Enantioselective Hydroformylation with the Chiral Bidentate *P,N*-Ligand 2-[1-(1*S*,2*S*,5*R*)-(−)menthoxydiphenylphosphino]pyridine Cationic Rhodium(I) Complexes

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Cationic rhodium(I) complexes containing the new chiral bidentate *P,N* ligand 2-[1-(1*S*,2*S*,5*R*)-(−)menthoxydiphenylphosphino]pyridine are prepared and used successfully in the enantioselective hydroformylation of olefinic substrates, styrene, 2-vinylnaphthalene, methylacrylate and vinylacetate.

The asymmetric hydroformylation of olefins is a useful synthetic method for preparing optically active aldehydes.[1] In these processes rhodium[2] or platinum[3] systems in the presence of optically active tertiary phosphines, flexible diphosphines and, recently, diphosphite ligands have been used as catalysts. To be effective the chiral ligand must remain coordinated to the metal centre during the catalytic process; for this reason enantioselective hydroformylations have been extensively studied using chiral ligands having *P*-donor atoms. The lack of knowledge on the effect of bidentate *P,N*-ligands in asymmetric hydroformylation of olefins prompts us to synthesize the ligand 2-[1-(1*S*,2*S*,5*R*)-(−)menthoxydiphenylphosphino]pyridine, and to use rhodium(I) cationic complexes with this ligand as catalyst precursor.

As shown in Scheme 1, we prepared the new ligand 2-[1-(1*S*,2*S*,5*R*)-(−)menthoxydiphenylphosphino]pyridine, [(−)-menthoxy-PPy], in a two-step reaction. Changes in the absolute configuration do not occur during the last step of the process because it does not involve carbon atoms.‡ The chiral ligand 2-[1-(−)menthoxydiphenylphosphino]pyridine is a yellowish liquid and its absolute configuration as 2-[1-(1*S*,2*S*,5*R*)-(−)menthoxydiphenylphosphino]pyridine was deduced from the X-ray crystal structure of $\{Rh(C_8H_{12})[2\text{-}(1S,2S,5R)\text{-}(-)\text{menthoxydiphenylphosphino}]\text{pyridine}\}ClO_4$.

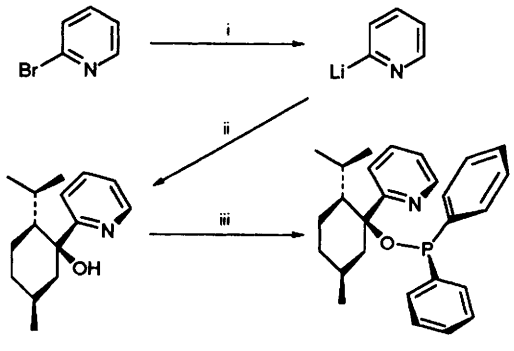
Thus, the same absolute configuration must be assigned to 2-(−)mentholpyridine.

The complex $\{Rh(C_8H_{12})[(-)\text{menthoxy-PPy}]\}ClO_4$, **1**, was prepared from $[Rh(C_8H_{12})(solv)_2]ClO_4$ (obtained from $[Rh(C_8H_{12})Cl]_2$ and $AgClO_4$, in the molar ratio 1:2, in THF at room temp.). The complex **1** was characterized from micro-analysis, IR and NMR spectroscopic data, and an X-ray crystal structure determination.§

CO was bubbled, at room temp., 1 atm, through a CH_2Cl_2 solution containing **1** and PPh_3 (1:1), the compound $\{Rh(CO)(PPh_3)[(-)\text{menthoxy-PPy}]\}ClO_4$, **2**, was formed almost quantitatively. A structure in which the phosphorus atoms of (−)-menthoxy-PPy and PPh_3 are *trans* to each other was assigned on the basis of the $^{31}P\{^1H\}$ NMR spectrum.¶

The results of the hydroformylation of olefinic substrates catalysed with cationic rhodium(I) complexes containing the chiral *P,N*-chelate ligand (−)-menthoxy-PPy are shown in Table 1. The presence of the *P,N*-chelate ligand (−)-menthoxy-PPy in the rhodium(I) catalyst allows good catalytic activity in the hydroformylation of the olefinic substrates styrene, 2-vinylnaphthalene, methylacrylate and vinylacetate.

The hydroformylation of styrene under 50 atm. of 1:1 CO/H_2 mixture at 70 °C proceeds almost quantitatively in 4 h with catalyst precursors **1** and **2**. As catalyst precursor in this reaction, **1** is less effective than **2**; at 30 atm and 70 °C the conversion of the styrene is 50% by **1** and 98% by **2**. The chemoselectivity of the reaction is very satisfactory, the linear 3-phenylpropanal and branched 2-phenylpropanal aldehydes being more than 99.5% of the reaction products. High regioselectivity for branched:linear (B/L) aldehyde was found (run 1, 2 and 3). The enantioselectivity achieved with (−)-menthoxy-PPy cationic rhodium(I) complexes in the hydroformylation of styrene was very low and the (*R*)-2-phenylpropanal was obtained with only 6% e.e. even at lower temperature resulting in a relatively low conversion of styrene to aldehyde. On changing the CO/H_2 ratio (2.1–0.4) and the total pressure (30 atm) the e.e. is the same.



Scheme 1 *Reagents and conditions*: i, Bu^{t}Li in THF at −78 °C; i, (−)menthone and hydrolysis;† iii, Bu^{t}Li, Ph_2PCl at 0 °C

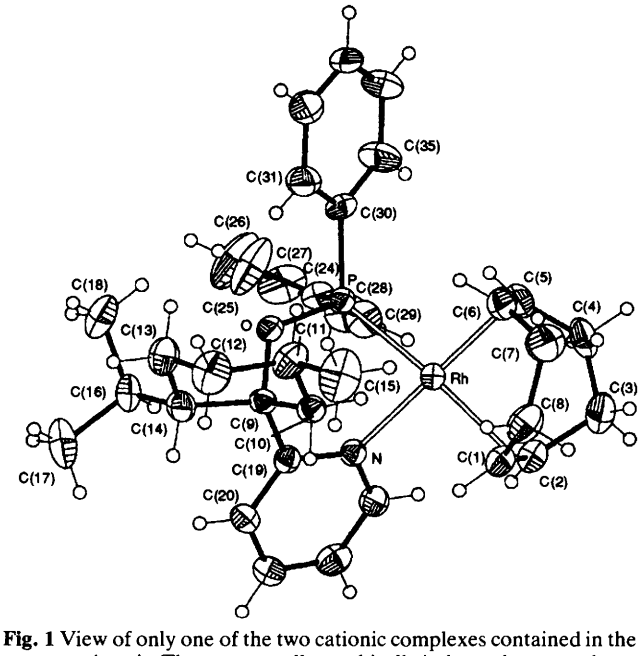


Fig. 1 View of only one of the two cationic complexes contained in the asymmetric unit. The two crystallographically independent complexes are similar and have the same numbering scheme for the corresponding atoms. Thermal ellipsoids are drawn at 40% of probability while hydrogen size is arbitrary and perchlorate anions are omitted for clarity. The rhodium coordination is mainly characterized by the bond lengths (Å) and angles (°) (with two values corresponding to the two complexes): Rh–N 2.133(4) [2.149(4)], Rh–P 2.221(1) [2.222(1)], Rh–centre$_{C1=C2}$ 2.208(6) [2.191(6)], Rh–centre$_{C5=C6}$ 2.030(7) [2.030(5)], N–Rh–P 81.0(1) [81.9(1)], centre$_{C1=C2}$–Rh–centre$_{C5=C6}$ 85.9(2) [85.4(2)], N–Rh–centre$_{C1=C2}$ 95.0(2) [96.0(2)], centre$_{C5=C6}$–Rh–P 98.3(2) [96.6(2)].

Table 1 Hydroformylation of olefins catalysed by rhodium complexes **1** and **2**[a]

Run	Catalyst	Substrate	*P*/atm	*T*/°C	*t*/h	Conversion (%)[b]	B/L[c]	ee (%)
1	**1**	Styrene	50	70	4	100	88/12	6(*R*)[d]
2	**1**	Styrene	30	70	4	50	82/18	6(*R*)[d]
3	**2**	Styrene	30	70	4	98	78/22	6(*R*)[d]
4	**2**	2-Vinylnaphthalene	80	100	16	100	100	78(*R*)[d]
5	**1**	Methylacrylate	60	60	16	100	99/1	45(*R*)[d]
6	**2**	Methylacrylate	60	60	16	95	97/3	92(*R*)[d]
7	**2**	Methylacrylate	60	100	16	100	100	53(*R*)[d]
8	**2**	Vinylacetate	60	75	16	100	100	Racemic[e]
9	**2**	Vinylacetate	60	50	16	50	100	12(*R*)[e]

[a] *Reaction conditions*: solvent benzene (10 ml); $CO:H_2$ = 1; rhodium:substrate = 1:500. [b] Determined by GLC analysis. [c] Determined based on ^1H NMR 300 MHz. [d] Determined by ^1H NMR 300 MHz using [Eu(hfc)$_3$]. [e] Determined by GLC analysis with 30 m cyclodex-β column (J & W Scientific).

Surprisingly, (*R*)-2-(2-naphthyl)propanal was obtained in 78% e.e. in the hydroformylation of 2-vinylnaphthalene using the catalyst precursor **2** under 80 atm (CO/H_2 1:1 mixture) and 100 °C for 16 h (run 4). Hydroformylation took place with 100% conversion and the branched aldehyde 2-(2-naphthyl)-propanal was the only product observed.

Methylacrylate hydroformylation with catalyst precursor **1** and **2** yielded a mixture; the process took place in 100% conversion, after 16 h at 60 atm and 60–75 °C, to yield the aldehydes with 100% selectivity. The regioselectivity to branched aldehyde was very high and increases to *ca.* 100% using the catalyst precursor **1**, and a pressure of 60 atm of a 1:1 mixture of CO/H_2 in the temperature range of 60–75 °C for 16 h (run 5). Comparable results were obtained with the catalyst precursors **2**. In all the experiments the hydrogenation product of methyl acrylate was not detected. The e.e. for *R*-product was high. The highest e.e. (92%) was obtained with **2** as catalyst precursor under CO/H_2 (1:1 ratio) pressure of 60 atm and 60 °C for 16 h (run 6); the temperature is a very important factor in determining the enantioselectivity of the process (run 6 and 7).

Hydroformylation of vinylacetate with catalyst precursor **2** proceeds with 100% conversion operating at 55 atm (CO/H_2 1:1 mixture) and 75 °C for 16 h (run 8 and 9). The regioselectivity is excellent under all experimental conditions the branched aldehyde 2-acetoxypropanal being the only reaction product.

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Footnotes

† The optical purity of 2-[1-(−)menthol]pyridine was confirmed by the $[\alpha]_D^{25}$ value.[4]

‡ *Selected data* for: [(−)-methoxy-PPy]: ^1H NMR (300 MHz, $CDCl_3$) δ 0.65 (d, *J* 6.85 Hz, CH_3, 3H), δ 0.85 (d, *J* 6.65 Hz, CH_3, 3H), δ 0.90 (d, *J* 6.41 Hz, CH_3, 3H), δ 8.50 (d, *J* 4.64 Hz, 6H-Py, 1H). $^{31}P\{^1H\}$ ($CDCl_3$) δ 91.35 (s).

§ *Selected data* for: **1**: ^1H NMR (300 MHz, $CDCl_3$) δ 0.89 (d, *J* 5.97 Hz, CH_3, 3H), δ 1.09 (d, *J* 6.63 Hz, CH_3, 3H), δ 1.20 (d, *J* 6.19 Hz, CH_3, 3H), δ 8.50 (d, *J* 5.52 Hz, 6H-Py, 1H). $^{31}P\{^1H\}$ ($CDCl_3$) δ 121.37 (d, $^1J_{RhP}$ 159.22 Hz).

Crystal Data: $C_{35}H_{44}NOPRh\cdot ClO_4$, *M* = 728.04, monoclinic, space group $P2_1$ (ITC No. 4), *a* = 9.316(2), *b* = 28.076(3), *c* = 13.441(2) Å, β = 103.95(1)°, *U* = 3412(1) Å^3, *Z* = 4, D_c = 1.42 g cm^{-3}, *F*(000) = 1512, μ(Mo-Kα) = 6.67 cm^{-1}, λ(Mo-Kα) = 0.71073 Å.

X-ray measurements were performed on an orange crystal at room temp. with a Siemens R3m/v automatic four-circle diffractometer using graphite-monochromated Mo-Kα radiation. The data collection was performed up to 2θ = 53° by the variable-speed ω-2θ scan method, measuring 9152 reflections of which 7570 were unique. No decay was observed. A semi-empirical absorption correction was applied by azimutal scan data.

Data reduction and structure solution (by using Patterson methods) were performed by SHELXTL-PLUS and then the model was refined with SHELXL-93 by the full-matrix least squares technique based on the F^2, considering 6084 observed reflection with $F_0 \geq 7\sigma(F_0)$.

The structure model, with all non-hydrogen atoms anisotropic and the hydrogens in calculated position by using the 'riding' model with a unique fixed isotropic thermal parameter, was refined by minimizing the function $\Sigma w(F_0^2 - F_c^2)^2$ and converged to $R = \Sigma|F_0 - F_c|/\Sigma F_0 = 0.030$ and $R' = [\Sigma w(F_0^2 - F_c^2)^2/\Sigma w(F_0^2)^2]^{1/2} = 0.072$ with the final weighting scheme w^{-1} ($\sigma^2(F_0^2)$ + {0.01647 [max(F_0^2) + 2.0*F_c^2]}^{2}), including an extinction parameter refined to 0.0015(2). Into the last refinement cycles an enantiomer parameter was included and converged to −0.03(2) equal to the theoretical value 0 expected for the right absolute configuration.

All computation were performed on DEC MicroVax/3400 computer. The final atomic coordinates, anisotropic temperature factors, bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

¶ *Selected data* for: **2**: IR (Nujol) ν_{CO} 2006 cm^{-1}. $^{31}P\{^1H\}$ (300 MHz, $CDCl_3$) δ 118.65 (dd, $^1J_{RhP}$ 125.12, $^2J_{RhP}$ 297.74 Hz), δ 31.11 (dd, $^1J_{RhP}$ 123.87, $^2J_{RhP}$ 297.74 Hz).

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