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Chiral-at-metal ruthenium(II) complexes as catalysts in the asymmetric cyclopropanation reaction

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Abstract

A family of five- and six-coordinate chiral-at-metal ruthenium complexes has been examined as catalysts in the asymmetric cyclopropanation reaction of styrene with ethyl diazoacetate. With complexes **5** and **6**, good *cis*-diastereoselectivity and enantioselectivity up to 74% were observed.

Keywords: Cyclopropanation; *cis*-Selectivity; Asymmetric catalysis; Ruthenium complexes; Stereogenic metal

1. Introduction

Catalytic asymmetric cyclopropanation of alkenes is one of the most efficient methods for the selective construction of chiral cyclopropanic compounds [1]. Over the last 15 years, many excellent metal-based methodologies have been developed, but most of them are *trans*-selective. Only recently, a few chiral *cis*-selective systems have been reported. Different ruthenium and cobalt(II) salen complexes [2,3] have proven to be very efficient catalysts to obtain *cis*-cyclopropanes with excellent enantio- and diastereoselectivities. Other systems based on N_2P_2-ligand ruthenium, [4] chiral iron carbene [5] or, more recently, dirhodium(II) complexes [6] have also been shown to be *cis*- enantio- and diastereoselective. On the other hand, some heterogeneous catalytic systems have been reported as *cis*-selective [7].

In general, the chirality of these catalytic systems remains exclusively in the substituents of the chelating skeleton. The utilization of organometallic complexes with stereogenic metal centers can provide a useful alternative to improve the stereoselectivity of organic reactions because the inductor of the chirality is the same metal atom at which catalysis takes place [8]. Moreover, the fixed configuration at the metal center of the organometallic complex used as catalyst can provide an interesting tool to understand the stereochemical pathway of the reaction. At present, the application of this kind of chiral-at-metal systems to the asymmetric synthesis has been mainly restricted to hydrogenation and Diels–Alder reactions [9].

In the last years, our research group has described different ruthenium(II), rhodium(III) and iridium(III) complexes with stereogenic metal atoms and their use as catalysts in enantioselective Diels–Alder [10], hydrogen transfer [11] or 1,3-dipolar cycloaddition [12] reactions. In some occasions, the complete characterization of intermediate complexes has been possible and a catalytic cycle could be proposed [10a,12]. In particular, we have experience in the synthesis of optically active phosphinooxazoline complexes where the nitrogen and phosphorus atoms of the phosphinooxazoline ligand co-ordinate the metal center in a chelate fashion [10a,d]. Herein, we examined a family of ruthenium(II) complexes with chirality at the metal having the chiral bidentate ligand (4*S*)-(2-diphenylphosphinophenyl)-

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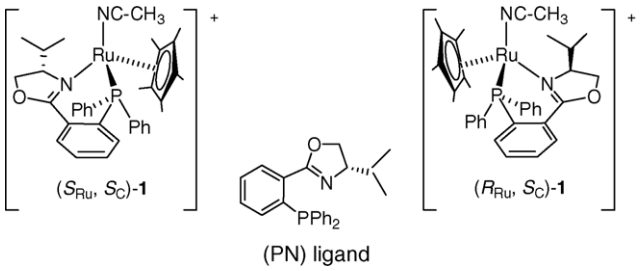


Fig. 1. Enantiopure (PN) ligand and structure of both diastereomers of complex **1**.

4-isopropyl-1,3-oxazoline [(PN), Fig. 1] as catalysts in a cyclopropanation reaction. When we started our work on this topic, mononuclear complexes containing stereogenic metals had not been reported as catalysts in asymmetric cyclopropanation of olefins. As far as we know, our complexes are the only catalysts with stereogenic metal centers that are *cis*- diastereo- and enantioselective in the asymmetric cyclopropanation of alkenes.

2. Experimental

2.1. General

All solvents were dried over appropriate drying agents, distilled under argon and degassed prior to being used. All preparations have been carried out under a argon atmosphere. Infrared spectra were recorded on a Nicolet Magna 550 spectrophotometer. ^{1}H and $^{31}P\{^{1}H\}$ were recorded on a Varian UNITY 300 (299.95 MHz), Varian GEMINI 2000 (300.10 MHz) or a Bruker 300 ARX (300.10 MHz). Chemical shifts are expressed in ppm upfield from $SiMe_4$ and 85% H_3PO_4 (^{31}P). NOEDIFF and ^{31}P, ^{1}H correlation spectra were obtained using standard procedures. Mass spectra were obtained in the FAB+ mode on a high resolution VG-autospectrometer using a NBA matrix; selective peaks and *m*/*z* percentage are given. Gas chromatographic (GC) analyses were performed using a Hewlett-Packard 58890 II with a flame ionisation detector. The yields of the cycloaddition reaction were determined by gas chromatography in a capillary column (cross-linked methyl silicone HP-1, 25 m × 0.2 mm × 0.33 μm) using *n*-decane as internal standard. The ee values were determined by GC with a chiral column (Cyclodex-B, 2,3,6-methylated, 30 m × 0.25 mm × 0.25 μm).

2.2. Synthesis of the complexes

2.2.1. Preparation of [(η^5-C_5Me_5)Ru(PN)(AN)]PF_6 (1)

A mixture of [{(η^5-C_5Me_5)RuCl}$_2$(μ-Cl)$_2$] (300 mg, 0.49 mmol), KPF_6 (252 mg, 1.37 mmol) and powdered Zn (128 mg, 1.96 mmol) in 15 mL of acetonitrile (AN) was stirred for 4 h. The solid (Zn) was separated by filtration to obtain an orange solution that was concentrated under vacuum to 1 mL. After addition of CH_2Cl_2 (15 mL), the newly appeared solid was separated again by filtration. To the resulting solution, the phosphinooxazoline ligand ((4*S*)-(2-diphenylphosphinophenyl)-4-isopropyl-1,3-oxazoline) [PN, 365 mg, 0.98 mmol] was added in 5 mL of dichloromethane. The colour of the solution turned immediately from orange to red-orange. The reaction mixture was partially concentrated under reduced pressure and the addition of diethyl ether gave an orange solid, which was filtered off, washed with Et_2O and dried under an argon atmosphere. Yield: 84%. (S_{Ru},S_C)-**1**: (R_{Ru},S_C)-**1** molar ratio 1.5:1. IR (nujol, cm^{-1}): ν(C≡N) 2268.2 (s), ν(C=N) 1641.3 (s), ν(C–O–C) 1230.5 (s). (S_{Ru},S_C)-**1**: ^{1}H NMR ($CDCl_3$) δ −0.22 (d, 3H, J_{HH} = 6.9 Hz, *Me*Me ^{i}Pr), 0.84 (d, 3H, J_{HH} = 6.9 Hz, Me*Me* ^{i}Pr), 1.44 (bs, 15H, C_5Me_5), 1.6–1.7 (m, 1H, C*H* ^{i}Pr), 1.96 (s, 3H, *Me*CN), 4.03–4.54 (m, 3H, *H* oxazoline-ring), 6.85–7.92 (m, 14 H, *Ph*). ^{13}C NMR ($CDCl_3$) δ 3.3 (*Me*CN), 10.3 (C_5Me_5), 13.1 (*Me*Me ^{i}Pr), 19.0 (Me*Me* ^{i}Pr), 29.0 (*C*H ^{i}Pr), 66.9 (C_4 oxazoline-ring), 86.9 (C_5Me_5), 75.2 (C_5 oxazoline-ring), 125.9 (Me*C*N), 128.0–136.3 (*Ph*), 163.9 (C_2 oxazoline-ring). ^{31}P NMR ($CDCl_3$) δ −144.6 (sp, J_{FP} = 716.5 Hz, uncoordinated *P*F_6^-), 51.2 (s). (R_{Ru},S_C)-**1**: ^{1}H NMR ($CDCl_3$) δ 0.52 (d, 3H, J_{HH} = 7.0 Hz, *Me*Me ^{i}Pr), 1.00 (d, 3H, J_{HH} = 6.9 Hz, Me*Me* ^{i}Pr), 1.35 (d, 15H, J_{PH} = 2.1 Hz, C_5Me_5), 1.6–1.7 (m, 1H, C*H* ^{i}Pr), 1.96 (s, 3H, *Me*CN), 4.03–4.54 (m, 3H, *H* oxazoline-ring), 6.85–7.92 (m, 14 H, *Ph*). ^{13}C NMR ($CDCl_3$) δ 3.5 (*Me*CN), 10.0 (C_5Me_5), 13.9 (*Me*Me ^{i}Pr), 18.7 (Me*Me* ^{i}Pr), 28.8 (*C*H ^{i}Pr), 67.7 (C_3 oxazoline-ring), 75.5 (C_4 oxazoline-ring), 86.9 (C_5Me_5), 125.9 (Me*C*N), 128.0–136.3 (*Ph*), 163.4 (C_2 oxazoline-ring). ^{31}P NMR ($CDCl_3$) δ −144.6 (sp, J_{FP} = 716.5 Hz, uncoordinated *P*F_6^-), 51.3 (s). MS [$M^+PF_6^-$, *m*/*z* (%)]: 610 (M^+−AN).

2.2.2. Preparation of [$RuCl_2$(PN)(PPh_3)] (2)

A mixture of [$RuCl_2(PPh_3)_3$] (500 mg, 0.52 mmol) and the phosphinooxazoline ligand (PN) (195 mg, 0.52 mmol) in 15 mL of toluene was stirred for 24 h. Solvent was vacuum-evaporated to dryness. The residue was dissolved in dichloromethane (10 mL) and the solution partially concentrated (5 mL) under reduced pressure. Slow addition of hexane (about 15 mL) gave a deep green solid, which was filtered off, washed with hexane and dried under an argon atmosphere. Free leaving triphenylphosphine was present in the obtained solid and it could not be removed by crystallization. IR (nujol, cm^{-1}): ν(C=N) 1630.3 (s), ν(C–O–C) 1242.1 (s). Major isomer of **2**: ^{1}H NMR ($CDCl_3$) δ 0.76 (d, 3H, J_{HH} = 6.8 Hz, *Me*Me ^{i}Pr), 0.98 (d, 3H, J_{HH} = 6.8 Hz, Me*Me* ^{i}Pr), 2.12–2.25 (m, 1H, C*H* ^{i}Pr), 4.42–4.50 (m, 2H, H_4,H_5 oxazoline-ring), 5.04–5.11 (m, 1H, $H_{5'}$ oxazoline-ring), 6.60–8.11 (m, *Ph*). ^{13}C NMR ($CDCl_3$) δ 13.9 (*Me*Me ^{i}Pr), 22.3 (Me*Me* ^{i}Pr), 32.5 (*C*H ^{i}Pr), 68.3 (C_4 oxazoline-ring), 77.1 (C_5 oxazoline-ring), 125.9–140.0 (*Ph*), 164.3 (C_2 oxazoline-ring). ^{31}P NMR ($CDCl_3$) δ 36.3 (d, J_{PP} = 34.6 Hz, coordinated *P*Ph_3), 84.3 [d, J_{PP} = 34.6 Hz, (*P*N)]. MS [*m*/*z* (relative abundance)]: 807 (M^+, 3%), 772 (M^+−Cl, 53%), 472 (100%).

*2.2.3. Preparation of [$RuCl_2$(PN)(PPh_3)(H_2O)] (**3**)*

Method A: A mixture of [$RuCl_2(PPh_3)_3$] (300 mg, 0.31 mmol) and the phosphinooxazoline ligand (PN) (117 mg, 0.31 mmol) in 15 mL of methanol was stirred for 24 h at room temperature. Solvent was vacuum-evaporated to dryness. The residue was dissolved in dichloromethane (10 mL) and the solution partially concentrated under reduced pressure. The addition of 20 mL of hexane gave an orange solid, which was filtered off, washed with hexane and dried under argon. Yield: 82%. *Method B*: A solution of [$RuCl_2$(PN)(PPh_3)] (**2**) (300 mg, 0.38 mmol) in 7 mL of methanol was stirred for 1 h at room temperature. During this time, the solution colour evolved from deep green to orange. The solution was partially concentrated under reduced pressure, and the slow addition of hexane gave an orange solid, which was filtered off, washed with hexane and dried under argon. Yield: 50%. IR (nujol, cm^{-1}): ν(C=N) 1593.1 (s), ν(C–O–C) 1236.1 (s), $\nu(H_2O)$ 3373.3 (s), 1629.8 (w). ^{1}H NMR ($CDCl_3$). δ −0.10 (d, 3H, J_{HH} = 6.8 Hz, *Me*Me ^{i}Pr), 0.27 (d, 3H, J_{HH} = 6.8 Hz, Me*Me* ^{i}Pr), 1.75 (bs, coordinated H_2O), 2.37 (m, 1H, C*H* ^{i}Pr), 3.50 (m, 2H, H_4, H_5 oxazoline-ring), 4.14 (m, 1H, $H_{5'}$ oxazoline-ring), 6.84–8.21 (m, *Ph*). ^{13}C NMR ($CDCl_3$) δ 13.2 (*Me*Me ^{i}Pr), 18.2 (Me*Me* ^{i}Pr), 27.4 (*C*H ^{i}Pr), 67.3 (C_4 oxazoline-ring), 77.2 (C_5 oxazoline-ring), 126.4–139.1 (*Ph*), 164.0 (C_2 oxazoline-ring). ^{31}P NMR ($CDCl_3$) δ 30.5 (d, J_{PP} = 32 Hz, co-coordinated *P*Ph_3), 59.9 [d, J_{PP} = 32 Hz, (*P*N)]. MS [*m*/*z* (relative abundance)]: 807 (M^+-H_2O, 7%), 772 (73%), 472 (100%).

*2.2.4. Preparation of [$RuCl_2$(PN)(PPh_3)(CO)] (**4**)*

Carbon monoxide was passed through a solution of [$RuCl_2$(PN)(PPh_3)] (**2**) (150 mg, 0.19 mmol) in 10 mL of dichloromethane. The change of solution colour from deep green to yellow was operated in a few minutes. The reaction was monitored by infrared spectroscopy until the IR spectrum remained unchangeable (about 1 h). Solvent was partially evaporated under reduced pressure and the addition of hexane gave a yellow solid, which was filtered off, washed with hexane and dried under argon. Yield: 54%. IR (nujol, cm^{-1}): ν(C=N) 1607.7 (s), ν(C–O–C) 1240.2 (s), ν(C≡O) 1957.7 (s). ^{1}H NMR ($CDCl_3$) δ −0.28 (d, 3H, J_{HH} = 6.9 Hz, *Me*Me ^{i}Pr), 0.41 (d, 3H, J_{HH} = 6.9 Hz, Me*Me* ^{i}Pr), 1.74 (m, 1H, C*H* ^{i}Pr), 3.54 (m, 1H, H_4 oxazoline-ring), 3.70 (pt, 1H, J_{HH} = 9.2 Hz, H_5 oxazoline-ring), 3.99 (dd, 1H, J_{HH} = 3.3 Hz, J_{HH} = 9.2 Hz, $H_{5'}$ oxazoline-ring), 6.84–8.21 (m, *Ph*). ^{13}C NMR ($CDCl_3$) δ 12.2 (*Me*Me ^{i}Pr), 18.4 (Me*Me* ^{i}Pr), 27.5 (*C*H ^{i}Pr), 66.2 (C_4 oxazoline-ring), 78.1 (C_5 oxazoline-ring), 126.4–136.0 (*Ph*), 165.4 (C_2 oxazoline-ring), 201.8 (pt, J_{PC} = 12.1 Hz, *C*O). ^{31}P NMR ($CDCl_3$) δ 15.3 (d, J_{PP} = 365 Hz), 34.8 (d, J_{PP} = 365 Hz) MS [*m*/*z* (relative abundance)]: 835 (M^+, 12%), 800 (M^+-Cl, 89%), 472 (100%).

*2.2.5. Preparation of [RuCl(PN)(PPh_3)$(AN)_2$]Cl (**5**) and solvato complex **6***

A solution of [$RuCl_2$(PN)(PPh_3)] (**2**) (300 mg, 0.38 mmol) in 7 mL of acetonitrile was stirred for 1 h at room temperature. The formation of the acetonitrile adduct was indicated by a colour change during this time (from deep green to yellow). The solution was partially concentrated under reduced pressure, and the slow addition of diethyl ether gave a yellow solid, which was filtered off, washed with diethyl ether and dried under argon. Yield: 46%. IR (nujol, cm^{-1}): ν(C=N) 1616.3 (s), ν(C–O–C) 1244.0 (s), ν(C≡N) 2279.8 (s). ^{1}H NMR ($CDCl_3$) δ −0.02 (d, 3H, J_{HH} = 6.9 Hz, *Me*Me ^{i}Pr), 0.76 (d, 3H, J_{HH} = 6.9 Hz, Me*Me* ^{i}Pr), 1.45 (s, 3H, *Me*CN), 1.90 (m, 1H, C*H* ^{i}Pr), 2.40 (s, 3H, *Me*CN), 4.34–4.49 (m, 2H, H_4, H_5 oxazoline-ring), 5.55–5.65 (m, 1H, $H_{5'}$ oxazoline-ring), 6.39–8.25 (m, *Ph*). ^{13}C NMR ($CDCl_3$) δ 3.8 (*Me*CN), 13.4 (*Me*Me ^{i}Pr), 19.5 (Me*Me* ^{i}Pr), 29.3 (*C*H ^{i}Pr), 68.2 (C_3 oxazoline-ring), 70.9 (C_4 oxazoline-ring), 123.7 (Me*C*N), 126.9–135.1 (*Ph*), 165.5 (C_2 oxazoline-ring). ^{31}P NMR ($CDCl_3$) δ 41.7 (d, J_{PP} = 23.9 Hz), 50.0 (d, J_{PP} = 23.9 Hz) MS [M^+Cl^-, *m*/*z* (relative abundance)]: 853 (M^+, 4%), 807 (M^+–AN, 4%), 772 (M^+–2AN, 100%), 472 (77%). Molar conductivity: 37.99 $\Omega^{-1}cm^{-1}\,mol^{-1}$ (5×10^{-4} M acetone solution).

When reaction between complex **2** and acetonitrile was carried out at reflux, a new complex (**6**) was appearing (reaction monitored by ^{1}H and ^{31}P NMR). After 3 days, the reaction did not more evolve. Then, the solution was concentrated and the solid precipitated by slow addition of diethyl ether to give a mixture of complexes **5** and **6** in a molar ratio of 1:5. As the formation of complex **6** is not quantitative, the characterization in the solid state was not attempted. Complex **6**: ^{1}H NMR ($CDCl_3$) δ −0.01 (d, 3H, J_{HH} = 6.9 Hz, *Me*Me ^{i}Pr), 0.74 (d, 3H, J_{HH} = 6.9 Hz, Me*Me* ^{i}Pr), 1.92 (m, 4H, *Me*CN, C*H* ^{i}Pr), 2.26 (s, 3H, *Me*CN), 4.29 (pt, 1H, J_{HH} = 7.8 Hz, H_4 oxazoline-ring), 4.41 (pt, 1H, J_{HH} = 9.8 Hz, H_5 oxazoline-ring), 5.22–5.38 (m, 1H, $H_{5'}$ oxazoline-ring), 6.73–8.16 (m, *Ph*). ^{31}P NMR ($CDCl_3$) δ 59.2 (s).

2.3. General procedure for asymmetric cyclopropanation

To a suspension containing AgOTf (12.85 mg, 0.05 mmol, except as indicated) and 0.025 mmol of the catalyst precursor in 2 mL of dry dichloromethane, a solution of 2.1 mL of styrene (18.75 mmol) and *n*-decane (49.8 mg, 0.35 mmol, used as internal standard for GC) in 1.5 mL of dry CH_2Cl_2 was added at room temperature under an inert atmosphere. A CH_2Cl_2 solution of ethyl diazoacetate (1.25 mmol in 40 mL) was slowly added dropwise (addition time indicated in Table 2). After the addition was complete, the resulting mixture was stirred for an additional time indicated in Table 2. The reaction was monitored by GC until the ratio between the formed cyclopropane compounds and the starting ethyl diazoacetate remained unchangeable. Yields, *cis*:*trans* ratios and dimerization percentage were determined by GC in a capillary column (cross-linked methyl silicone HP-1, 25 m × 0.2 mm × 0.33 μm). Previously to the chromatographic analysis, samples were treated with hexane (for catalyst **2**–**4**) or diethyl ether (for catalyst **1**, **5**, **6**) and the

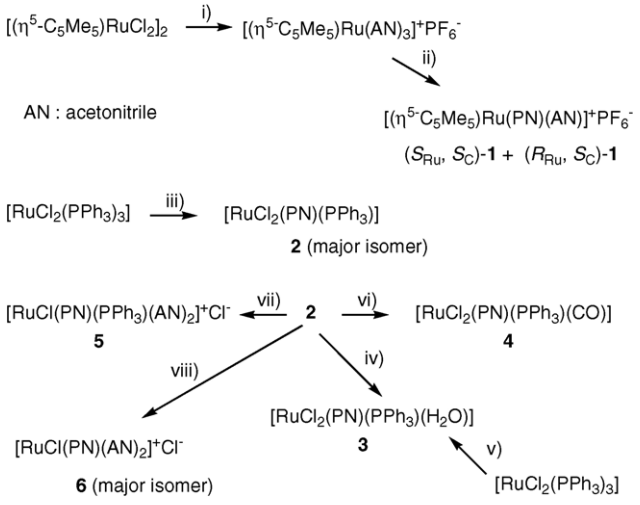
organometallic compound filtrated. Enantiomeric excess of the products was determined by GC using a chiral column (Cyclodex-B, 2,3,6-methylated, 30m × 0.25mm × 0.25 μm) [13]. Absolute configuration of the cyclopropanes was determined by the comparison of the elution order found in the literature [13].

3. Results and discussion

3.1. Synthesis of complexes 1–6

Half-sandwich complexes as $[(\eta^5\text{-}C_5H_5)Ru(AN)_3]^+$ (AN, acetonitrile) or $[(\eta^5\text{-}C_5H_5)RuCl(PPh_3)_2]$ and five-coordinate compounds as $[RuCl_2(PPh_3)_3]$ have proven to be excellent catalysts for olefin cyclopropanation [14,15]. We therefore synthesised similar systems including the chiral bidentate ligand (PN). Complexes **1**–**6** (Figs. 1 and 2) were prepared as described in Scheme 1. The proposed structures are based on their spectroscopic data, as no crystals of any complex have been obtained so far. As it has been shown by other authors [4a], the analysis of the ^{31}P NMR spectra can be very useful to assign the stereochemistry in octahedral ruthenium complexes since chemical shifts depend on the coordinate atom (Cl, O or N) in the *trans* P–Ru–ligand arrangements, whereas coupling constant values indicate *cis* or *trans* P–Ru–P dispositions. Table 1 shows the ^{31}P NMR data of complexes **1**–**6**.

Half-sandwich complex $[(\eta^5\text{-}C_5Me_5)Ru(PN)(AN)]^+PF_6^-$ (**1**), where a molecule of the solvent (acetonitrile, AN) occupy a labile position of the metal coordination sphere, was prepared by reaction of (PN) ligand with dimer $[(\eta^5\text{-}C_5Me_5)RuCl_2]_2$ in acetonitrile at room temperature (Scheme 1). The mass spectrum (FAB+) displays the peak of the cationic fragment with a loss of acetonitrile (*m*/*z* 610, 100%) and the solvated nature of the complex



Scheme 1. Synthesis of complexes **1**–**6**: (i) KPF_6, Zn, AN, r.t., 4 h; (ii) (PN), CH_2Cl_2, r.t.; (iii) (PN), toluene, r.t., 24 h; (iv) MeOH, r.t., 24 h; (v) (PN), MeOH, r.t., 24 h; (vi) CO, CH_2Cl_2, r.t., 1 h; (vii) AN, r.t., 1 h; (viii) AN, reflux, 3 days.

Table 1
^{31}P NMR data of complexes **1**–**6**

Complex	^{31}P NMR, δ (ppm)	^{31}P NMR, J_{PP} (Hz)
(S_{Ru},S_C)-**1**	51.2 (s)	
(R_{Ru},S_C)-**1**	51.3 (s)	
2	84.3 (d), 36.3(d)	34.6
3	59.9 (d), 30.5 (d)	32.0
4	15.3 (d), 34.8 (d)	365
5	50.0 (d), 41.7 (d)	23.9
6	59.2 (s)	

was characterized by the corresponding features of the coordinate acetonitrile molecule in ^{13}C and ^{1}H NMR. Similar solvato-complexes derived from rhodium(III) and iridium(III), whose structures were determined by X-ray diffraction, have been prepared and used as catalyst in the Diels–Alder reaction [10d]. The analysis of the spectroscopic data of complex **1** and the similarities with those of the rhodium(III) and iridium(III) analogs have permitted to propose the structure of the ruthenium complex. Fig. 1 shows for complex **1** a "three-legged piano stool" geometry, where chiral metal center is in a pseudo-octahedral environment, being bonded to the η^5-C_5Me_5 ring, to the nitrogen and phosphorus atoms of the phosphinooxazoline ligand in a chelate fashion, and to the solvent molecule.

The cationic complex $[(\eta^5\text{-}C_5Me_5)Ru(PN)(AN)]^+PF_6^-$ (**1**) was obtained as a mixture of (S_{Ru},S_C)-**1** and (R_{Ru},S_C)-**1** in a 1.5:1 ratio (Fig. 1) that could not been resolved. Each diastereomer was characterized by ^{1}H, ^{13}C and ^{31}P NMR and their absolute configurations assigned by comparing with those of rhodium(III) and iridium(III) analogs [10d].

The five-coordinate complex $[RuCl_2(PN)(PPh_3)]$ (**2**) was obtained from $[RuCl_2(PPh_3)_3]$ by displacement of two molecules of PPh_3 by the ligand (PN) in toluene at reflux (Scheme 1). Under these conditions, a mixture of five isomers was obtained, one of which was the major component (71% by ^{1}H NMR). The mass spectrum displays the molecular ion (*m*/*z* 807, 3%), the loss of a chloride anion to form the cationic specie $[RuCl(PN)(PPh_3)]^+$ (*m*/*z* 772, 53%) and the peak of $[RuCl(PPh_3)]^+$ (*m*/*z* 472, 100%). The ^{31}P NMR spectrum showed an AX system with the two phosphorus atoms in a *cis*-disposition for all the isomers. From the ^{31}P NMR spectrum of the main isomer (Table 1) and taking into account that the P atom involved in a *trans* P–Ru–Cl arrangement displays high ^{31}P NMR chemical shifts (δ) and that typical δ's for *trans* P–Ru–N dispositions are around 35–50 ppm [4a], a square pyramidal structure (Fig. 2) could be proposed. This fact agrees with that shown by other authors: when d^6 complexes can be induced to be five-coordinate, they are best classified as square pyramidal [16]. In an attempt to obtain a single isomer, we tried to prevent the equilibrium between different coordination polyhedra by preparing more stable 18-electron complexes derived from compound **2**. Thus, six-coordinate complexes $[RuCl_2(PN)(PPh_3)(H_2O)]$ (**3**), $[RuCl_2(PN)(PPh_3)(CO)]$ (**4**) and the cationic $[RuCl(PN)(PPh_3)(AN)_2]^+$ Cl^- (**5**) were pre-

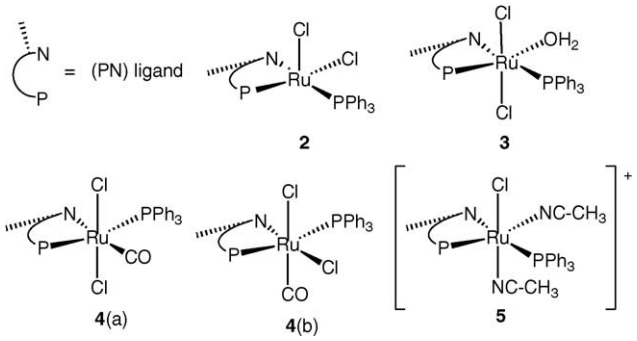


Fig. 2. Structures of complexes **2**–**5**. For structures **2**, **4**(b) and **5,** only one epimer at the metal is shown.

pared by reaction of **2** with methanol, CO and acetonitrile, respectively, at room temperature.

$[RuCl_2(PN)(PPh_3)(H_2O)]$ (**3**) was synthesised as a single isomer (*cis* P–Ru–P arrangement) by reacting $[RuCl_2(PPh_3)_3]$ with (PN) in methanol. The same product was also obtained when complex **2** was left to react with methanol. This aquo-complex **3** was characterized by the corresponding features of the water molecule in IR and ^{1}H NMR (see Section 2). The water molecule proceeds from traces of water in the solvent, as we have previously observed in other related phosphoxazoline-Ru aquo-complex [10a]. The aquo-solvated nature of complex **3** was also confirmed by the following experiment: to a solution of complex **2** in dichloromethane, small amounts of water were added and the reaction monitored by ^{31}P NMR. When we added an equimolecular amount of water, aquo-complex **3** was detected, but as a minor component of the mixture. An excess of water and a reaction time of 12 h enhanced the presence of complex **3** and decreased the concentration of isomers of **2**, suggesting an equilibrium between the five-coordinate complexes **2** and the six-coordinate aquo-solvate **3**. The FAB mass spectrum showed a peak at *m*/*z* 807 (M^+–H_2O, 7%) but not that of the molecular ion, suggesting that the water molecule is loosely bonded. ^{31}P NMR chemical shifts and coupling constant $J_{PP'}$ (Table 1) indicate *trans* P–Ru–O, *trans* P–Ru–N and *cis* P–Ru–P arrangements. On the basis of all analytical data, we propose for complex **3** the structure represented in Fig. 2.

Treatment of complex **2** with carbon monoxide over a short period (1 h) gave $[RuCl_2(PN)(PPh_3)(CO)]$ (**4**) as a single isomer with a *trans* P–Ru–P disposition (Table 1). The FAB mass spectrum displays the molecular ion (*m*/*z* 835, 12%) and the loss of a chloride anion to form the cationic specie $[RuCl(PN)(PPh_3)(CO)]^+$ (*m*/*z* 800, 89%). Two structures can be proposed with this condition, **4**(a) and **4**(b) (Fig. 2), and we were a priori unable to determine which of these corresponds to compound **4**. It is known that values for ruthenium–chlorine stretching frequencies are characteristic of *trans* Cl–Ru–ligand disposition depending on the nature of the ligand [17]. Unfortunately, next to complex **4**, a minor side compound, probably a dicarbonyl complex, was detected by IR. This by-product difficulted the characterization because we could not unequivocally assign the bands present in the far-IR spectrum. Although different carbonyl stretching frequencies have been reported for monocarbonyl complexes having the CO group *trans* to a Cl (1945–1949 cm^{-1}) or to a phosphine (1961 cm^{-1}) [17a], our compound shows an intermediate value (1958 cm^{-1}). Without any more references, it was not possible to assign the relative stereochemistry of compound **4**.

In a similar way, we investigated the reaction of complex **2** with acetonitrile to obtain the corresponding solvate-complex. Under the conditions reflected in Scheme 1, the cationic compound $[RuCl(PN)(PPh_3)(AN)_2]^+Cl^-$ (**5**) (molar conductivity in 5×10^{-4} M acetone solution: 37.99 Ω^{-1} cm^{-1} mol^{-1}) was obtained, whose spectroscopic analyses reflect the presence of two molecules of acetonitrile. Likewise, mass spectrum shows the molecular peak at *m*/*z* 853 (4%), the loss of one molecule of acetonitrile (*m*/*z* 807, 4%) and the loss of a second molecule (*m*/*z* 772, 100%). This new complex has typical ^{31}P NMR chemical shifts for *trans* P–Ru–N dispositions [4a] and a $J_{PP'}$ corresponding to a *cis* P–Ru–P arrangement (Table 1), suggesting the structure depicted in Fig. 2.

Thus, from the starting mixture of isomers of the 16-electron complex **2**, a single stereoisomer of each 18-electron complex **3**–**5** was formed in all cases. It is reasonable to assume that the chiral (PN) ligand controls the absolute configuration at octahedral ruthenium so that a single stereoisomer was obtained. Unfortunately, the absolute configuration at the ruthenium center is unknown; single-crystals suitable for X-ray diffraction could not be obtained for any of these compounds.

The obtention of complex **5** was not easy to control because the formation of the complex was indicated by the colour change of the solution. Then, when complex **2** was reacted with acetonitrile for long times or under heating, a new ruthenium complex (**6**) was detected. Refluxing of the reaction enhanced the presence of complex **6**, and the mixture of complexes became enriched in **6** after long reaction times (80% after 3 days of reaction under reflux). Complex **6** could not be purified from the mixture and, then, the characterization in the solid state was not attempted. The FAB mass spectrum obtained from the enriched mixture is quite similar to mass spectrum of **5**, and did not allow proposing a structure for complex **6**. The ^{1}H NMR spectrum of complex **6** reveals the presence of two molecules of acetonitrile and the (PN) ligand and the ^{31}P NMR spectrum confirms the absence of any other phosphorus atom. It seems that **6** is a five-coordinate complex arising from the loss of a PPh_3 ligand from **5**.

3.2. Catalytic asymmetric cyclopropanation of styrene using *1*–*6* Ru(II) complexes

Complexes **1**–**6** were examined as catalyst precursors in the cyclopropanation reaction between styrene and ethyl di-

Table 2
Asymmetric cyclopropanation of styrene with ethyl diazoacetate catalyzed by complexes **1**–**6**

Entry	Catalyst (molar ratio)	*t* addition/ *t* reaction (h)[a]	Yield (%)[b]	*cis*:*trans*[c]	ee *cis*[d] (major isomer)[e]	ee *trans*[d] (major isomer)[e]	Dimerization (%)[f]
1	–[g]	2/6	3	51:49	–	–	0
2	**1** (2%)	2/15	19	46:54	4% (1*S*,2*R*)	−2% (1*R*,2*R*)	23
3	**2** (2%)	2/6	28	58:42	22% (1*S*,2*R*)	20% (1*S*,2*S*)	31
4	**3** (2%)	2/6	31	54:46	22% (1*S*,2*R*)	30% (1*S*,2*S*)	41
5	**4** (2%)	2/6	17	55:45	18% (1*S*,2*R*)	0%	12
6	**5** (2%)	2/6	39	68:32	56% (1*S*,2*R*)	0%	4
7	**5** (2%)[h]	2/4	14	41:58	4% (1*S*,2*R*)	−2% (1*R*,2*R*)	52
8	**5** (2%)	2/0	40	68:32	56% (1*S*,2*R*)	0%	6
9	**5** (2%)	24/0	33	74:26	68% (1*S*,2*R*)	12% (1*S*,2*S*)	0
10	**6** (2%)	2/0	34	67:33	74% (1*S*,2*R*)	42% (1*S*,2*S*)	0
11	**6** (2%)	24/0	32	75:25	74% (1*S*,2*R*)	20% (1*S*,2*S*)	0
12	**6** (6%)[i]	2/0	36	32:68	74% (1*S*,2*R*)	34% (1*S*,2*S*)	0

[a] Reaction time was considered as stirring time after the addition was complete.
[b] Yield was calculated as the ratio between the formed cyclopropane compounds (determined by GC) and the starting ethyl diazoacetate.
[c] Ratio of *cis* and *trans* isomers was determined by GC analysis.
[d] Enantiomeric excess of the products was determined by GC using a chiral column (Cyclodex-B).
[e] Absolute configuration was determined by the comparison of the elution order found in the literature [13].
[f] Dimerization percentage was calculated as 2 × (fumarate mmol + maleate mmol) (mmol starting ethyl diazoacetate)$^{-1}$.
[g] Two blank tests without any ruthenium complex were carried out, one of them without silver triflate and another one with 0.05 mmol of AgOTf, and the same results were obtained.
[h] This experiment was carried out without AgOTf.
[i] 0.15 mmol of AgOTf was added.

azoacetate. Reactions were carried out by slowly adding a much-diluted solution of ethyl diazoacetate (EDA) to a solution containing styrene and the catalyst precursor. Under these conditions, the formation of maleic and fumaric acid esters, by-products of the metal-carbene dimerization, is kept to a minimum [13]. In accordance with the literature method, silver triflate was used as an activating agent to precipitate either part or all of the chloride anions [4c,18]. The results using these activated catalysts and two blank tests without any catalyst (with and without silver triflate) are summarised in Table 2. These tests make clear that, in the studied reaction conditions, AgOTf does not catalyse EDA decomposition in an appreciable extension.

Preliminary cyclopropanation tests in similar conditions (entries 2–6) indicated that, after activation by AgOTf, the complexes **1**–**5** showed catalytic activity. The yields were from low to moderate (17–39%) and the best results were found for complex **5**, with a moderate *cis*- enantio- and diastereoselectivity (*cis*: 56% ee, *cis*:*trans* ratio 68:32). Complex **5** was then more investigated (entries 7–9). Because complexes **5** and **6** were related, this last compound was also tested as catalyst. As complex **6** could not be isolated, the referred as "complex **6**" in Table 2 was really a mixture of complexes **6** and **5** in a ratio 5/1 (entries 10–12).

Half-sandwich complex $[(\eta^5\text{-}C_5Me_5)Ru(PN)(AN)]^+ PF_6^-$ (**1**) catalyzed the cyclopropanation reaction with low yield, enantio- and diastereoselectivity (entry 2). The loss of enantioselectivity could be consistent with the presence in the catalyst of the two diastereomers of reversed configuration at the metal, (S_{Ru},S_C)-**1** and (R_{Ru},S_C)-**1**. The low cyclopropane yield (19%) even after 15 h of reaction time, a much longer time than in the experiments with catalyst **2**–**6**, can be partially explained by the competitive dimerization of the carbene. However, as unreacted ethyl diazoacetate was still present in the solution reaction, the most probable explanation of the low cyclopropane yield is the intrinsic low activity of the catalyst. This poor catalytic behaviour (low yield and diastereoselectivity) is similar to reported in a recent work that described the use of ruthenium half-sandwich complexes with a non-stereogenic metal center, $[RuCl_2(\eta^6\text{-}p\text{-cymene})P^*]$ (P* = chiral fosforamidite) as catalysts in asymmetric cyclopropanation of olefins [19].

On the contrary, under the standard conditions (2% catalyst, presence of AgOTf), the family of complexes **2**–**6** showed a *cis* preference (entries 3–6, 8–11). Likewise, all of them catalyzed the cyclopropanation reaction with *cis*-enantioselectivity (from 18 to 74% ee). About the sense of the enantioselectivity, all the complexes **2**–**6** showed the same trend, being *cis*-(1*S*,2*R*) cyclopropane the major isomer. For catalysts **2**–**4**, the dimerization percentage is slightly higher than the cyclopropanation reaction. However, acetonitrile complexes **5** and **6** led predominantly (exclusively, for complex **6**) to the cyclopropane products.

The catalytic behaviour of five-coordinate complex **2** was very similar to that found for aqua-complex **3**, with a moderate enantioselectivity for both *cis* and *trans* cyclopropanes. The water molecule probably occupies a very labile position and, under the reaction conditions, complexes **3** and **2** evolve to the same catalytic intermediate. Compound **4**, however, showed quite different behaviour: a lower yield and enantioselectivity only for the *cis*-isomer. Thus, complex **4** is similar to compound **5** in terms of the catalytic trend (cf. entries 5 and 6). Complexes **5** and **6** led to the highest *cis*-diastereo- and enantioselectivities (56 and 74% ee, respec-

tively, entries 8 and 10). Slower addition of ethyl diazoacetate improved the *cis*- diastereo- and enantioselectivity for both complexes (entries 9, 11). Nevertheless, additional reaction time after the addition of EDA did not modify either yield or steroselectivities of the reaction (compare entries 6 and 8).

The presence of AgOTf proved to be essential for complex **5**. When the reaction was carried out in its absence, dimerization was much more significant than cyclopropanation, the *cis*-enantioselectivity fell and the *cis*:*trans* ratio was reversed (cf. entries 6 and 7).

Complex **6** is the most effective catalyst, with good *cis*- and moderate *trans*- selectivities (*cis*: 74% ee, *trans*: 42% ee). Since in all reactions no pure complex **6** was used, but an enriched mixture, it is possible that it was even more active. Any way, the catalytic behaviour of **6**, showing enantioselectivity for both diastereoisomers, is more similar to that found for the five-coordinate complex **3** than showed for six-coordinate complex **5** (cf. entries 4, 6 and 10), suggesting complex **6** as a coordinatively unsaturated 16-electron species.

It is notable that an increase in the ratio of catalyst **6** (from 2 to 6%) reversed the diastereoselectivity of the reaction, whereas the enantioselectivity for *cis*- and *trans*-diastereomers remained almost unchangeable (compare entries 10 and 12). It is possible that this different stereoselection was dependent on the association state (monomeric or aggregated) of complex **6**, which in turn would be dependent on the catalyst concentration. Taking this fact into account, we were able to perform both *cis*- and *trans*-selective asymmetric cyclopropanations with the same catalyst.

In conclusion, we have reported a family of ruthenium complexes that have a stereogenic metal center as catalysts for the asymmetric *cis*-selective cyclopropanation between styrene and ethyl diazoacetate. Although the absolute configuration of complexes **2**–**6** is not known, it is clear that it should be related with the configuration of the major cyclopropane isomer obtained in all the reactions, *cis*-(1*S*,2*R*). These preliminary results open the way to the use of enantiopure chiral-at-metal ruthenium complexes as catalyst in cyclopropanation reactions for a better understanding of the reaction mechanism.

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