ELSEVIER

Journal of Molecular Catalysis A: Chemical 196 (2003) 27–38

JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL

www.elsevier.com/locate/molcata

Binaphthalene-templated N,S- and N,P-heterobidentate ligands with an achiral oxazoline pendant Synthesis and assessment in asymmetric catalysis

Serafino Gladiali*, Giovanni Loriga, Serenella Medici, Rossana Taras

Dipartimento di Chimica, Università di Sassari, Via Vienna 2, 07100 Sassari, Italy

Received 17 June 2002; accepted 10 October 2002

Abstract

Novel chiral binaphthalene-core ligands where an oxazoline pendant is flanked by a sulfur **6**, or by an atropisomeric phosphite donor **5**, have been synthesized using the hydroxy binaphthyl oxazoline **7** as the common starting material. This intermediate is obtained in high e.e. by Ni-catalyzed asymmetric heterocoupling of two suitably 1,2-disubstituted naphthalene derivatives. Ligands **5** and **6** feature a stereogenic axis as the unique source of chirality. They display chelate binding towards Rh(I) centres affording cationic complexes which have been inspected for their catalytic activity in several asymmetric reactions with modest success. The Pd catalyst derived from the sulfur-containing oxazoline **6a** provides up to 66% e.e. in the allylic alkylation of 1,3-diphenylallyl esters with dimethyl malonate.

Keywords: Binaphthyl oxazoline ligands; Axial chirality; N,X-heterodonor ligands; Rh(I) complexes; Pd-catalyzed allylic alkylation

1. Introduction

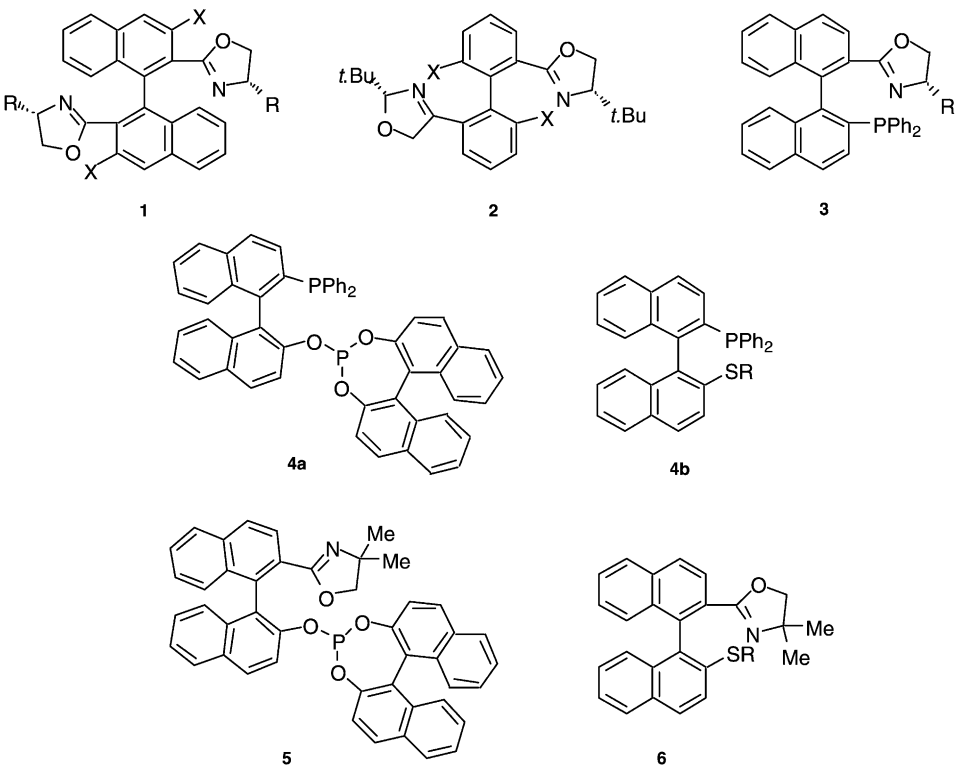
Chiral oxazoline ligands enjoy a widespread diffusion in the field of transition metal-catalyzed asymmetric reactions. Given that most of these ligands originate from a chiral aminoalcohol, the source of chirality in the large majority of them resides exclusively in the stereogenic carbon adjacent to the nitrogen within the heterocyclic ring. Some of these derivatives, however, combine in their structures diverse chiral elements, such as stereogenic axes or planes or heteroatoms, in the place of (or in addition to) the stereogenic carbon(s) of the oxazoline fragment.

A few atropisomeric oxazoline ligands derived from axially chiral templates have been developed in the last decade. The C_2 symmetry binaphthyl and biphenyl derivatives **1** (X = H) and **2** (X = Me), respectively (Scheme 1), featuring three stereogenic elements of the same notation (two centres and one axis), are chiral inducers of high efficiency in stereoselective catalysis. The Cu(I) complex derived from (*R*,*R*,*R*)-**2** (X = Me) was successfully used for addressing in 90% e.e. the enantioselective intramolecular cyclopropanation reaction required in the key step of the asymmetric synthesis of (−)-sirenin [1].

Ligand **1** provides remarkably high e.e. in the Cu(I)-catalyzed asymmetric cyclopropanation of olefins [2] and in the Pd(II)-catalyzed Wacker-type cyclization of *o*-allylphenols [3]. In the latter reaction, comparable results have been recorded on a variety of different substrates with the 3,3′-disubstituted

* Corresponding author. Tel.: +39-079-229-546; fax: +39-079-229-559/212-069.
E-mail address: gladiali@uniss.it (S. Gladiali).

1381-1169/02/$ – see front matter
PII: S1381-1169(02)00632-5



Scheme 1.

bisoxazolines analogues of **1** (X ≠ H) featuring a stereogenic axis as the unique chiral element [4]. Good to excellent e.e. have been obtained as well in the Cu(I)-catalyzed asymmetric cyclopropanation of styrene even when the axially chiral diaryl scaffold is configurationally labile as in the case of the bisoxazolines **2** where X = H [5].

In the course of the last 5 years, the synthesis of binaphthyl P,X-heterodonor ligands has been a hot topic which has attracted much attention from the groups active in the area of asymmetric catalysis [6]. This interest was basically the result of the excellent perfomances displayed by (*R*,*S*)-BINAPHOS **4a** in the Rh-catalyzed hydroformylation of olefins [7]. The phosphino-oxazolines **3** were among the most desired targets of the researchers working in this field and their preparation was simultaneously accomplished by two independent teams separately [8]. The (*S*,*aR*)-diastereoisomer of **3** performed quite well in the Pd(II)-catalyzed asymmetric allylic alkylation of 1,3-diphenylallyl acetate with dimethyl malonate where over 95% e.e. was recorded [8].

The high stereoselectivities provided by the binaphthalene-templated oxazoline ligands **1** and **3** reported above prompted us to design novel binaphthyl derivatives where an achiral oxazoline pendant is flanked either by an axially chiral phosphite, as in **5**, or by an alkylsulfide substituent, as in **6**. Compounds **5** and **6** are closely related to the known ligands BINAPHOS **4a** and BINAPS **4b** [9], respectively, from which they can be formally derived by exchanging the oxazoline for the diphenylphosphino substituent. This structural relationship was sought in the aim to compare the behaviour of nitrogen versus phosphorus as a donor in the relevant chelate complexes with the purpose to obtain some useful insights in the modeling of chiral modifiers for suitable transition metal catalysts.

The chelating P,N-heterodonor ligand **5** arising from the combination of the oxazoline nitrogen with a strong π-acidic P-donor has one very encouraging precedent in asymmetric catalysis [10]. Furthermore,

it offers the chance to exploit the matching–mismatching interplay of axial chiralities for addressing the stereoselectivity of the reaction.

A few chiral N,S-heterodonor ligands capable of good efficiency in asymmetric catalysis have been reported in the literature [11]. No one of them features a stereogenic axis as the unique chiral source [11e].[1]

Here we like to report on the preparation of the new ligands **5** and **6** as well as on synthesis and characterization of the relevant cationic Rh(I) complexes and on their applications in asymmetric catalysis.

2. Experimental

2.1. General procedures

All reactions were carried out under a dry nitrogen or argon atmosphere using standard Schlenk techniques unless otherwise specified. Commercial chemicals (Aldrich) were used as received. Solvents were dried by standard procedures and stored under nitrogen. ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded on a Varian VXR-300 spectrometer. Chemical shifts are in parts per million relative to TMS and were referenced by use of the residual solvent signal (^{1}H and ^{13}C NMR spectra) and a capillary containing 85% H_3PO_4. Gas chromatographic analyses were performed using a Hewlett-Packard 5890/A gas chromatograph equipped with a HP 3396 integrator on a 25 m × 0.25 mm capillary column coated with diethyl-*t*-butylsilyl-β-cyclodextrin. Optical rotations were measured on a Perkin-Elmer Model 241 polarimeter. Melting points were obtained with a Leitz Laborlux S melting point apparatus and are not corrected. Elemental analyses were performed with a Perkin-Elmer Analyzer 240B by Mr. A. Canu (Dipartimento di Chimica, Universita' di Sassari).

Compounds **7**–**9** have been prepared following the procedures of Wilson and Cram detailed in [13].

2.1.1. (S)-2′-[2-(4,4-Dimethyl-Δ^2-oxazolinyl)]-1,1′-binaphth-2-ol (**10**)

To a solution of (*S*)-methoxy-2′-[2-(4,4-dimethyl-Δ^2-oxazolinyl)]-1,1′-binaphthyl (**9**) (8 g, 21 mmol) in CH_2Cl_2 (150 ml), cooled at 0 °C, BBr_3 (10.5 g, 42 mmol) was added. The color of the solution immediately changed from pale yellow to dark green. The mixture was stirred at 0 °C for 3 h, then at the same temperature cold 1% KOH (200 ml) was added. The aqueous solution was extracted with CH_2Cl_2, the combined organic layers dried over Na_2SO_4 and the solvent evaporated to give the pure product as a white solid (7.65 g, quantitative yield). A sample of analytical purity was obtained by flash chromatography.

$[\alpha]_D^{25} = -62$ ($c = 1$, THF); mp: 220 °C. ^{1}H NMR ($CDCl_3$) δ (ppm): 0.88 (s, 3H, CH_3), 1.14 (s, 3H, CH_3), 3.75 (dd, AB system, $J = 8.7$ Hz, 2H, CH_2), 6.77 (d, $J = 8.7$ Hz, 1H, Ar), 7.08–8.20 (series of m, 11H, Ar). Anal. Calcd. for $C_{25}H_{21}NO_2$ (367.44): C, 81.72; H, 5.76; N, 3.81. Found: C, 81.26; H, 5.70; N, 3.34.

2.1.2. (S)-2′-[2-(4,4-Dimethyl-Δ^2-oxazolinyl)]-1,1′-binaphth-2-ol N,N-dimethylamino thiocarbamate (**12**)

NaH (233 mg, 9.7 mmol) was added to a solution of **10** (2.1 g, 5.7 mmol) in DMF (20 ml), cooled at 0 °C. The reaction mixture was stirred for 1 h at RT, then *N*,*N*-dimethylaminothiocarbamoylchloride (742 mg, 6 mmol) was added, and the solution heated at 85 °C and stirred at the same temperature for 6 h. The mixture was allowed to warm to RT and poured into 1% KOH (300 ml). The solid thus obtained was filtered, dissolved in CH_2Cl_2, and dried over Na_2SO_4. The solvent was evaporated and the crude product was crystallized (CH_2Cl_2/MeOH) to obtain 1.60 g of an orange solid (65% yield).

$[\alpha]_D^{25} = +22.3$ ($c = 1$, THF); mp: 203–207 °C. ^{1}H NMR ($CDCl_3$) δ (ppm): 1.03 (s, 3H, C–CH_3), 1.18 (s, 3H, C–CH_3), 2.63 (s, 3H, N–CH_3), 3.06 (s, 3H, N–CH_3), 3.48 (dd, AB system, $J = 8.0$ Hz, 2H, CH_2), 7.16–7.51 (series of m, Ar, 6H), 7.57 (d, $J = 8.8$ Hz, Ar, 1H), 7.89–8.04 (series of m, Ar, 5H). Anal. Calcd. for $C_{28}H_{26}N_2O_2S$ (454.58): C, 73.98; H, 5.76; N 6.16. Found: C, 73.95; H, 5.58; N, 6.21.

2.1.3. (S)-2′-[2-(4,4-Dimethyl-Δ^2-oxazolinyl)]-1,1′-binaphthalene-2-thiol N,N-dimethylamino carbamate (**13**)

In the flask of a Büchi distillation apparatus **12** (2 g, 4.4 mmol) was heated at 280 °C for 17 min.

[1] In the biphenyl sulfur oxazolines reported by Ikeda and coworkers a stereogenic carbon is always associated to the chiral axis.

After cooling to RT, the brown solid was dissolved in CH_2Cl_2, and purified by flash chromatography (light petroleum/acetone 4:1) to give the pure product as a pale yellow solid (1.14 g, 57% yield).

$[\alpha]_D^{25} = -35.4$ ($c = 1$, $CHCl_3$); mp: 77 °C. ^{1}H NMR ($CDCl_3$) δ (ppm): 0.94 (s, 3H, C–CH_3), 1.10 (s, 3H, C–CH_3), 2.70 (bs, 3H, N–CH_3), 2.82 (bs, 3H, N–CH_3), 3.43 (dd, AB system, $J = 7.8$ Hz, 2H, CH_2), 7.08 (d, $J = 8.3$ Hz, Ar, 1H), 7.19–7.50 (series of m, Ar, 5H), 7.75 (d, $J = 8.7$ Hz, Ar, 1H), 7.87–8.03 (series of m, Ar, 5H). Anal. Calcd. for $C_{28}H_{26}N_2O_2S$ (454.58): C, 73.98; H, 5.76; N, 6.16. Found: C, 73.61; H, 5.50; N, 6.08.

*2.1.4. (S)-2′-[2-(4,4-Dimethyl-Δ^2-oxazolinyl)]-1,1′-binaphthalene-2-thiol (**14**)*

To a solution of **13** (500 mg, 1.10 mmol) in THF (7 ml) and MeOH (2 ml), a solution of KOH (105 mg, 1.87 mmol) in MeOH (2 ml) was added dropwise via syringe. The reaction mixture was heated at reflux temperature for 4.5 h, then the solvents were evaporated. Water (10 ml) was added and the solution neutralized. After extraction with CH_2Cl_2 the combined organic layers were dried (Na_2SO_4) and the solvent evaporated, to obtain 300 mg of an orange solid (71% yield).

Melting point: 82 °C decomposition. ^{1}H NMR ($CDCl_3$) δ (ppm): 0.94 (s, 3H, C–CH_3), 1.10 (s, 3H, C–CH_3), 3.32 (d, AB system, $J = 8.1$ Hz, 1H, CH_2), 3.57 (d, $J = 8.1$ Hz, 1H, CH_2), 6.99–8.05 (series of m, 12H). Anal. Calcd. for $C_{25}H_{21}NOS$ (383.51): C, 78.30; H, 5.52; N, 3.65. Found: C, 77.88; H, 5.50; N, 3.35.

*2.1.5. (S)-2-Methylthio-2′-[2-(4,4-dimethyl-Δ^2-oxazolinyl)]-1,1′-binaphthalene (**6a**)*

To a solution of **14** (650 mg, 1.69 mmol) in MeOH (20 ml) containing Et_3N (0.47 ml, 3.39 mmol), methyl iodide (0.12 ml, 1.86 mmol) was added. The reaction mixture was stirred at RT for 16 h. The solvent was evaporated and the residue was dissolved in CH_2Cl_2. The organic phase was washed with water and dried (Na_2SO_4). The solvent was evaporated and the crude was purified by flash chromatography (light petroleum/ethyl acetate 2:1) to give 440 mg of pure product (60% yield).

$[\alpha]_D^{25} = -42.2$ ($c = 0.5$, THF); mp: 78–80 °C. ^{1}H NMR ($CDCl_3$) δ (ppm): 0.89 (s, 3H, C–CH_3), 1.06 (s, 3H, C–CH_3), 2.39 (s, 3H, S–CH_3), 3.26 (d, AB system, $J = 7.8$ Hz, 1H, CH_2), 3.56 (d, $J = 7.8$ Hz, 1H, CH_2), 7.04 (d, $J = 8.4$ Hz, Ar, 1H), 7.21–7.54 (series of m, Ar, 6H), 7.57 (d, $J = 8.8$ Hz, Ar, 1H), 7.84–8.04 (series of m, Ar, 4H). Anal. Calcd. for $C_{26}H_{23}NOS$ (397.53): C, 78.55; H, 5.83; N, 3.52. Found: C, 78.65; H, 5.91; N, 3.50.

*2.1.6. (S)-2-iso-Propylthio-2′-[2-(4,4-Dimethyl-Δ^2-oxazolinyl)]-1,1′-binaphthalene (**6b**)*

To a solution of **14** (700 mg, 1.82 mmol) in MeOH (20 ml) containing Et_3N (364 mg, 3.65 mmol), iso-propyl iodide (388 mg, 2.28 mmol) was added. The reaction mixture was stirred for at RT 24 h, then the solvent was evaporated and the residue dissolved in CH_2Cl_2. The organic phase was washed with water, dried over Na_2SO_4 and the solvent removed under vacuum. The crude product was purified by flash chromatography (light petroleum/ethyl acetate 1:1) to give 320 mg of a yellow solid (41% yield).

$[\alpha]_D^{25} = -124.1$ ($c = 0.5$, THF); mp: 66–68 °C. ^{1}H NMR ($CDCl_3$) δ (ppm): 0.83 (s, 3H, C–CH_3), 1.06 (s, 3H, C–CH_3), 1.12 (d, $J = 6.9$ Hz, 3H, S–CH–CH_3), 1.17 (d, $J = 6.9$ Hz, 3H, S–CH–CH_3), 3.32 (d, AX system, $J = 7.8$ Hz, 1H, CH_2), 3.50 (sept, $J = 8.1$ Hz, S–CH, 1H), 3.54 (d, AX system, $J = 8.1$ Hz, 1H, CH_2) 7.04 (d, $J = 7.8$ Hz, Ar, 1H),7.16–7.54 (series of m, Ar, 6H), 7.63 (d, $J = 8.7$ Hz, Ar, 1H), 7.82–8.09 (series of m, Ar, 4H). Anal. Calcd. for $C_{28}H_{27}NOS$ (425.59): C, 79.02; H, 6.39; N, 3.29. Found: C, 79.12; H, 6.28; N, 3.15.

*2.1.7. Synthesis of ligand [(R,S)-**5**]*

To a solution of (*R*)-binaphthyl chlorophosphite **11** (490 mg, 1.41 mmol) in toluene (10 ml) cooled at −40 °C, a solution of (*S*)-(**2**) (500 mg, 1.36 mmol) in THF (5 ml) and Et_3N (0.19 ml, 1.36 mmol) was added. The reaction mixture was stirred for 12 h at RT, then the precipitate was filtered and the filtrate was evaporated. The crude material was purified by flash chromatography (CH_2Cl_2/ethyl acetate 10:1) to give the product as a yellow solid (520 mg, 56% yield).

$[\alpha]_D^{25} = -16.5$ ($c = 1$, THF); mp: 122–124 °C. ^{1}H NMR ($CDCl_3$) δ (ppm): 0.88 (s, 3H, CH_3), 1.02 (s, 3H, CH_3), 3.25 (d, AX system, $J = 8.1$ Hz, 1H, CH_2), 3.62 (d, AX system, $J = 7.8$ Hz, 1H, CH_2), 5.62 (d, $J = 9.0$ Hz, Ar, 1H), 7.13–8.22 (series of m,

Ar, 23H). ^{31}P NMR ($CDCl_3$) δ (ppm): 147.6 (s). Anal. Calcd. for $C_{45}H_{32}NO_4P$ (681.71): C, 79.28; H, 4.73; N, 2.05. Found: C, 79.08; H, 4.58; N, 2.10.

2.1.8. Synthesis of ligand [(S,S)-5]

To a solution of (*S*)-binaphthyl chlorophosphite **11** (490 mg, 1.41 mmol) in toluene (10 ml) cooled at −40 °C, a solution of (*S*)-(**2**) (500 mg, 1.36 mmol) in THF (5 ml) and Et_3N (0.19 ml, 1.36 mmol) were added. The reaction mixture was stirred for 26 h at RT, then elaborated as before. The crude material was purified by flash chromatography (CH_2Cl_2/ethyl acetate 10:1) to give 50 mg of pure product (5.4% yield).

$[\alpha]_D^{25} = 73.9$ ($c = 1$, THF). ^{1}H NMR ($CDCl_3$) δ (ppm): 0.91 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 3.19 (d, AB system, $J = 8.1$ Hz, 1H, CH_2), 3.50 (d, $J = 8.1$ Hz, 1H, CH_2), 6.42 (d, $J = 8.7$ Hz, Ar, 1H), 7.15–8.24 (series of m, Ar, 23H). ^{31}P NMR ($CDCl_3$) δ (ppm): 145.6 (s). Anal. Calcd. for $C_{45}H_{32}NO_4P$ (681.71): C, 79.28; H, 4.73; N 2.05. Found: C, 79.12; H, 4.61; N, 2.00.

*2.1.9. Synthesis of [(**6a**)Rh(nbd)]$^+BF_4^-$ (**15**)*

To a solution of $[Rh(nbd)Cl]_2$ (181 mg, 0.39 mmol) in THF (10 ml) $AgBF_4$ (152 mg, 0.78 mmol) was added. After stirring 30 min, the suspension was filtered through Celite and ligand **6a** (311 mg, 0.78 mmol) was added. The solution turned from yellow to brilliant orange. After stirring for 2 h at RT, the solvent was evaporated, the residue was washed with ether and crystallized (CH_2Cl_2–ether) to give the pure product as an orange solid (235 mg, 45% yield).

Melting point: 210 °C decomposition. ^{1}H NMR ($CDCl_3$) δ (ppm): 0.67 (s, 3H, CH_3), 1.20 (s, 3H, CH_3), 1.33 (s, 2H, nbd–CH_2), 2.13 (s, 3H, S–CH_3), 3.23 (d, AX system, $J = 8.7$ Hz, 1H, CH_2), 3.85 (bs, 2H, nbd–CH), 3.96 (bs, 2H, nbd–CH), 4.01 (d, AX system, $J = 8.4$ Hz, 1H, CH_2), 4.33 (bs, 2H, nbd–CH), 6.96 (d, $J = 8.4$ Hz, Ar, 1H), 7.06 (d, $J = 8.4$ Hz, Ar, 1H), 7.32 (dt, $J = 6.9$ Hz, $J = 0.9$ Hz, Ar, 1H), 7.39 (dt, $J = 7.5$ Hz, $J = 0.8$ Hz, Ar, 1H), 7.55 (t, $J = 7.8$ Hz, Ar, 1H), 7.67 (t, $J = 7.2$ Hz, Ar, 1H), 7.68 (d, $J = 8.4$ Hz, 1H), 7.94 (d, $J = 8.4$ Hz, Ar, 1H), 8.10 (d, $J = 8.4$ Hz, Ar, 1H), 8.17 (d, $J = 8.4$ Hz, Ar, 1H), 8.26 (d, $J = 8.4$ Hz, Ar, 1H), 8.47 (d, $J = 8.4$ Hz, Ar, 1H). Anal. Calcd. for $C_{35}H_{30}BF_4NORhS$ (678.38): C, 58.43; H, 4.46; N 2.06. Found: C, 58.20; H, 4.62; N, 2.03.

2.1.10. Synthesis of [((R,S)-5)Rh(nbd)]$^+BF_4^-$ [(R,S)-16]

To a solution of $[Rh(nbd)Cl]_2$ (34 mg, 7,4 mmol) in CH_2Cl_2 (15 ml), the ligand (*R*,*S*)-**5** (100 mg, 14.8 mmol) was added. The solution was stirred 1 h, then $AgBF_4$ (28.6 mg, 14.8 mmol) was added and the reaction mixture stirred further 12 h at RT The suspension was filtered through Celite and the filtrate was evaporated. The residue was washed with ether and then crystallized (CH_2Cl_2–ether) to give the pure product as a yellow solid (50 mg, 36% yield).

Melting point: 230 °C decomposition. ^{1}H NMR ($CDCl_3$) δ (ppm): 0.72 (s, 2H), 1.35 (bm, 2H), 1.51 (s, 3H, CH_3), 1.70 (bm, 2H), 2.35 (s, 3H, CH_3), 3.22 (d, AX system, $J = 8.7$ Hz, 1H, CH_2), 3.60 (bm, 2H), 4.19 (d, AX system, $J = 7.8$ Hz, 1H, CH_2), 6.76–8.43 (series of m, Ar, 24H). ^{31}P NMR ($CDCl_3$) δ (ppm): 129.09 (d, $J_{Rh\text{-}P} = 306.0$ Hz). Anal. Calcd. for $C_{52}H_{40}BF_4NO_4RhS$ (964.67): C, 64.75; H, 4.18; N, 1.45. Found: C, 64.62; H, 4.08; N, 1.25.

2.1.11. Synthesis of [((S,S)-5)Rh(nbd)]$^+BF_4^-$ [(S,S)-16]

Following the procedure reported above, 17 mg of $[Rh(nbd)Cl]_2$ (3.7 mmol) and 50 mg of ligand (*S*,*S*)-**5** (7.4 mmol) gave 18 mg of complex [(*S*,*S*)-**16**] (25% yield).

^{1}H NMR ($CDCl_3$) δ (ppm): 1.04 (s, 2H), 1.21 (s, 3H, CH_3), 1.26 (bm, 2H), 1.56 (s, 3H, CH_3), 1.90 (bm, 2H), 3.50 (d, AX system, $J = 6.6$ Hz, 1H, CH_2), 3.99 (bm, 2H), 4.15 (d, AX system, $J = 6.9$ Hz, 1H, CH_2), 5.54 (d, $J = 6.6$, Ar, 1H) 6.91–8.35 (series of m, Ar, 21H), 8.75 (d, $J = 6.0$ Hz, Ar, 1H), 8.84 (d, $J = 6.0$ Hz, Ar, 1H). ^{31}P NMR ($CDCl_3$) δ (ppm): 118.86 (d, $J_{Rh\text{-}P} = 299.6$ Hz). Anal. Calcd. for $C_{52}H_{40}BF_4NO_4RhS$ (964.67): C, 64.75; H, 4.18; N, 1.45. Found: C, 64.71; H, 4.09; N, 1.48.

2.2. Hydroformylation of styrene

In a typical experiment the suitable complex (0.008 mmol) and styrene (8 mmol) were dissolved in benzene (2 ml) under argon. The solution was transferred into a 100 cm^3 autoclave and pressurized by $CO/H_2 = 1{:}1$ mixture to 80 bar. The reaction mixture was stirred in an oil bath heated at the required temperature. At the end of the reaction the autoclave was cooled to room temperature, vented

and the solution was immediately analyzed. Conversions, chemo-, regio- and enantio-selectivities were determined by gaschromatographic analysis: initial temperature: 60 °C; heating rate: 2 °C/min; final temperature: 150 °C. Retention times: branched aldehyde, 21 min (*S*), 21.5 min (*R*); linear aldehyde, 26.7 min.

2.3. Hydroboration of styrene

Styrene (156 mg, 1.5 mmol) was added to a solution of the suitable complex (0.03 mmol) in THF (2 ml). The solution was stirred for 5 min and then catecholborane (180 mg, 1.5 mmol) was added. Stirring was continued at room temperature for 12 h, then the reaction mixture was quenched with EtOH (0.4 ml). NaOH (2 ml, 2 M in H_2O) and H_2O_2 (0.2 ml) were added and the mixture was stirred for 10 h. The reaction mixture was extracted with Et_2O, washed (2 M NaOH, H_2O, brine) and dried over Na_2SO_4. Conversions, regioselectivity and the e.e. were determined by gaschromatographic analysis at 105 °C. Retention times: 13.8 min (*R*)-phenylethanol; 14.8 min (*S*)-phenylethanol; 14.1 min 2-phenylethanol.

2.4. Hydrogenation of methyl acetamidoacrylate

Methyl acetamidoacrylate (143 mg, 1 mmol) and the suitable complex (0.01 mmol) were placed in a pressure bottle. The flask was purged with nitrogen, the solvent (benzene/methanol 1:1, 10 ml) was added by syringe through a serum cap and the bottle was connected to the hydrogen reservoir of a Parr mid-pressure apparatus. The nitrogen was evacuated and purged twice with hydrogen. Then hydrogen (2 bar) was admitted into the bottle and the reaction mixture was shaken for 16 h at RT.

Conversions and e.e. of methyl alaninate were determined by GC analysis operated at 95 °C using He (60 kPa) as the carrier. Retention times: substrate, 13.7 min; (*S*)-methyl alaninate, 14.8 min; (*R*)-methyl alaninate 19.1 min.

2.5. Reduction of acetophenone via hydrogen transfer

A solution of complex **15** (4.7 mg, 0.007 mmol) and KOH (0.5 M in *i*PrOH, 0.1 ml) in *i*PrOH (11 ml) was heated at reflux temperature for 1 h. A solution of acetophenone (0.41 ml, 3.5 mmol) in *i*PrOH (11 ml) was then added to the resulting yellow solution.

Yield, conversion and e.e. were determined by GC analysis operated at the following conditions: initial temperature: 60 °C (3 min); heating rate: 3 °C/min; final temperature: 150 °C. Retention times: acetophenone, 10.5 min; (*R*)-carbinol, 24.0 min; (*S*)-carbinol, 24.5 min.

2.6. Allylic alkylation of 1,3-diphenylallyl acetate with dimethyl malonate

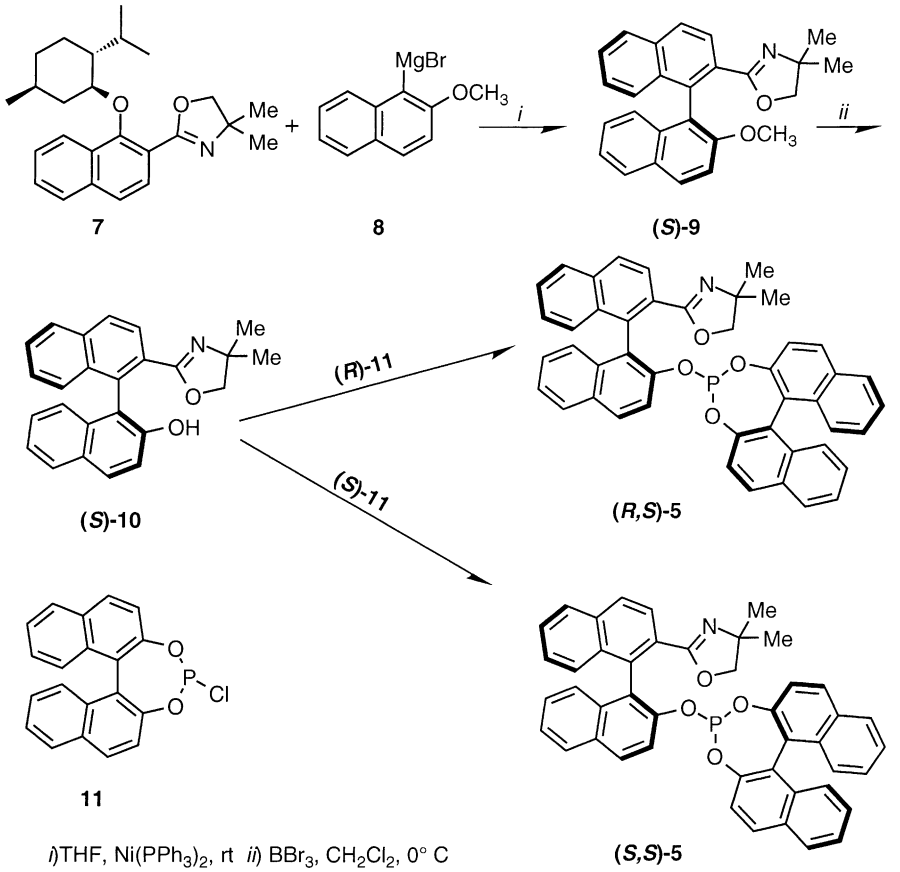
A solution of $[Pd(h^3\text{-}C_3H_5)Cl]_2$ (2.2 mg, 0.006 mmol) and the free ligand (0.02 mmol) in CH_2Cl_2 (1 ml) was stirred at RT under nitrogen. After 30 min a solution of 1,3-diphenylprop-2-enyl acetate (50 mg, 0.2 mmol) in CH_2Cl_2 (0.5 ml) was added. Dimethyl malonate (80 mg, 0.6 mmol), *N*,*O*-bis(trimethylsilyl)-acetamide (BSA) (122 mg, 0.6 mmol) and potassium acetate (0.6 mg, 0.006 mmol) dissolved in CH_2Cl_2 (3.5 ml) were added to the reaction mixture via syringe. Stirring was continued at the required temperature until complete conversion was attained. The reaction mixture was diluted with ether (25 ml) and washed with saturated NH_4Cl. The organic phase was dried (Na_2SO_4), concentrated under reduced pressure and the residue purified by flash chromatography (light petroleum/ether, 3:1) to give dimethyl[(*S*)-1,3-diphenylprop-2-enyl]malonate.

The e.e. were determined from the integrals of the methoxy groups of (1,3-diphenylprop-2-enyl)-malonate, as split by the chiral shift reagent europium tris[3-(trifluoromethylhydroxymethylene)-(+)-camphorate].

3. Results and discussion

3.1. Synthesis of the ligands

The preparation of 2,2′-unsymmetrically disubstituted 1,1′-binaphthalene derivatives can be dealt with either by heterocoupling of the appropriate 2-substituted naphthalenes or by asymmetrization of a suitable C_2-symmetric 2,2′-homodisubstituted binaphthalene. Where possible, the second route is more practical, as pointed out by the fact that, with quite



Scheme 2.

few significant exceptions [12],[2] it has been consistently exploited for the synthesis of C_1-symmetric P,X-binaphthyl derivatives using 1,1′-binaphthalene 2,2′-diol (BINOL) as the starting material [6].

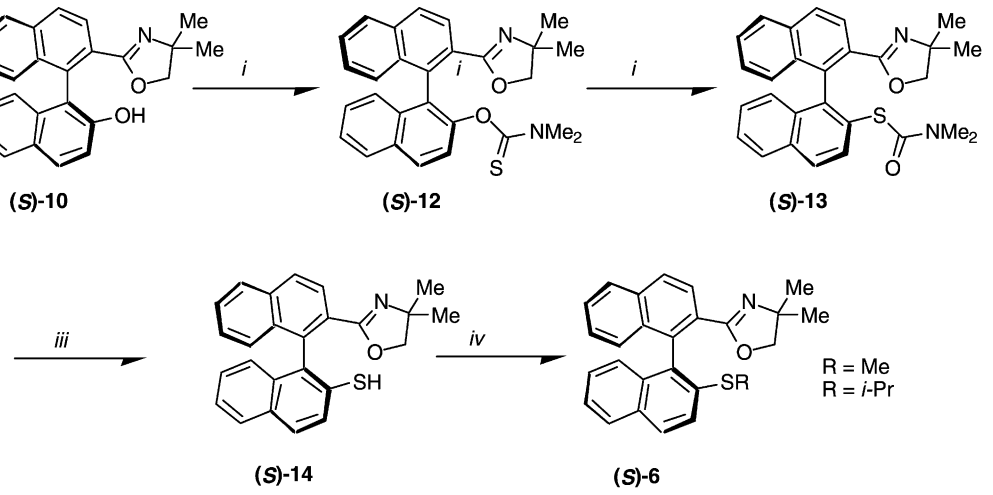
For the synthesis of our targets **5** and **6**, however, the heterocoupling strategy turned out to be more appropriate because it could provide a straightforward entry to the methoxy oxazoline **9** in high enantiopurity through the Ni-catalyzed reaction of **7** and **8**, two substrates easily available from inexpensive starting materials (Scheme 2).

This reaction was reported by Cram several years ago [13]. The coupling proceeds quite well on the dimethyl substituted naphthyl oxazoline **7** giving the key intermediate (*S*)-**9** in high chemical yield and in 85% optical purity as inferred from the specific rotation. Unfortunately, the scope of this reaction is fairly limited and, in our hands, even modest variations in the structure of the naphthyl oxazoline **7** resulted in low yields or in unpractical mixtures of products. This fact precluded us from preparing congeners of **9** with one or two hydrogens in the place of the two methyl groups in the oxazoline ring.

Demethylation of **9** with BBr_3 at 0 °C gave the hydroxy oxazoline **10** in quantitative yield. From this, the synthesis of the phosphito oxazoline **5** was eventually accomplished by reaction of **10** with the chlorophosphite **11** [14].

(*S*)-**10** reacted with (*R*)-**11** to give (*R*,*S*)-**5** isolated in 56% yield after column chromatography. The ^{31}P

[2] The first synthesis of ligand **1** was accomplished by enantioselective Ullmann coupling of the corresponding 1-bromo-2-(oxazolyl)naphthalenes.



i) NaH, DMF then $Me_2NC(S)Cl$, 85° C, 6 h; *ii*) 280° C, 17'; *iii*) KOH, MeOH, reflux 4.5 h; *iv*) RI, Et_3N, MeOH, rt

Scheme 3.

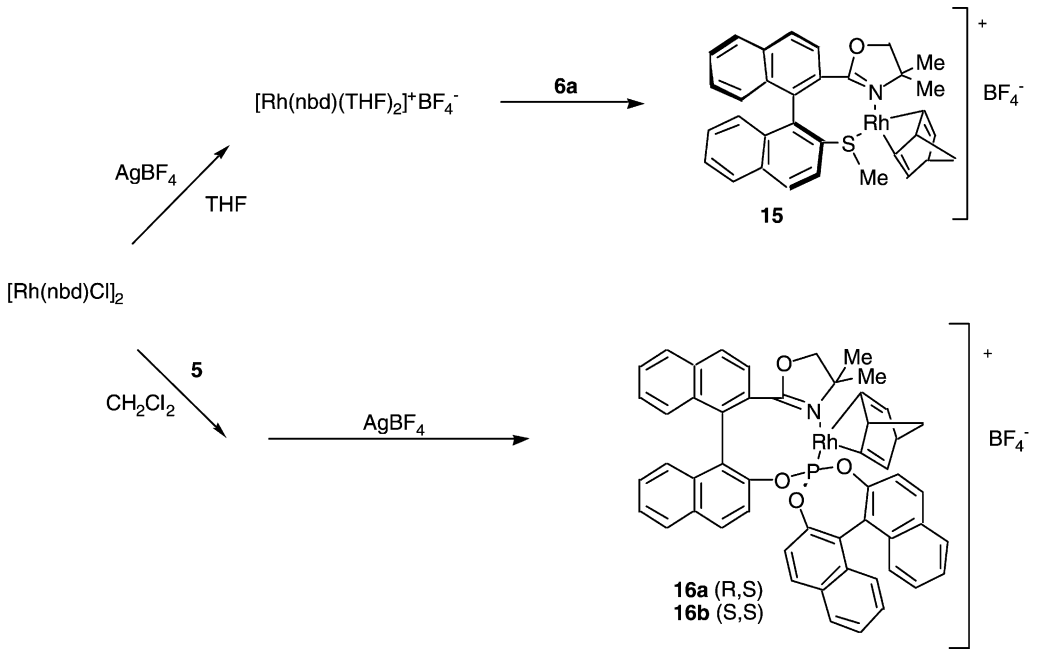
NMR spectrum of the purified product shows only one peak at 147.6 ppm, whereas in the crude product a small peak, corresponding to (*R*,*R*)-**5** and accounting for less than 5%, was also present at 145.6 ppm. Since the enantiomeric purity of the starting hydroxy oxazoline (*S*)-**10** was confidently assumed to be the same of its precursor **9** (about 85%), this implies either that the enantiomeric purity of (*S*)-**10** is higher than the one suggested by the optical rotation of **9** (more than 95% instead of 85%) or that a kinetic resolution had occurred in the course of the reaction of (*S*)-**10** with (*R*)-**11**. Whichever the case, the (*R*,*S*)-stereoisomer was eluted pure from the chromatographic column.

Unlike the previous case, the condensation between (*S*)-**10** and (*S*)-**11** gave a mixture of (*S*,*S*)-**5** and (*R*,*S*)-**5** in about 80:20 as determined by ^{31}P NMR. From this mixture a sample of (*S*,*S*)-**5** impure of (*R*,*S*)-**5** (about 20%) was isolated in very low yield (about 5%) after chromatographic purification. This result points out how different is the reactivity of (*S*)-**10** towards the two enantiomers of **11** and corroborates the hypothesis that a kinetic resolution could have occurred in the reaction between (*S*)-**10** and (*R*)-**11**.

For the preparation of the second target, compound (*S*)-**10** was acylated with *N*,*N*-dimethylaminothiocarbamoyl chloride to give **12** in 65% yield after crystallization (Scheme 3). The thiocarbamate **12** was subjected to Newmann–Kwart (N–K) rearrangement (280 °C, 17 min) [15] producing the corresponding thiolcarbamate (*S*)-**13** which was isolated in 57% yield after flash chromatography. Hydrolysis of (*S*)-**13** (KOH in methanol, 71%) afforded the thiol **14** which was alkylated with the suitable alkyl iodide to give the corresponding thioether (*S*)-**6** in moderate overall yields (12–25% from (*S*)-**9**). The enantiomeric purity of **6** was not determined directly. From previous experiences in N–K chemistry [10,16] and from the results observed in the preparation of **5**, it should be not lower than the value (85% e.e.) confidently assumed for the starting methoxyoxazoline **9**.

3.2. Synthesis of the Rh(I) complexes

The preparation of the Rh(I) complex containing the ligand (*S*)-**6a** was accomplished by reacting $[Rh(nbd)(THF)_2]^+BF_4^-$ (nbd: 1,4-norbornadiene) with a stoichiometric amount of the ligand (Scheme 4). The required THF adduct was prepared in situ from the corresponding chloro-bridged dimer, $[Rh(nbd)Cl]_2$ and $AgBF_4$ [17]. Complex **15** was isolated in 45% yield as an orange solid.



Scheme 4.

Its ^{1}H NMR spectrum shows a sharp set of multiplets for the ligand backbone and four broad signals for the norbornadiene protons. This indicates that a dynamic process is occurring in solution which averages the protons of the nbd ligand in the bound state.

The chelate coordination of the ligand was demonstrated in the ^{1}H NMR by the upfield shift of the *S*-methyl group (0.3 ppm with respect to the free ligand) and by the downfield shift experienced by one arm of the AB system of the diastereomeric protons of the methylene of the oxazoline ring. Upon coordination to rhodium, the more deshielded doublet was displaced about 0.6 ppm with respect to the free ligand, while the position of the second doublet of the AB system remained substantially unchanged after chelation. This turned out to be a general feature of all the Rh complexes with these oxazoline ligands.

Notably, in the ^{1}H NMR the *S*-methyl peak resonates as a sharp singlet and all the peaks of the ligand framework are very sharp. These data may be indicative that: (a) the binding of the Rh to the sulfur center has occurred with complete stereoselectivity affording only one diastereoisomer; (b) at room temperature the complex **15** is locked in a single conformation; and (c) at room temperature the ligand fragment of the complex is not involved in any significant dynamic process. All these facts may have significant bearings in view of the use of this complex in asymmetric catalysis.

According to what we have recently described for a similar Rh(I)–nbd complex containing *S*-methyl BINAPS **4b** (R = Me) as the heterobidentate ligand, we ascribe this dynamic behaviour to a pseudo-rotation of the nbd fragment [9c].

The preparation of the cationic Rh(I) complexes derived from (*R*,*S*)-**5** and (*S*,*S*)-**5** has been accomplished following a slightly different procedure [18], by adding one equivalent of $AgBF_4$ to a solution of $[Rh(nbd)Cl]_2$ in CH_2Cl_2 containing the appropriate ligand **5**. Complexes **16** were isolated in modest yields (25–35%).

The ^{1}H NMR spectrum of (*R*,*S*)-**16** shows broad peaks both in the aromatic and in the aliphatic region. The sole exception are the signals of the oxazoline fragment, where the two methyl groups and the AB pattern of the methylene are quite sharp. These peaks are shifted downfield some 1.3 and 0.6 ppm, respectively, compared to the free ligand. Again, the

norbornadiene protons give only four signals, only the methylene bridge being sharp. The ^{31}P NMR spectrum shows a doublet at 129.09 ppm due to the coupling with Rh ($J_{Rh\text{-}P} = 306.0$ Hz), with an upfield shift of 18.5 ppm respect to the free ligand.

Complex (*S*,*S*)-**16** gives similar spectra. Also in this case, the four signals of the norbornadiene are broad with the exception of the methylene bridge (sharp singlet at 1.04 ppm). Compared to the free ligand the two methyl groups of the oxazoline ring are shifted downfield of 0.3 and 0.5 ppm, respectively, and the two doublets of the AB system of the diastereotopic methylene of 0.3 and 0.55, respectively. In the ^{31}P spectrum the doublet ($J_{Rh\text{-}P} = 299.6$ Hz) appears at 118.86 ppm.

These data are in agreement with a *P*,*N*-chelate coordination of ligands **5** to the metal center and with a dynamic behaviour of the diolefin in both the complexes.

3.3. Assessment in asymmetric catalysis

Complexes (*R*,*S*)-**16**, (*S*,*S*)-**16** and **15** have been assessed in several Rh-catalyzed reactions with modest results.

In the hydroformylation of styrene the two Rh complexes **15** and (*R*,*S*)-**16** gave slightly different results. With the sulfur-containing derivative **15** a 80% conversion with complete chemoselectivity was attained in 2 h. The branched aldehyde accounted for 90%, but was racemic. With the phosphito-containing complex (*R*,*S*)-**16** the conversion into aldehydes was complete and the amount of the branched isomer was as high as 98%. While these figures compare favorably with the ones recorded with (*R*,*S*)-BINAPHOS **4a** in the same reaction, the e.e. of (*R*)-**2**-phenylpropanal was miserable (6 versus 94%).

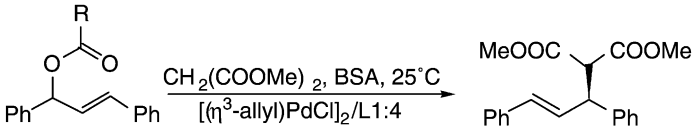
In the hydroboration of styrene complex **15** produced a 95% conversion with a 70% share of the linear carbinol. The branched isomer was almost racemic. With the complex (*R*,*S*)-**16** a quantitative conversion was obtained with a 68:32 ratio in the favor of the linear product. The e.e. of the branched alcohol was low (16% for the *R* enantiomer). The (*S*,*S*)-analogue was less effective and produced a lower conversion (50%) with a higher share (64%) of the branched racemic product.

The Rh complex **15** was devoid of catalytic activity in the hydrogenation of methyl acetamidoacrylate at room temperature and pressure and in the reduction of acetophenone transfer hydrogenation from 2-propanol. The phosphito analogue (*R*,*S*)-**16** is a catalyst of modest activity in the hydrogenation of methyl acetamidoacrylate where it gave 30% conversion in 24 h with a 11% e.e. for the *R*-configured methyl alaninate.

A comparison of these results with the ones recorded in the same reactions with the Rh complexes of BINAPHOS **4a** or BINAPS **4b** shows that these latter are by far more stereoselective in the hydrogenation (both) and in the hydroformylation (BINAPHOS). It appears that the substitution of the diphenylphosphino group with a nitrogen donor is detrimental for the stereoselection ability of the ligand, while it may lead to a definite improvement in the chemo- and regio-selectivity of the hydroformylation.

Both the sulfide-oxazoline ligands **6a** and **6b** have been tested in the Pd-catalyzed allylic alkylation of 1,3-diphenylallyl esters with dimethyl malonate under standard conditions (Scheme 5). In this reaction, the methyl-substituted ligand **6a** led to complete conversion in few hours and to fair e.e., whereas the *i*-propyl analogue **6b** produced a catalyst of poor activity (50% conversion within 22 h) which gave rise to a racemic product.

The effect of the solvent, of the temperature and of the leaving group in the substrate was examined in



17a, R = CH_3
17b, R = OCH_3

Scheme 5.

Table 1
Asymmetric allylic alkylation of 1,3-diphenylallyl esters with dimethyl malonate in the presence of sulfide-oxazoline ligand **6a**

Entry	Substrate	Solvent	T (°C)	t (h)	Conversion (%)	e.e. (%)	Configuration
1	**17a**	CH_2Cl_2	25	3	100	56	*S*
2	**17a**	CH_2Cl_2	0	7.5	100	59	*S*
3	**17a**	$CHCl_3$	25	2	100	65	*S*
4	**17a**	$CHCl_3$	0	36	70	66	*S*
5	**17b**	CH_2Cl_2	25	1.6	100	60	*S*
6	**17b**	CH_2Cl_2	0	8	100	65	*S*
7	**17b**	$CHCl_3$	25	15	100	63	*S*

Table 2
Asymmetric allylic alkylation of 1,3-diphenylallyl acetate with dimethyl malonate in the presence of phosphito-oxazoline ligands **5**

Entry	Ligand	Solvent	T (°C)	t (h)	Conversion (%)	e.e. (%)	Configuration
1	*(R,S)*-**5**	CH_2Cl_2	25	5	100	38	*S*
2	*(R,S)*-**5**	CH_2Cl_2	0	7	100	40	*S*
3	*(R,S)*-**5**	CH_2Cl_2	−20	24	70	40	*S*
4	*(R,S)*-**5**	$CHCl_3$	25	24	50	43	*S*
5	*(S,S)*-**5**	CH_2Cl_2	25	1	100	27	*S*
6	*(S,S)*-**5**	$CHCl_3$	25	24	50	11	*S*

some detail in the case of ligand **6a**. The results of this study are reported in Table 1.

While variations of these parameters had some influence on the reaction rate, the stereoselectivity was only marginally affected and fluctuated within a short range attaining 66% e.e. in the best run. If the ligand **6** used was not enantiopure, the stereoselectivity of this reaction might be actually a bit higher than expressed by this value. It remains, however, lower the best result obtained with ligand **4b** in the same reaction (91%) [19].

The two diastereomeric phosphito-oxazolines (*R*,*S*)-**5** and (*S*,*S*)-**5** have been as well tested in the same reaction of 1,3-diphenylallyl acetate. The results reported in Table 2 show that the matching of the chiral elements is attained with the (*R*,*S*)-combination.

The trends observed with the temperature and the solvents were comparable with the previous case, but the e.e. recorded in these runs were lower (up to 43% with the matching ligand) than those obtained with the sulfur-derivatives.

Notably the configuration of the reaction product was always the same and did not change upon changing the chirality of the phosphite fragment. Thus, the enantioselection of the Pd-catalyzed allylic alkylation is basically dictated by the axial chirality of the main scaffold where the two donors are appended and the additional chiral elements, either the new stereocentre originated upon the binding at the S donor or the chirality of the phosphite pendant, play a modest role in the transfer of the chiral information.

In conclusion the results obtained in the course of this work show that the introduction of an oxazoline in the place of a diphenylphosphino group as a chelating arm of binaphthalene-core heterobidentate ligands has a negative influence on the stereoselection ability of the resulting ligands in a variety of Rh- and Pd-catalyzed asymmetric reactions, but may exert a moderate positive effect on the catalytic activity and on the chemo-/regio-selectivity of some process.

Acknowledgements

This work was carried out in the frame of the COST Chemistry Action D12 “Organic Transformations: Selective Processes and Asymmetric Catalysis”, project 0009/98. The financial support of the University of Sassari and of MIUR (Rome) is gratefully acknowledged.

References

[1] T.G. Gant, M.C. Noe, E.J. Corey, Tetrahedron Lett. 36 (1995) 8745.

[2] Y. Uozumi, H. Kyota, E. Kishi, K. Kitayama, T. Hayashi, Tetrahedron: Asymmetry 6 (1996) 1603.

[3] (a) Y. Uozumi, K. Kato, T. Hayashi, J. Am. Chem. Soc. 119 (1997) 5063;
(b) Y. Uozumi, K. Kato, T. Hayashi, J. Org. Chem. 63 (1998) 5071.

[4] Y. Uozumi, H. Kyota, K. Kato, M. Hayashi, T. Ogasawara, J. Org. Chem. 64 (1999) 1620.

[5] Y. Imai, W. Zhang, T. Kida, Y. Nakatsuji, I. Ikeda, J. Org. Chem. 65 (2000) 3326.

[6] M. McCarthy, P.J. Guiry, Tetrahedron 57 (2001) 3809.

[7] (a) N. Sakai, S. Mano, K. Nozaki, H. Takaya, J. Am. Chem. Soc. 115 (1993) 7033;
(b) N. Sakai, K. Nozaki, H. Takaya, J. Chem. Soc., Chem. Commun. (1994) 395.

[8] (a) Y. Imai, W. Zhang, T. Kida, Y. Nakatsuji, I. Ikeda, Tetrahedron Lett. 39 (1998) 4343;
(b) M. Ogasawara, K. Yoshida, H. Kamei, K. Kato, Y. Uozumi, T. Hayashi, Tetrahedron: Asymmetry 9 (1998) 1779.

[9] (a) S. Gladiali, A. Dore, D. Fabbri, Tetrahedron: Asymmetry 5 (1994) 1143;
(b) S. Gladiali, S. Medici, G. Pirri, S. Pulacchini, D. Fabbri, Can. J. Chem 79 (2001) 670;
(c) S. Gladiali, F. Grepioni, S. Medici, A. Zucca, Z. Berente, L. Kollàr, EJIC, in press.

[10] R. Pretot, A. Pfaltz, Angew. Chem. Int. Ed. Engl. 37 (1998) 323.

[11] (a) C.G. Frost, J.M.J. Williams, Tetrahedron Lett. 34 (1993) 2015;
(b) C.G. Frost, J.M.J. Williams, Tetrahedron: Asymmetry 4 (1993) 1785;
(c) C.G. Frost, J.M.J. Williams, Synlett (1994) 551;
(d) X.-L. Hou, X.-W. Wu, L.-X. Dai, B.-X. Cao, J. Sun, Chem. Commun. (2000) 195;
(e) Y. Imai, W. Zang, T. Kida, Y. Nakatsuji, I. Ikeda, Synlett (1999) 1319.

[12] T.D. Nelson, A.I. Meyers, J. Org. Chem. 59 (1994) 2655.

[13] J. Wilson, D. Cram, J. Org. Chem. 49 (1984) 4930.

[14] (a) G. Franciò, F. Faraone, W. Leitner, Angew. Chem. Int. Ed. Engl. 39 (2000) 1428;
(b) G.C. Arena, G.P. Calabrò, F. Faraone, Tetrahedron: Asymmetry 11 (2000) 2387.

[15] D. Fabbri, G. Delogu, O. Delucchi, J. Org. Chem. 58 (1993) 1748.

[16] (a) A. Dore, D. Fabbri, S. Gladiali, G. Valle, Tetrahedron: Asymmetry 6 (1995) 779;
(b) D. Fabbri, S. Pulacchini, S. Gladiali, Synlett (1996) 1054.

[17] P. Pertici, F. D'Arata, C. Rosini, J. Organomet. Chem. 163 (1996) 515.

[18] R.R. Schrock, J.A. Osborn, J. Am. Chem. Soc. 93 (1971) 2397.

[19] J. Kang, S. Hoon Yu, J.I. Kim, H.G. Cho, Bull. Korean Chem. Soc. 16 (1995) 439.