, 1; (*g*) A. Aaliti, N. Ruiz, J. Forniés, A. Ruiz, C. Claver, C. J. Cardin, D. Fabbri and S. Gladiali, *J. Organomet. Chem.*, in the press.
7 F. Fache, P. Gamez, F. Nour and M. Lemaire, *J. Mol. Catal.*, 1993, **85**, 131.
8 H. B. Kagan, in *Comprehensive Organometallic Chemistry*, eds. G. Wilkinson, F. G. A. Stone and E. W. Abel, Pergamon, Oxford, 1982, vol. 8, ch. 53; H. Takaya, T. Onta and R. Noyori, in *Catalytic Asymmetric Synthesis*, ed. I. Ojima, VCH, New York, 1993, ch. 1; R. Noyori, in *Asymmetric Catalysis in Organic Synthesis*, Wiley, New York, 1994, ch. 2, p. 16; J. M. Brown, *Chem. Soc. Rev.*, 1993, 25; H. Brunner, in *Top. Stereochem.*, 1988, **18**, 129; J. M. Brown, in *Insights into Speciality Inorganic Chemicals*, ed. D. Thompson, The Royal Society of Chemistry, Cambridge, 1995, ch. 6.
9 (*a*) S. Akutagawa, in *Asymmetric Hydrogenation with Ru–BINAP: Chirality in Industry*, eds. A. N. Collins, G. N. Sheldrake and J. Crosby, Wiley, Chichester, 1992, p. 325; (*b*) S. Akutagawa, in *Asymmetric Hydrogenation with Ru–BINAP: Catalysis of Organic Reactions*, eds. M. Scaros and M. L. Prunier, Marcel Dekker, New York, 1994, p. 135; (*c*) S. Akutagawa, *Appl. Catal. A, Gen.*, 1995, **128**, 171.
10 *Asymmetric Synthesis*, ed. J. D. Morrison, Academic Press, New York, 1985, vol. 5; R. Noyori, *Science*, 1990, **245**, 1194; W. S. Knowles, *Acc. Chem. Res.*, 1983, **16**, 106; *Asymmetric Catalysis*, Maryinus Nijhoff, Boston, MA, 1984; J. M. Brown, *Nature (London)*, 1991, **350**, 191.
11 W. S. Knowles, *J. Chem. Educ.*, 1986, **63**, 222.
12 W. A. Nugent, T. V. RajanBabu and M. J. Burk, *Science*, 1993, **259**, 479; G. M. Ramos Tombo and D. Bellus, *Angew Chem., Int. Ed. Engl.*, 1991, **30**, 1193; J. Alberecht and U. Nagel, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 407.
13 M. J. Burk, J. E. Feaster and R. L. Harlow, *Organometallics*, 1990, **9**, 2653; M. J. Burk, J. E. Feaster, W. A. Nugent and R. L. Harlow, *J. Am. Chem. Soc.*, 1993, **115**, 10 125.
14 T. V. RajanBabu, T. A. Ayers and A. L. Caslnuovo, *J. Am. Chem. Soc.*, 1994, **116**, 4101.
15 T. Ohta, H. Takaya, M. Kitamura, K. Nagai and R. Noyori, *J. Org. Chem.*, 1987, **52**, 3174.
16 (*a*) P. A. Chaloner, M. A. Esteruelas, F. Joó and L. A. Oro, in *Homogeneous Hydrogenation*, Kluwer, Dordrecht, 1994, ch. 4; (*b*) L. A. Oro, J. A. Cabeza, C. Cativiela, M. D. Díaz de Villegas and E. Meléndez, *J. Chem. Soc., Chem. Commun.*, 1983, 1383; (*c*) J. A. Cabeza, C. Cativiela, M. D. Díaz de Villegas and L. A. Oro, *J. Chem. Soc., Perkin Trans. 1*, 1988, 1881.
17 H. B. Kagan and T. P. Dang, *J. Am. Chem. Soc.*, 1972, **94**, 6429.
18 M. Carmack and C. J. Kelley, *J. Org. Chem.*, 1969, **33**, 2171.
19 R. D. Feltham and R. G. Hayter, *J. Chem. Soc.*, 1964, 4587; R. Uson, J. Gimeno, J. Fornies and F. Martínez, *Inorg. Chim. Acta*, 1981, **50**, 173; A. Ruiz, C. Claver, J. C. Rodríguez, M. Aguiló, X. Solans and M. Font-Altaba, *J. Chem. Soc., Dalton Trans.*, 1984, 2665.
20 W. J. Hälg, L. R. Öhrström, H. Rüeggh, L. M. Venanzi, T. Gerfin and V. Gramlich, *Helv. Chim. Acta*, 1993, **76**, 788.

21 Ph. Kalck and R. Poilblanc, *Inorg. Chem.*, 1975, **14**, 2779; J. C. Rodriguez, A. Ruiz and C. Claver, *Transition Met. Chem.*, 1984, **9**, 237.
22 M. Green, T. A. Kuc and H. Taylor, *J. Chem. Soc. A*, 1971, 2334.
23 J. C. Rodriguez, C. Claver and A. Ruiz, *J. Organomet Chem.*, 1985, **293**, 115.
24 D. Sellmann, H.-P. Neumer and F. Knoch, *Inorg. Chim. Acta*, 1991, **190**, 61.
25 R. H. Crabtree, H. Felkin, T. Fillebeen-Khan and G. E. Morris, *J. Organomet. Chem.*, 1979, **168**, 183.
26 (*a*) D. G. Hamilton and R. H. Crabtree, *J. Am. Chem. Soc.*, 1988, **110**, 4126; (*b*) J. C. Lee, jun., W. Yao and R. H. Crabtree, *Inorg. Chem.*, 1996, **35**, 695.
27 K. Nakamoto, in *Infrared and Raman Spectra of Inorganic and Coordination Compounds*, Wiley, New York, 1978.
28 I. Ojima, T. Kogure and N. Yoda, *J. Org. Chem.*, 1980, **45**, 4728.
29 J. L. Herde, J. C. Lambert and C. V. Senoff, *Inorg. Synth.*, 1974, **15**, 18.
30 J. Chatt and J. M. Davidson, *J. Chem. Soc. A*, 1965, 843.
31 C. Cativiela, J. Fernandez, J. A. Mayoral, E. Melendez, R. Usón, L. A. Oro and M. J. Fernandez, *J. Mol. Catal.*, 1992, **16**, 19.
32 H. Frank, C. J. Nickolson and E. Bayer, *J. Chromatogr. Sci.*, 1977, **15**, 174.

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