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Aminophosphonite-phosphite and aminophosphonite-phosphinite ligands with mixed chirality: preparation and catalytic applications in asymmetric hydrogenation and hydroformylation

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Dedicated to Professor Renato Ugo on the occasion of his 65th birthday

Abstract

Aminophosphonite-phosphite and aminophosphonite-phosphinite chiral ligands with mixed stereogenic elements have been prepared in good yields from chiral α-aminoalcohols such as 2-(hydroxymethyl)pyrrolidine and 2-*N*-ethylammino-1-butanol. These new ligands have been fully characterized; the Rh(I) complexes have been tested in catalytic hydrogenation and hydroformylation reactions. Enantioselectivities up to 70% have been obtained in asymmetric hydrogenation of α-acetamidocinnamic acid, methyl ester; enantioselectivities higher than 30% and regioselectivities higher than 98% have been obtained in asymmetric hydroformylation of vinyl acetate.

Keywords: Aminophosphonite-phosphite; Aminophosphonite-phosphinite; Rh(I) complexes; Asymmetric hydrogenation; Asymmetric hydroformylation

1. Introduction

In recent years, metal complexes have become increasingly important in the field of organic synthesis: reactions such as catalytic asymmetric hydrogenation, hydroformylation, hydrocianation and isomerization are now recognized as effective alternatives in the strategic preparation of compounds which were believed to be impossible to carry out by conventional methods [1–3].

The greater part of the transition metals known as being excellent catalysts for asymmetric synthesis have optically active diphosphine ligands as a source of chirality but inspite of the wide variety of chiral ligands available there is still a demand for the development of catalysts which display the requirements of high enantioselectivity, diastereoselectivity and productivity in fine chemicals, fragrances, flavors and agrochemicals [4].

The development of new catalysts is closely connected to the development of new chiral ligands and particularly of those containing chiral phosphorous.

Today thousands of optically active phosphines are available but only a few of them produce catalysts

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which are able to show enantiomeric excesses higher than 95% enantiomeric eccesses (e.e.).

This implies that in the field of asymmetric catalysis there is still space and opportunity for research and development.

Since the early 1980s, one of us (EC) has been involved in the synthesis, characterization and use of aminophosphine-phosphinites in Rh(I) and Pt(II) catalyzed hydrogenations and hydroformylations.

We first demonstrated how it was possible to easily obtain viz. *N*-(diphenylphosphino)-2-((diphenylphosphinoxy)methyl)pirrolidine ((*S*)- and (*R*)-Prolophos) and 1-(diphenylphosphinoxy)-2-(*N*-ethyl-*N*-(diphenylphosphino)amino)butane ((*S*)- and (*R*)-Butaphos) (see Fig. 1a) from cheap α-aminoalcohols valuable and versatile aminophosphine-phosphinite [5].

The cationic rhodium(I) complexes $[Rh(COD)(P\text{-}P')]^+$ were shown to be efficient homogeneous hydrogenation catalysts toward several prochiral substrates [6]. The dichloro complexes of Pt(II) with the same ligands, in the presence of tin(II) chloride, were found to catalyze the hydroformylation of styrene to 2-phenylpropionaldehyde with an optical purity of up to 37% e.e. [7].

The palladium(II) complexes of the formula $[Pd(\eta^3\text{-allyl})(P\text{-}P')]X$, where P-P′ is (*S*)-Prolophos, catalyzed the reaction of racemic 1,3-dimethylprol-2-enylacetate or 1,3-diphenyl-2-enylacetate with sodium dimethyl-

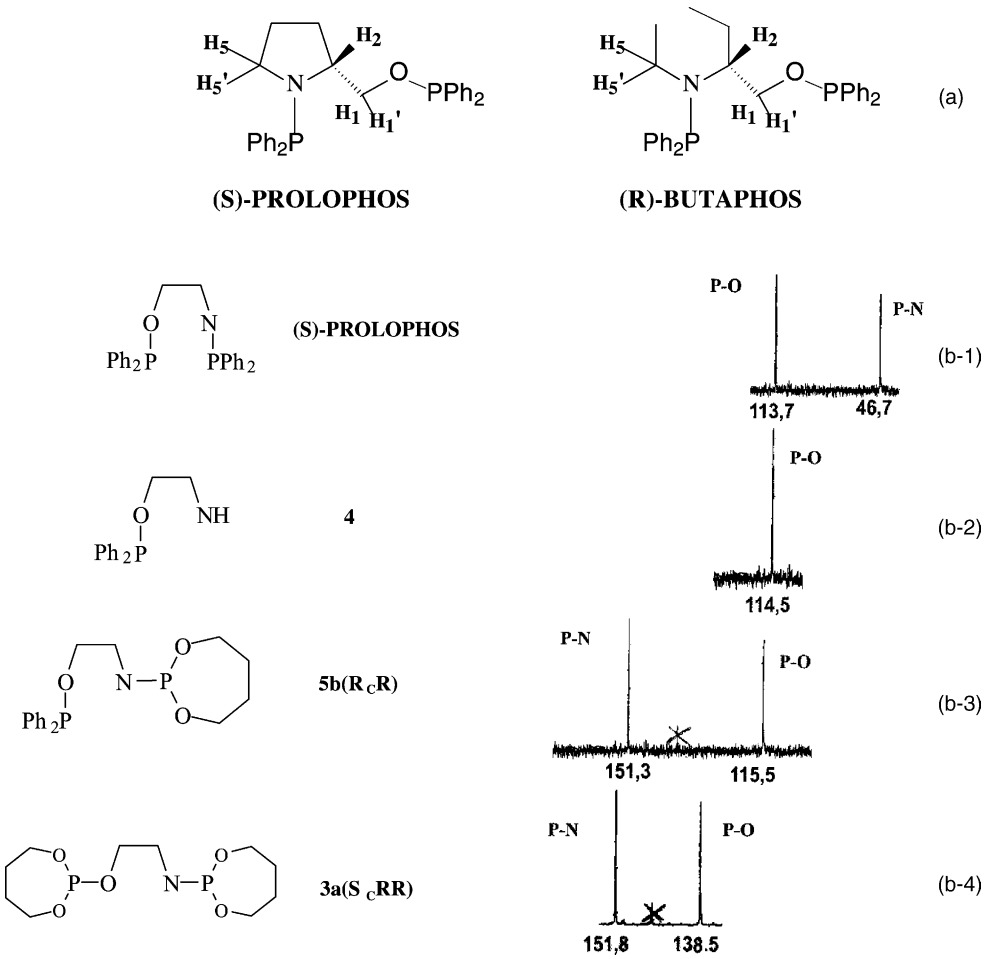


Fig. 1. Structures of the chiral ligands (a) and ^{31}P-NMR assignments (b1–4, c).

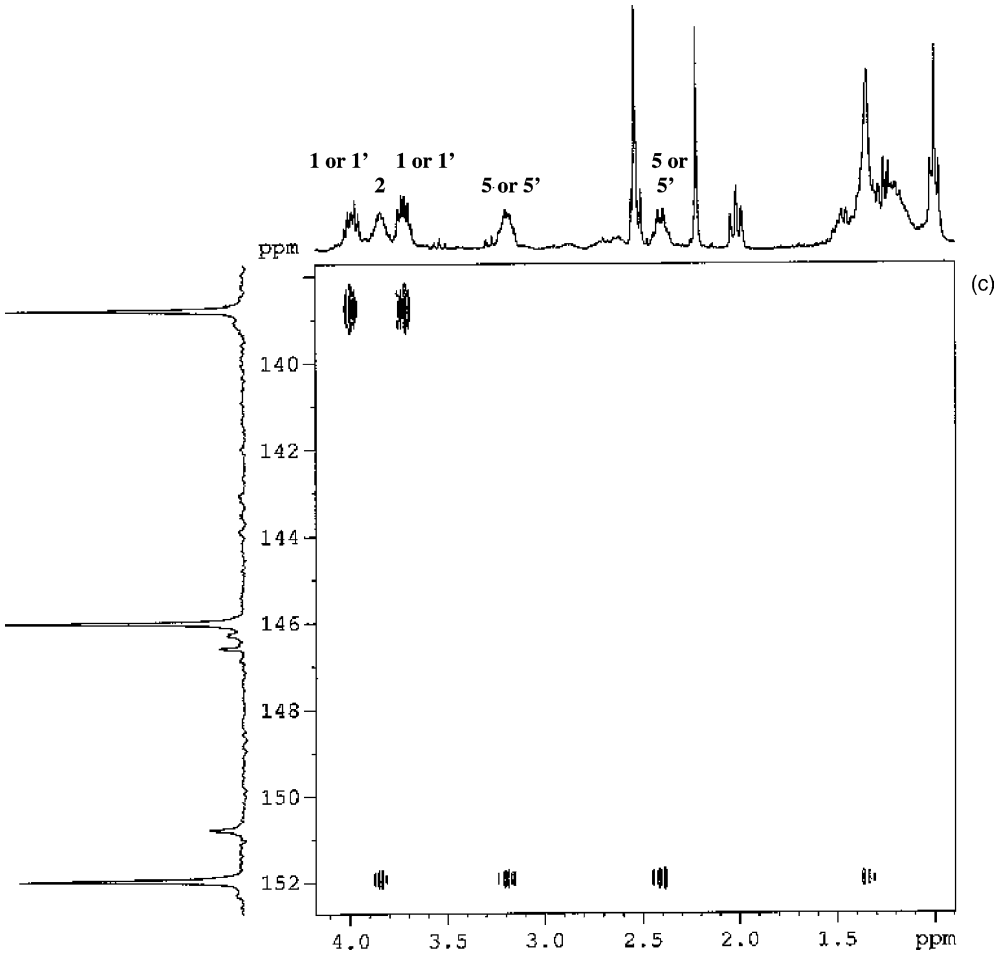


Fig. 1. (*Continued*).

malonate to give the allylic alkylation products in 20 and 30% e.e., respectively [8].

Our interest in the field together with the results achieved by the development of a new class of atropisomeric ligands based on biheteroaromatic rings [9–11] prompted us to investigate the development of new "mixed" electrondeficient aminophosphonite-phosphite and aminophosphonite-phosphinite. The term "mixed" indicates that the ligands gather one stereogenic sp^3 carbon atom of the aminoalcohol backbone with the stereogenic axis of the 1,1′-binaphthyl moiety; we describe here, the synthesis and the use of these ligands in the Rh(I) enantioselective hydrogenations and hydroformylations of different prochiral substrates.

2. Experimental

General: Preparation of both ligands and catalysts are performed under inert atmosphere (argon) using the standard Schlenk techniques. The catalytic reactions are performed in a 200 ml stainless steel autoclave equipped with temperature control and magnetic stirrer.

^{1}H- and ^{31}P-NMR spectra are recorded on a Bruker AC300 equipped with a non-reverse probe and also on a Bruker DRX300 Avance (see Fig. 1 for the numbering of the hydrogen atoms).

Elemental analysis are performed on a Perkin-Elmer 2400 CHN; GC analysis: DANI GC86.10 equipped with a capillary column with a chiral stationary phase

MEGA DAcTButSilBETA (25 m, internal diameter 0.35 mm); HPLC analysis: Merck-Hitachi L-7100 equipped with Detector UV6000LP; polarimetric analysis: Perkin-Elmer model 343 Plus.

2.1. Preparations of the ligands

2.1.1. Preparation of 2

2 is prepared according to ref. [12][1].

^{1}H-NMR (C_6D_6): $\delta = 6.9$-7-7 (m 12 H, aromatic); ^{31}P-NMR (C_6D_6): $\delta = 179.5$ ppm (s 1P).

2.1.2. Preparation of ***3a(S$_C$RR)***

Seventy-seven milligram (0.76 mmol) of (*S*)-2-pyrrolidinemethanol and 0.32 ml (2.3 mmol) of triethylamine are dissolved in 10 ml of toluene. The solution is cooled at 0 °C and a solution of the ligand **2** (532 mg, 1.52 mmol) in toluene (5 ml) is added dropwise within 30 min.

The reaction mixture is stirred overnight, then 10 ml of diisopropylether are added to the reaction mixture. After filtration of the ammonium salt the solvent is evaporated leaving a sticky solid. This solid is washed in hexane (3 × 10 ml) leaving 460 mg, 83% yield, of **3a(S$_c$RR)**.

^{1}H-NMR (C_6D_6): δ = 6.8–8 ppm (m 24 H, aromatic); 4.0 ppm (m 1H, hydrogen 1 or 1′); 3.8–3.9 ppm (broad m 1H, hydrogen 2); 3.7 ppm (m 1H, hydrogen 1′ or 1); 3.2 ppm (m 1H, hydrogen 5 or 5′); 2.4 ppm (m 1H, hydrogen 5′ or 5); 1.2–1.6 ppm (broad m 4H, –CH_2–CH_2–); ^{31}P-NMR (C_6D_6): δ = 151.8 ppm (s $P(O)_2(N)$); 138.5 ppm (s $P(O)_2(O)$). Elemental analysis calculated for $C_{45}H_{33}NO_5P_2$: C, 74.07; H, 4.56; N, 1.9, found: C, 73.96; H, 4.45; N, 1.87. $[\alpha]_D^{25} = -424.2$ ($c = 0.108$, $C_6H_5CH_3$).

2.1.3. Preparation of ***3b(S$_C$SS)***

The ligand is prepared as **3a(S$_c$RR)**.

^{1}H-NMR (C_6D_6): δ = 6.9–8.1 ppm (m 24 H, aromatic); 4.1 ppm (broad m 1H, hydrogen 1 or 1′); 3.7–4.0 ppm (broad m 1H, hydrogen 2); 3.7 ppm (m 1H, hydrogen 1′); 3.3 ppm (m 1H, hydrogen 5); 2.3 ppm (m 1H, hydrogen 5′); 1.2–1.7 ppm (broad m 4H, –CH_2-CH_2-); ^{31}P-NMR (C_6D_6): δ = 149.2 ppm (s $P(O)_2(N)$); 137.9 ppm (s $P(O)_2(O)$). Elemental analysis calculated for $C_{45}H_{33}NO_5P_2$: C, 74.07; H, 4.56; N, 1.9, found: C, 74.02; H, 4.52; N, 1.88. $[\alpha]_D^{25} = +463.9$ ($c = 0.099$, $C_6H_5CH_3$).

2.1.4. Preparation of ***5b(R$_C$R)***

Sodium hydride (125 mg, 5.21 mmol) is suspended in 10 ml of THF and stirred for 10 min at room temperature. To the suspension a solution of (*R*)-(−)-2-ethylamino-1-butanol (604 mg, 5.16 mmol) in 10 ml of THF is added dropwise and the mixture is stirred until no more evolution of hydrogen is observed; the suspension is cooled at 0 °C and a solution of chlorodiphenylphosphine (1.137 g, 5.15 mmol) in 5 ml of THF is added dropwise.

The suspension is heated at room temperature and stirred for 1 h, treated with 10 ml of diisopropylether, filtered and evaporated to dryness leaving **4** as a white solid in 60% yield; the product is used immediately without further purification. It is dissolved in 10 ml of toluene, triethylamine (0.42 ml, 3.0 mmol) is added and the solution is cooled at 0 °C. A solution of **2** (595 mg, 1.69 mmol) in 5 ml of toluene is added dropwise and the raction mixture is stirred overnight. Ten milliliter of diisopropylether are added to the reaction mixture; after filtration of the ammonium salt the solvent is evaporated leaving a sticky solid. This solid is washed in hexane (3 × 10 ml) leaving 1.17 g of **5b(R$_c$R)** (37% yield based on (*R*)-(−)-2-ethylamino-1-butanol).

^{1}H-NMR (C_6D_6): δ = 6.9–7.8 ppm (m 22 H, aromatic); 4.0 ppm (m 1H, hydrogen 1 or 1′); 3.9 ppm (m 1H, hydrogen 1′ or 1); 3.4 ppm (m 1H, hydrogen 2); 2.9 ppm (m 1H, hydrogen 5 or 5′); 2.7 ppm (m 1H, hydrogen 5′ or 5); 1.6 ppm (m 2H, hydrogens 3 and 3′); 1.0 ppm (t 3H, methyl); 0.8 ppm (t 3H, methyl); ^{31}P-NMR (C_6D_6): δ = 151.0 ppm (s $P(O)_2(N)$); 115.5 ppm (s $P(Ph)_2(O)$). Elemental analysis calculate for $C_{38}H_{35}NO_3P_2$: C, 74.14; H, 5.73; N, 2.28, found, C, 74.07; H, 5.68; N, 2.22. $[\alpha]_D^{25} = -212.87$ ($c = 0.101$, $C_6H_5CH_3$).

2.1.5. Preparation of ***5a(R$_C$S)***

The ligand is prepared as **5b(R$_c$R)**.

^{1}H-NMR (C_6D_6): δ = 6.8–7.9 ppm (m 22 H, aromatic); 3.9 ppm (m 1H, hydrogen 1 or 1′); 3.8 ppm (m 1H, hydrogen 1′ or 1); 3.6 ppm (m 1H, hydrogen 2); 2.9 ppm (m 1H, hydrogen 5 or 5′); 2.8 ppm (broad

[1] The (*S*)- or (*R*)- 1,1′-binaphthyl-2,2′ diylphosphite chloride is prepared following the method suggested by Prof. Faraone with minor modifications.

m 1H, hydrogen 5′ or 5); 1.6 ppm (broad m 2H, hydrogens 3 and 3′); 1.1 ppm (t 3H, methyl); 0.7 ppm (t 3H, methyl); ^{31}P-NMR (C_6D_6): $\delta = 151.3$ ppm (s $P(O)_2(N)$); 115.5 ppm (s $P(Ph)_2(O)$). Elemental analysis calculated for $C_{38}H_{35}NO_3P_2$: C, 74.14; H, 5.73; N, 2.28, found: C, 74.09; H, 5.68; N, 2.23. $[\alpha]_D^{25} = +206.1$ ($c = 0.098$, $C_6H_5CH_3$).

2.2. General procedure for hydrogenation of *6a* and *6b*

The ligands (0.012 eq.) and $[Rh(COD)_2]ClO_4$ (0.01 eq.) are placed in a Schlenk tube sealed with a rubber septum under an argon atmosphere; CH_2Cl_2 (5 ml) is added and the homogeneous yellow solution is stirred for 15 min, evaporated to dryness and kept under vacuum for 1 h. The catalyst is used without further purification. The substrate (1 eq.) is added to the solid phosphine–Rh(I) complex, followed by 30 ml of THF. The solution is stirred for 30 min and then transferred to an autoclave with a cannula.

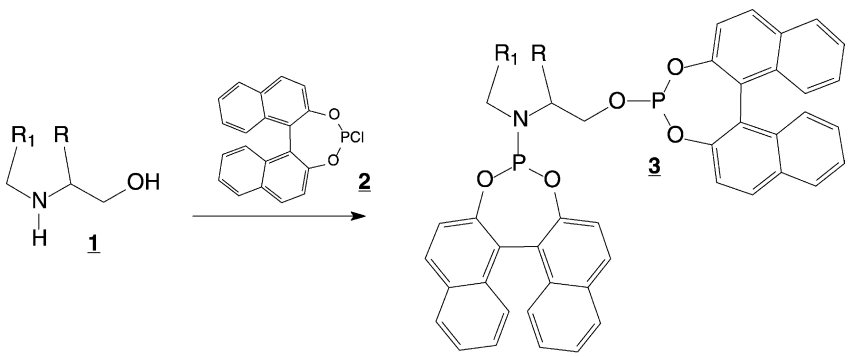
The stainless steel autoclave (200 ml), equipped with temperature control and magnetic stirrer, is purged five times with hydrogen before use. After the transfer of the reaction mixture, the autoclave is pressurized. At the end of the reaction, the autoclave is vented, the catalyst is removed by filtration on a short pad of cellulose and the solvent is evaporated. The conversion is determined by ^{1}H-NMR. The enantiomeric excess of **7b** is determined by HPLC on a chiral stationary phase column (Diacel Chiralcel OD, *n*-hexane/isopropanol = 9/1 0.8 ml/min, $\lambda = 210$ nm); the enantiomeric excess of **7a** is determined as for **7b**, after esterification with $(CH_3)SiCHN_2$ or CH_2N_2. The absolute configuration is determined by the sign of the optical rotation.

2.3. General procedure for hydroformylation of *8*

The ligands (0.01–0.03 eq.), $[Rh(CO)_2acac]$ (0.01 eq.) and vinylacetate **8** (6–20 eq.) are placed in a Schlenk tube, THF (1 ml) is added to assure homogeneous conditions and the resulting solution is stirred for 30 min and then transferred to a stainless steel autoclave previously purged five times with a H_2/CO mixture. At the end of the reaction, the autoclave is vented and the residue is vacuum distilled. The branched/linear ratio (**9**/**10**) and the conversion are determined by ^{1}H-NMR and GC-MS; the enantiomeric excess of **9** is determined by GC on a chiral stationary phase column (Mega DAcTButSilBETA 25 m, internal diameter 0.35 mm).

3. Results and discussion

Scheme 1 describes the preparation of aminophosphonite-phosphite "symmetrically" disubstituted with (*S*)- or (*R*)-binaphthyldiylphosphite at the nitrogen and oxygen atoms, **3**.



3 = Aminophosphonite-phosphite

3a : R = R$_1$= (CH$_2$)$_2$
3b : R =-CH$_2$-CH$_3$ R$_1$=H

Scheme 1.

This "one pot" reaction closely resembles the preparation of (*S*)-Prolophos and (*S*)- or (*R*)-Butaphos described by one of the authors (EC) some years ago [5,6].

The reaction between the suitable chiral aminoalcohol and (*S*)- or (*R*)- 1,1′-binaphthyl-2,2′ diylphosphite chloride, (*R*)-(+)-**2** or (*S*)-(−)-**2**, is performed in toluene at 0 °C in the presence of a stoichiometric amount of triethylamine.

The course of the reactions is monitored by ^{31}P-NMR-(C_6D_6): the 1,1′-binaphthyl-2,2′-diylphosphite chloride, characterized by a signal at approximately 179 ppm [12], disappears completely in 12 h. The ligands of type **3** show two signals at approximately 151 and 138 ppm, attributed to P(N) and P(O), respectively.

^{31}P-NMR signals of minor intensities, usually less than 20%, appear at 140–145 ppm and around 0 ppm; these signals however disappear after several washings with hexane.

After the filtration of the ammonium salt the clear solutions are evaporated to dryness leaving sticky white solids.

The ligands are obtained in 80% yield or more as colourless solids after the usual work up and accurate washing with hexane.

The ligands are fully characterized by elemental analysis, ^{1}H- and ^{31}P-NMR spectroscopy.

The "dissymmetric" aminophosphonite-phosphinite ligands of type **5** are prepared in a similar manner as reported in Scheme 2.

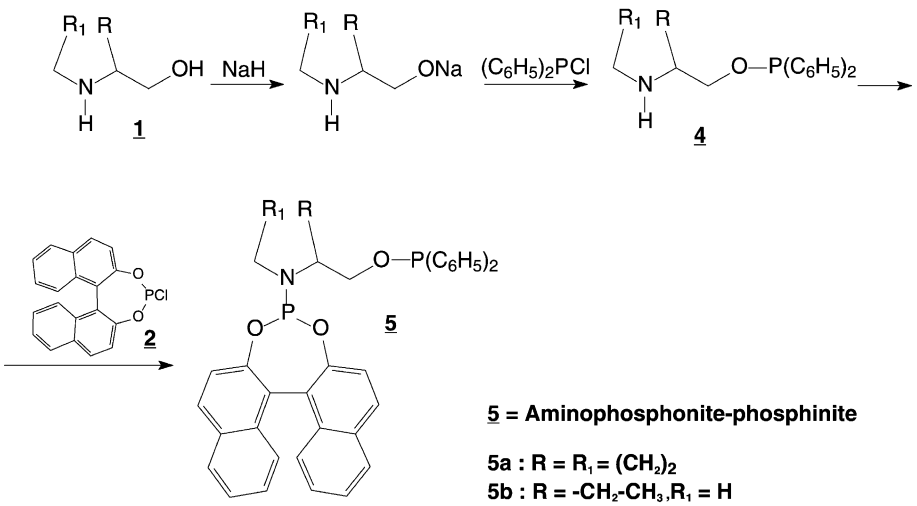
The chiral aminoalcohols are transformed into the corresponding sodium alcoholates with an equivalent amount of sodium hydride in THF; chlorodiphenylphosphine is then added slowly to give the corresponding monosubstituted aminophosphinite **4** characterized by a singlet at 114.5 ppm in the ^{31}P-NMR spectra.

The aminophosphinites **4** react with (*R*)-(+)-**2** or (*S*)-(−)-**2** in toluene in the presence of triethylamine to quantitatively give the corresponding "disimmetrically" substituted aminophosphonite-phosphinites **5**.

The reactions are monitored by ^{31}P-NMR and they are complete when the signal at approximately 179 ppm of (*R*)-(+)-**2** or (*S*)-(−)-**2** disappears, while a new signal at approximately 151 ppm joins the signal at approximately 115 ppm of the phosphinite group. Evaporation of the solvent, followed by the usual work up, leaves the aminophosphonite-phosphinites as white solids in an almost pure form.

The ligands are fully characterized by elemental analysis, ^{1}H- and ^{31}P-NMR spectroscopy.

The ^{1}H-NMR spectra of all **3a**, **5a**, **3b** and **5b** are almost superimposable and closely resemble the



Scheme 2.

^{1}H-NMR spectra of Prolophos and Butaphos that have already been fully described in terms of multiplicity and chemical shift [8,13].

This observation let us assign the ^{31}P-NMR signals of the new ligands by a combination of ^{1}H- and ^{31}P-NMR selective decoupling and heteronuclear multiple quantum correlation (HMQC).

Fig. 1 contains the ^{31}P-NMR of the new ligands of the intermediate products and that of (*S*)-Prolophos for comparison.

Spectrum b-1 shows the ^{31}P-NMR spectra of (*S*)-Prolophos in which the two signals at 113.7 and 46.7 ppm are unambiguously assigned to diphenylphosphinite [$Ph_2P(O)$] and to diphenylphosphine [$Ph_2P(N)$], respectively [8,13].

Spectrum b-2 shows the ^{31}P-NMR signals of the monophosphinite intermediate **4** with a singlet located at 114.5 ppm, quite close to the corresponding signal of the P(O) group in the (*S*)-Prolophos.

Spectrum b-3 shows the ^{31}P-NMR spectra of the ligand **5b(R_cR)** in which only two singlets are present at 151.3 and 115.5 ppm.

These results support the theory that the signal located at approximately 115 ppm can be assigned to the phosphinite $P(Ph)_2(O)$ and, as a consequence, the signal at approximately 151 ppm should be assigned to the aminophosphonite $P(O)_2(N)$ group.

Spectrum b-4 shows the ^{31}P-NMR of the ligand **3a(S_cRR)** "symmetrically" disubstituted, in which the binaphthyl moieties are bound to the nitrogen and to the oxygen atoms; the spectra shows two singlets at 151.8 and 138.5 ppm.

Assuming that the signal at approximately 151 ppm is correctly assigned to the aminophosphonite group (vide supra) then the signal at approximately 138 ppm can be assigned to phosphite O-$P(O)_2$. The ^{1}H-^{31}P selective decoupling (spectra not reported) shows that the multiplets at 4.0 (1 or 1′), 3.82 (2), 3.75 (1′ or 1), 3.2 (5′ or 5) and 2.4 (5′ or 5) ppm are hydrogen atoms which are more strongly coupled with the phosphorous atoms (see Fig. 1a for the numbering of hydrogen atoms); however, the HMQC plot obtained at 5.0 Hz (Fig. 1c) clearly indicates that the signal at approximately 151 ppm is coupled with the hydrogens marked as 2, 5 and 5′ but not with the hydrogens 1 and 1′; the signal at approximately 138 ppm is exclusively coupled with 1 and 1′ hydrogens but not with the other hydrogen atoms of the chiral skeleton.

The only possible conclusion is that the signals at approximately 151 ppm belong to the aminophosphonite and the signal at approximately 138 ppm belong to phosphite group, confirming the previous observation based on the comparison of the chemical shifts.

Analogous NMR experiments on the ligands **3b**, **5a** and **5b** give similar results, allowing us to assign the NMR signals of the phosphorous atoms unambiguously in all ligands prepared.

The ligands react smoothly with $[Rh(COD)_2]^+ClO_4^-$ to give the corresponding $[Rh(COD)(P\text{-}P')]^+ClO_4^-$ compounds according to standard procedures.

These type of cationic complexes are well-known catalysts for the asymmetric hydrogenation of prochiral substrates, mainly (*Z*)-α-*N*-acylaminoacrylic acids and esters.

Table 1 summarizes the results of the asymmetric reduction of the *N*-acetyldehydrocinnamic acid **6a** and of its methylester **6b**.

All the asymmetric hydrogenations are carried out in THF with a 100/1 ratio of substrate/catalyst. The same reactions carried out in MeOH, which is the solvent of choice for this catalytic reductions, are slow and the protic solvents lead to an extensive decomposition of the ligands.

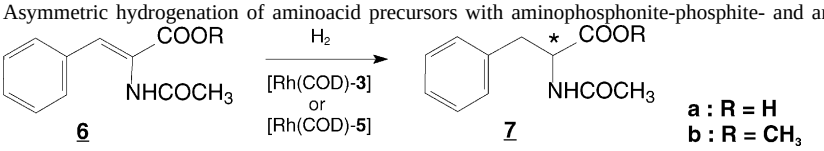
All the catalysts tested give 100% conversion in a reaction time ranging from 3 min to 6 h; the methylester **6b** usually gives enantiomeric eccesses slightly higher than the corresponding acid **6a**.

The highest e.e.% is obtained with catalyst Rh(I)-**3a**(S_cRR), in which the *S* configuration of the stereogenic carbon atom of the ligand backbone (S_c) is matched with the *R* axial configuration of the two binaphthyl moieties (entries 1–3).

The lowering of the temperature from 30 to 0 °C and the increasing of the partial pressure from 1 to 100 atm. do not modify significantly the stereochemical outcome; the e.e.% changes from 59 to 67% (entries 2 and 3) and the prevailing configuration of the product is *R*. When the axial configuration is changed from *R* to *S*, the steric control of the catalyst is dramatically decreased to 24 and 12% (entries 4 and 5) and the prevailing configuration of the product becomes *S*.

A similar trend is observed with the catalysts of type Rh(I)-**5**, in which the configuration of the stereogenic carbon atom is matched with only one binaphthyl group bound to the nitrogen atom; the Rh(I)-**5b**R_cS catalysts give only a modest 7% e.e.

Table 1
Asymmetric hydrogenation of aminoacid precursors with aminophosphonite-phosphite- and aminophosphonite-phosphinite-Rh(I)



6 7

Entry	Substrate	Catalyst	T (°C)	t (min)	H_2 (atm)	e.e. (%)	Configuration
1	6b	Rh(I)-**3a**(ScRR)	30	90	10	63	*R*
2	6b	Rh(I)-**3a**(ScRR)	0	60	100	67	*R*
3	6a	Rh(I)-**3a**(ScRR)	30	360	1	59	*R*
4	6b	Rh(I)-**3a**(ScSS)	30	30	10	12	*S*
5	6a	Rh(I)-**3a**(ScSS)	30	300	1	24	*S*
6	6b	Rh(I)-**5b**(RcR)	30	3	100	44	*S*
7	6a	Rh(I)-**5b**(RcR)	30	210	1	24	*S*
8	6b	Rh(I)-**5b**(RcS)	30	40	10	17	*R*
9	6a	Rh(I)-**5b**(RcS)	30	300	1	7	*R*

(entry 9) compared to Rh(I)-**5b**(R_cR) (entry 7); with the substrate **6b** when the axial configuration changes from *S* to *R*, an even greater variation in the steric control is obtained and the e.e.% changes from 17 to 44% (entries 6 and 8).

It is worth mentioning; however, that the *R* axial configuration in catalysts of type Rh(I)-**3**, in which two atropisomeric binaphthyl moieties are present, invariably produces the *N*-acetylphenylalanine and its methyl ester with *R* configuration; the same *R* atropisomeric chirality in complex of type Rh(I)-**5**, in which only one atropisomeric binaphthyl group is present, produces the aminoacid and its methyl ester with the opposite *S* configuration.

The catalytic hydroformylation reaction, in its asymmetric variant, is an extremely powerful synthetic tool for the preparation of optically active aldehydes. These compounds are extremely valuable precursors for a variety of drugs, agrochemicals and food additives [14,15].

In recent years, the major breakthrough in asymmetric hydroformylation is related to the development of Binaphos, a phosphane-phosphite ligand; the Binaphos Rh(I) complexes give high stereoselectivities together with good chemo- (hydroformylation against hydrogenation) and regioselectivity [16,17]; due to the close similarities between Binaphos and the ligands developed in this work, we have extended our investigation to the asymmetric hydroformylation with Rh(I)-complexes derived from the aforementioned ligands; some preliminary results concerning the asymmetric hydroformylation of vinyl acetate **8** are reported in Table 2.

We have used $Rh(CO)_2(acac)$ as the catalyst precursor; the catalysts are prepared "in situ" mixing the appropriate ligand with [$Rh(CO)_2$acac]; the molar ratio ligand:metal is varied from 1:1 to 3:1; all hydroformylation reactions are performed at 60 °C with a 1:1 mixture of H_2 and CO and the pressure of the H_2/CO mixture is varied from 30 to 100 atm.; a minimum amount of THF (usually 1 ml) is added to both catalyst and substrates to assure homogeneous conditions. All the catalysts show a remarkably high regioselectivity, the ratio of branched to linear acetoxypropanal being **9**/**10** is usually higher than 96/4 and we have never observed hydrogenation to ethylacetate.

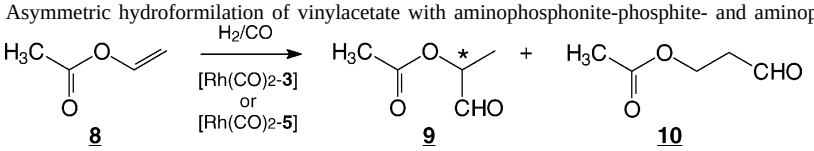
All the catalysts show that the chirality of the prevailing enantiomer in **9** is mainly due to atropisomeric chirality of the binaphthyl group.

The best results are obtained with catalyst Rh(I)**3a(S_cRR)** (entry 1).

The rise of the substrate/catalyst ratio dramatically reduces the activity of the catalyst even if the branched acetoxypropanal remains the only product of the reaction (entry 2).

It is worth mentioning that usually the hydroformylation with Rh(I) complexes is performed with an excess of ligand to prevent the formation of [$Rh(H)(CO)_4$] which is an active catalyst for the synthesis of the linear aldeydes [18].

Table 2
Asymmetric hydroformilation of vinylacetate with aminophosphonite-phosphite- and aminophosphonite-phosphinite-Rh(I)



8 **9** **10**

Entry	Catalyst	P-P/Rh	*T* (°C)	H_2/CO (atm)	S/Cat	Conversion % (h^{-1})	Binaphos/ligands (b/l)	e.e. (%)
1	Rh(I)-**3a**(ScRR)	1	50	50	675	90 (24)	97/3	32
2	Rh(I)-**3a**(ScRR)	3	60	40	2076	5 (20)	>99/1	32
3	Rh(I)-**3a**(ScSS)	3	60	35	2076	3 (20)	>99/1	18
4	Rh(I)-**5b**(RcR)	3	60	40	2076	40 (20)	96/4	14
5	Rh(I)-**5b**(RcR)	2	60	30	1285	35 (96)	99/1	19
6	Rh(I)-**5b**(ScS)	2	70	100	1350	98 (60)	98/2	2
7	Rh(I)-**5b**(ScR)	2	70	100	1350	90 (60)	96/4	6
8	Rh(I)-**5a**(ScR)	2	60	70	1350	35 (60)	95/5	12

We have used a ligand/Rh ratio of 2 or higher in order to compare chemo-, regio- and enantioselectivities with those of other catalytic systems. In our case, the rise of the ligand/Rh ratio does not affect the enantioselectivity but strongly reduces the activity of the catalyst (entries 1 and 2).

When the chirality of the binaphthyl group is changed from *R* to *S*, the regioselectivity remains unaffected but the enantiselectivity is almost halved (entry 3) in favour of the opposite enantiomers.

The catalysts Rh(I)**5** appear to be less reactive than the corresponding Rh(I)**3** complexes and show lower enantioselectivities.

The increase of the total pressure results in a significant enhancement of the reaction rate with a pronounced loss of enantioselectivity (entries 6 and 7).

This trend is opposed to that observed in the BINAP-Rhodium(I) catalyzed conversion of **8** to **9** where decreasing the total pressure of the 1:1 mixture of CO/H_2 from 50 to 10 atm. causes a significant enhancement of the reaction rate (BINAP: 2,2′-bis(diphenylphosphino)-1,1′-binaphtyl) [19].

4. Conclusions

Aminophosphonite-phosphite and aminophosphonite-phosphinite ligands with mixed stereogenic elements produce Rhodium(I) complexes which are active catalysts for the asymmetric hydrogenation of *N*-acetyl dehydroalanine and of its methyl ester (enantiomeric excess up to 70% are achieved).

The Rhodium(acac) $(CO)_2$ complexes with the same ligands are active in the asymmetric hydroformylation of vinylacetate; very high regioselectivities of the branched aldehyde **8** are obtained with enantiomeric excesses up to 32%.

The data seem to assign a primary importance to axial chirality and minor role to the chirality of the stereogenic sp^3 carbon atoms both in hydrogenation and in hydroformylation.

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