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New optically active amido-phosphinite ligand and ruthenium complexes

Pierre Le Gendre, Martin Offenbecher, Christian Bruneau * and Pierre H. Dixneuf *
Laboratoire de Chimie de Coordination et Catalyse, UMR 6509: CNRS, Université de Rennes, Campus de Beaulieu, 35042 Rennes, France

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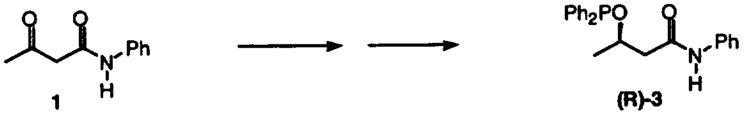
Abstract

The hydrogenation of acetoacetanilide in the presence of optically active ruthenium catalysts leads to 3-hydroxy-*N*-phenylbutanamide in good yield and high enantioselectivity (ee>95%). Its direct phosphinylation with chlorodiphenylphosphine affords a new bifunctional amido-phosphinite ligand that can easily be coordinated to [(arene)RuCl$_2$] and to the CpRuCl(PPh$_3$) moiety with very good stereoselectivity from CpRuCl(PPh$_3$)$_2$. © 1998 Elsevier Science Ltd. All rights reserved.

1. Introduction

Efficient asymmetric catalysis in the presence of metal complexes requires the utilization of functional mono- or polydentate optically active ligands. A breakthrough in this area was the preparation of a variety of chiral diphosphine ligands with C$_2$ symmetry.[1] Unsymmetrical ligands and molecules containing two different phosphorus chelating groups have also found useful applications in enantioselective hydrogenation of olefins, ketones and imines associated with transition metals such as rhodium, ruthenium or iridium.[2] Recently, new heterobidentate P–O,[3] P–N,[2d,3,4] P–S[5] ligands exhibiting efficient stereoinduction properties have appeared. It has also been shown that phosphinite ligands have potential in asymmetric hydrovinylation of olefins,[6] dimerization of dienes,[7] hydrocyanation,[8] allylic substitution,[9] and hydrogenation of C–C double bonds[10] and ketones.[11] We report here the synthesis of a new amido-phosphinite ligand and its use in the preparation of new ruthenium complexes.



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* Corresponding authors. E-mail: christian.bruneau@univ-rennes1.fr

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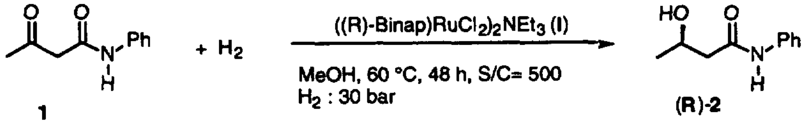
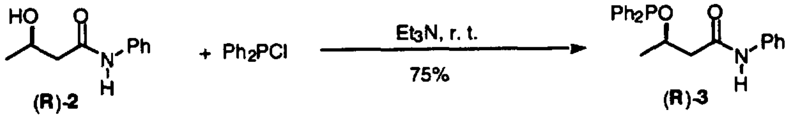
2. Results and discussion

The preparation of optically active 3-hydroxy-*N*-butanamide **2** has already been reported in a five step synthesis starting from commercially available sodium 3-hydroxybutyrate.[12] This preparation was considerably shortened by performing the enantioselective hydrogenation of acetoacetanilide **1** in the presence of an enantiomerically pure ruthenium catalyst containing an atropoisomeric ligand. Thus, 2 g of acetoacetanilide **1** was hydrogenated in methanol under 30 bar of hydrogen at 60°C in the presence of 0.2 mol% of [((R)-Binap)RuCl$_2$]NEt$_3$[13] to give (R)-3-hydroxy-*N*-butanamide **2** in 99% isolated yield and more than 95% ee (Eq. 1). The absolute configuration of **2** was established from the literature data[12] and the enantiomeric excess was determined by HPLC with a chiral (S,S)-Whelk 0-1 column. Under similar conditions the catalytic species [((R)-Binap)RuCl$_2$] generated in situ from ((R)-Binap)Ru(2-methylallyl)$_2$ and HCl[14,15] led to the same result, whereas ((R)-Binap)Ru(O$_2$CCF$_3$)$_2$ afforded **2** in almost quantitative yield but with less than 10% ee. These results are in perfect agreement with the literature data concerning the nature of the achiral ligands in asymmetric hydrogenation of functional ketones with ruthenium catalysts.[15]



(1)

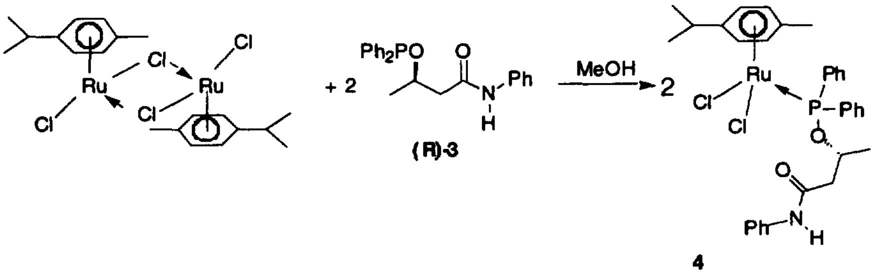
After treatment at room temperature for 72 h of 1 g (5.6 mmol) of (R)-**2** with 1.26 ml (7 mmol) of chlorodiphenylphosphine in 200 ml of diethyl ether in the presence of 10 ml of triethylamine, the new phosphinite **3** was collected by filtration, redissolved in diethyl ether, purified over alumina and isolated in 75% yield (Eq. 2) according to a reported protocol.[16]



(2)

Only one signal characteristic of a phosphinite group was detected in ^{31}P NMR at 111.29 ppm. Satisfactory elemental analyses and spectroscopic data were obtained for this phosphinite showing an optical rotation of −82 (c=1 g l^{-1}, EtOH).

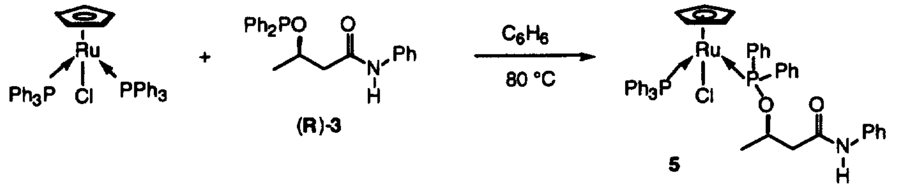
This ligand was expected to cleave the [(arene)RuCl$_2$]$_2$ dimers to give the corresponding (arene)RuCl$_2$(phosphinite) complexes *via* monohapto coordination of the phosphinite group. Indeed, **3** reacted with [(*p*-cymene)RuCl$_2$]$_2$ in methanol at room temperature for 20 h to afford complex **4** as red needles in 95% yield after evaporation of the solvent, washing with diethyl ether and recrystallization from a dichloromethane–hexane mixture (Eq. 3). The chemical purity of the compound was confirmed by a single ^{31}P NMR signal at 115.50 ppm.



(3)

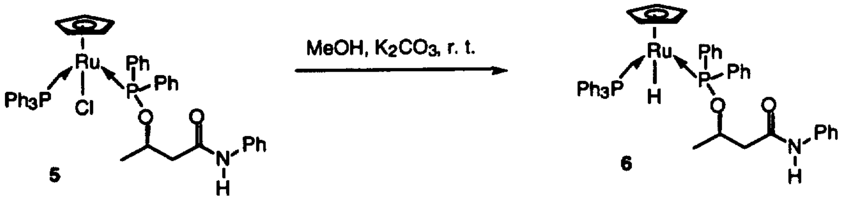
Our attempts to prepare a cationic ruthenium(II) complex *via* elimination of a chloride by NH_4PF_6 and η^2-coordination of the ligand **3** involving both the phosphinite and the amido group failed. This can be explained by the high lability of the amido group and can be compared to the difficulty of phosphinoesters to give a bidentate ligand,[17] but contrasts with the easy obtention of cationic ruthenium(II) complexes from aminophosphine–phosphinite ligands,[18] showing that the coordinating ability of an amido group is much weaker than that of a phosphorus group.

It was also possible to prepare a cyclopentadienyl ruthenium(II) complex by treating the $(Cp)RuCl(PPh_3)_2$ precursor with **3** in benzene at 80°C for 1.5 h. After evaporation of the solvent, washing with diethyl ether and recrystallization from a CH_2Cl_2/ether mixture, orange crystals of **5** were isolated in 90% yield (Eq. 4).



(4)

The ^{31}P NMR analysis of the crude mixture indicated a diastereomeric excess of 95%, similar to the enantiomeric excess of the free ligand. This result shows that the coordination of the phosphinite to the prochiral $CpRuCl(PPh_3)$ moiety takes place with an excellent diastereoselectivity. One recrystallization of the crude reaction mixture made possible the isolation of only one diastereomer **5**; its ^{31}P NMR spectrum exhibited two singlets at 43.9 and 143.51 ppm, corresponding to the phosphine and phosphinite group, respectively.



(5)

The cleavage of the Ru–Cl bond could be easily achieved in methanol in the presence of K_2CO_3 (Eq. 5) but racemization occurs and the ruthenium hydride complex **6** was isolated as a mixture of two diastereomers in a 70:30 ratio.

3. Conclusion

We have synthesized a new optically active bifunctional amido-phosphinite ligand *via* enantioselective hydrogenation of a β-ketoamide, and prepared optically pure ruthenium complexes containing this ligand. The use of the new complexes **4** and **5** for the reduction of the ketonic C=O bond of ketoamides either under hydrogen pressure or hydrogen transfer conditions is under investigation.

4. Experimental section

4.1. *(R)-(−)-3-Hydroxy-*N*-phenylbutanamide 2*

Acetoacetanilide **1** (2 g) and $[((R)\text{-Binap})RuCl_2]_2\cdot NEt_3$ (20 mg) were placed into a 125 ml autoclave. After degassing, 125 ml of distilled methanol was added and the autoclave was pressurized to 30 bar with dihydrogen. After heating at 60°C for 48 h, the resulting 3-hydroxy-*N*-phenylbutanamide was purified over a silica column eluted with diethyl ether and collected as a white powder. The enantiomeric excess was determined by HPLC with an (S,S)-Whelk 0-1 column eluted with a hexane:isopropanol (90:10) mixture. Yield 99%, mp 105°C. IR ν (cm^{-1}): 1552, 1607, 1672, 3290, 3410. ^1H NMR (200 MHz, $CDCl_3$), δ ppm 1.26 (d, 3H, *J*=6.3 Hz, CH_3), 2.36–2.55 (m, 2H, CH_2), 3.20 (s, 1H, OH), 4.10–4.31 (m, 1H, CHOH), 7.09 (t, 1H, *J*=7.2 Hz, Ph), 7.30 (dd, 2H, *J*=7.6 and 7.2 Hz, Ph), 7.47 (d, 2H, *J*=7.6 Hz, Ph), 7.83 (s, 1H, NH). ^{13}C NMR {^1H} (50 MHz, $CDCl_3$), δ ppm 23.12 (s, CH_3), 45.23 (s, CH_2), 65.06 (s, CH), 120.29 (s, 2*o*-C(Ph)), 124.58 (s, *p*-C(Ph)), 129.01 (s, 2*m*-C(Ph)), 137.62 (s, *ipso*-C(Ph)), 170.60 (s, CO). $[\alpha]_D^{20}$ −37 (c=1.0 g l^{-1}, $CHCl_3$); ee 95%. Anal. found: C 66.91, H 7.31, N 7.81; calcd for $C_{10}H_{13}NO_2$: C 67.02, H 7.32, N 7.81.

4.2. *(R)-(−)-3-Diphenylphosphinito-*N*-phenylbutanamide 3*

Amidoalcohol **2** (1 g, 5.6 mmol) and degassed triethylamine (10 ml) were added to a Schlenk tube containing 200 ml of diethyl ether. Ph_2PCl (1.26 ml, 7 mmol) was added dropwise under nitrogen and a white solid immediately appeared. After 72 h of stirring at room temperature, the solution was filtrated and the solvent was removed. The remaining white solid was redissolved in diethyl ether and purified over a neutral alumina column. Yield 75%, m.p. 104. IR ν (cm^{-1}) 351, 1433, 1539, 1600, 1675. ^{31}P NMR (81 MHz, $CDCl_3$), δ ppm 111.29 (s, $OPPh_2$). ^1H NMR (200 MHz, $CDCl_3$), δ ppm 1.39 (d, 3H, CH_3, *J*=6.3 Hz), 2.54–2.77 (m, 2H, CH_2), 4.39–4.62 (m, 1H, CH), 6.95–7.49 (m, 15H, Ph), 7.79 (s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$), δ ppm 22.05 (qd, CH_3, *J*=125.8 Hz, J_{CP}=5.8 Hz), 42.27 (td, CH_2, *J*=127.9 Hz, J_{CP}=5.2 Hz), 74.55 (dd, CH, *J*=142.1 Hz, J_{CP}=21.9 Hz), 119.74 (d, CH(Ar), *J*=162,6 Hz), 124.07 (d, CH(Ar), *J*=160.2 Hz), 127.30–130.84 (m, CH(Ar)), 137.87 (s, *ipso*-C PhNH), 141.50 (d, *ipso*-C(Ph), *J*=30.5 Hz), 141.80 (d, *ipso*-C(Ph), J_{CP}=32.0 Hz), 168.75 (s, CO). $[\alpha]_D$ −82 (c=1 g l^{-1}, EtOH). Anal. found: C 71.72, H 5.97, N 3.76; calcd for $C_{22}H_{22}NO_2P$: C 72.71, H 6.10, N 3.85.

4.3. *(*p*-Cymene)(η^1-amido-phosphinite)$RuCl_2$ 4*

Amido-phosphinite **3** (0.348 g, 0.95 mmol) and 0.264 g (0.43 mmol) of $[(p\text{-cymene})RuCl_2]_2$ were dissolved under an inert atmosphere of nitrogen in 14 ml of degassed methanol. After stirring for 20 h, the solvent was evaporated and the resulting red solid was purified by washing with 2×5 ml of diethyl ether. Yield 95%. IR ν (cm^{-1}) 1539, 1600, 1617, 1630, 1682, 3414, 3445, 3478, 3550. ^{31}P NMR (81 MHz, $CDCl_3$), δ ppm 115.50 (s, $OPPh_2$). ^1H NMR (200 MHz, $CDCl_3$), δ ppm 0.83 (d, 3H, CH_3, *J*=6.9 Hz), 1.03 (d, 3H, isopropyl CH_3, *J*=7.0 Hz), 1.04 (d, 3H, isopropyl CH_3, *J*=5.9 Hz), 1.86 (s, 3H, CH_3–Ar), 2.36–2.65 (m, 3H, CH_2+isopropyl CH), 4.53–4.81 (m, 1H, OCH), 5.03 (d, 1H, =CH *p*-cymene, *J*=5.8 Hz), 5.15 (d, 1H, =CH *p*-cymene, *J*=5.4 Hz), 5.22–5.40 (m, 2H, =CH *p*-cymene), 6.96–7.93 (m, 15H, Ph), 9.04 (s, 1H, NH). ^{13}C NMR {^1H} (75 MHz, $CDCl_3$), δ ppm 15.32, 17.35 (2s, CH_3 *p*-cymene), 21.23 (d, $CH_3CHOPPh_2$, J_{CP}=3.2 Hz), 22.48 (s, CH_3 *p*-cymene), 30.09 (s, CH *p*-cymene), 53.54 (d, CH_2, J_{CP}=2.9 Hz), 73.76 (d, $CHCH_2$, J_{CP}=6.0 Hz), 86.30 (d, =CH *p*-cymene, J_{CP}=5.1 Hz), 88.80 (d, 2=CH *p*-cymene, J_{CP}=7.5 Hz), 93.46 (d, =CH *p*-cymene, J_{CP}=5.9 Hz), 96.14, 110.81 (2s, C quat., *p*-

cymene), 119.54–133.88 (15s, =CH(Ph)), 135.59 (d, C ipso Ph, J_{CP}=46.1 Hz), 138.88 (s, C ipso PhNH), 139.24 (d, C ipso Ph, J_{CP}=54.4 Hz), 168.71 (s, CO). $[\alpha]_D$ −12 (c=1.2 g l^{-1}, $CHCl_3$). Anal. found: C 57.88, H 5.38, N 2.09, P 3.55; calcd for $C_{32}H_{36}NO_2PCl_2Ru$: C 57.40, H 5.42, N 2.09, P 4.62.

4.4. (Cyclopentadienyl)(η^1-amido-phosphinite)RuCl(PPh_3) 5

Amido-phosphinite **3** (0.15 g, 0.40 mmol) and 0.24 g (0.33 mmol) of (cyclopentadienyl)RuCl$(PPh_3)_2$ were dissolved under an inert atmosphere of nitrogen in 10 ml of benzene. After stirring at 80°C for 1.5 h, the solvent was evaporated, the resulting orange solid was washed with 15 ml of diethyl ether, dried under vacuum, dissolved in dichloromethane and recrystallized by diffusion in the presence of diethyl ether. Orange crystals were obtained in 90% yield. IR ν (cm^{-1}) 696, 1434, 1538, 1598, 1679, 3052. ^{31}P NMR (81 MHz, $CDCl_3$), δ ppm 43.90 (d, PPh_3, J_{PP}=59.0 Hz), 143.51 (d, $OPPh_2$, J_{PP}=59.0 Hz). ^1H NMR (200 MHz, $CDCl_3$), δ ppm 1.01 (d, 3H, CH_3, J=6.5 Hz), 1.83 (dd, 1H, CH_2, J=13.5 and 4.0 Hz), 2.23 (dd, 1H, CH_2, J=13.5 and 3.8 Hz), 3.64–3.90 (m, 1H, CH), 4.14 (s, 5H, Cp), 6.81–6.93 (m, 30H, Ph), 9.53 (s, 1H, NH). ^{13}C NMR {^1H} (50 MHz, $CDCl_3$), δ ppm 21.22 (s, CH_3), 46.09 (s, CH_2), 72.74 (d, CH, J_{CP}=16.7 Hz), 82.55 (s, Cp), 120.14–134.73 (20s, =CH(Ph)), 137.56 (d, C ipso PPh_3, J_{CP}=40.3 Hz), 139.41 (d, C ipso $OPPh_2$, J_{CP}=34.6 Hz), 139.56 (s, C ipso PhNH), 142.16 (d, C ipso $OPPh_2$, J_{CP}=40.1 Hz), 169.26 (s, CO). $[\alpha]_D$ +190 (c=0.7 g l^{-1}, $CHCl_3$). Anal. found: C 65.34, H 5.08, N 1.88, P 7.35; calcd for $C_{45}H_{42}NO_2P_2ClRu$: C 65.33, H 5.11, N 1.69, P 7.49.

4.5. (Cyclopentadienyl)(η^1-amido-phosphinite)RuH(PPh_3) 6

Complex **5** (0.233 g, 0.28 mmol) and 0.071 g (0.56 mmol) of K_2CO_3 were dissolved in 15 ml of degassed methanol under nitrogen. The solution was stirred at room temperature for 20 h. After filtration, the solvent was evaporated and the solid was dissolved in diethyl ether, filtered again and the solution was evaporated to dryness. A yellow powder was collected. Yield 80%. IR ν (cm^{-1}) 683, 1088, 1477, 1499, 1540, 1599, 1669, 1959, 3130. ^{31}P NMR (81 MHz, C_6D_6), δ ppm *dia 1*: 67.77 (d, PPh_3, J_{PP}=36.6 Hz), 158.15 (d, $OPPh_2$, J_{PP}=36.6 Hz); *dia 2*: 68.48 (d, PPh_3, J_{PP}=36.6 Hz), 158.15 (d, $OPPh_2$, J_{PP}=36.6 Hz). ^1H NMR (200 MHz, C_6D_6), δ ppm (*dia 1*/*dia 2*=1/2) *dia 1*: −11.57 (dd, 1H, Ru–H, J_{HP}=32.3 and 30.5 Hz), 1.23 (d, 3H, CH_3, J=6.1 Hz), 2.25–2.62 (m, 2H, CH_2), 4.70 (s, 5H, Cp), 5.12–5.56 (m, 1H, CH), 6.95–7.93 (m, 31H, Ph+NH); *dia 2*: −11.55 (dd, 1H, Ru–H, J_{HP}=33.6 and 31.2 Hz), 1.40 (d, 3H, CH_3, J=6.2 Hz), 2.25–2.62 (m, 2H, CH_2), 4.76 (s, 5H, Cp), 5.12–5.56 (m, 1H, CH), 6.95–7.93 (m, 31H, Ph+NH).

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