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Note

Cymantrene-derived monodentate phosphites: New ligands for Rh-catalyzed enantioselective hydrogenation

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Abstract

Novel chiral monodentate phosphite ligands bearing cymantrene fragment have been prepared. Phosphite **4** with PPh_3, instead of CO-ligand, in cymantrene moiety provided higher enantioselectivity than its unsubstituted analogue **3** in hydrogenation of (*Z*)-methyl-2-acetamido-3-phenylacrylate.

Keywords: Phosphite ligands; Cymantrene; Asymmetric hydrogenation

1. Introduction

Bidentate derivatives of ferrocene, cymantrene, and some tricarbonyl complexes of chromium and rhenium have been actively investigated and demonstrated from good to excellent enatioselectivity in asymmetric hydrogenation, allylation, hydrosilylation and conjugate addition (for example, see [1–8]). Despite the encouraging performance of many bidentate ligands, especially phosphines, recent breakthroughs have shown that the use of bidentate ligands is not essential to obtain high enantioselectivity. Chiral monodentate phosphines [9], phosphonites [10], phosphites [11] and phosphoramidites [12] have been reported to be excellent ligands in the rhodium-catalyzed asymmetric hydrogenation. Undoubted leaders among modern P-monodentate ligands are phosphite and phosphoramidite derivatives of BINOL [11–13, and references cited therein]. They may have either only axial chirality or contain additional stereogenic centers. The latter group has been well developed during the last years; for example, ferrocenylethyamine-derived phosphoramidites showed up to 99.5% ee in hydrogenation of enamides and dehydroamino acids [12]. But ligands containing only axial chirality are more attractive because of their synthetic availability and low cost [14].

Herein, we report synthesis of BINOL-based monodentate phosphites derived from accessible cymantrenylcarbinol and its derivative obtained by changing a CO-ligand for PPh_3. Due to the lack of additional stereocentres, correct correlation between the ligands structure and their efficiency in the Rh-catalyzed asymmetric hydrogenation can be made.

2. Results and discussion

Cymantrenylcarbinol was easily prepared from formylcymantrene [15]. To increase the electron-donor and steric demands of **1** the photochemical substitution of a CO ligand by PPh_3 was carried out (Scheme 1). Compound **2** showed two multiple signals for Cp-protons at δ 4.16 (2H) and δ 4.52 (2H) in the ^{1}H NMR spectrum in acetone-d_6 but only first of them possessed a PH-coupling of 3.2 Hz. Analysis of the NOESY spectrum of **2** and synthe-

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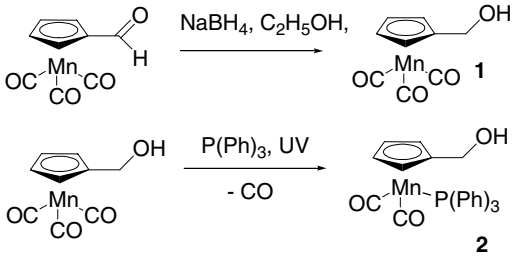


Scheme 1. Synthesis of cymantrenylcarbinols.

sis of its 2,5-D labeled analogue starting from 2,5-D labeled alcohol **1** [15] revealed that a PH-coupling exists between the P-atom of PPh_3 and protons at 3,4-positions of the Cp-ring. Selectivity of the observed coupling is connected with the hindered conformational rotation of the $Mn(CO)_2PPh_3$ moiety.

Novel BINOL-based ligands were readily synthesized by direct phosphorylation of the corresponding cymantrene alcohols **1** and **2** (Scheme 2).

They represent crystalline compounds stable in prolonged storage in dark place.

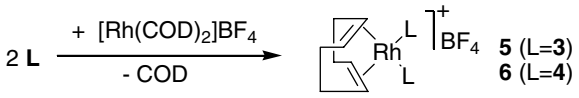
To examine the catalytic behavior of the both cymantrene-based ligands **3** and **4** in asymmetric hydrogenaton cationic rhodium(I) complexes **5** and **6** were obtained (Scheme 3).

Significantly larger ν(CO) frequency for the ligand **3** and its Rh(I) complex **5** (Table 1) prove higher π-acidity of phosphite **3** in comparison to **4** having a more efficient electron-donating ligand $P(Ph)_3$ than CO in the cymantrene part. We supposed that the different electron-donating properties of the ligands should have influence on the catalytic behavior of the complexes.

Complexes **5** and **6** were first used in the hydrogenation of (*Z*)-methyl 2-acetamido-3-phenylacrylate **7** (Scheme 4).

Both complexes showed excellent chemical yields. In the case of **5** poor enantioselectivety were obtained in all solvents used (Table 2, entries 1 and 2).

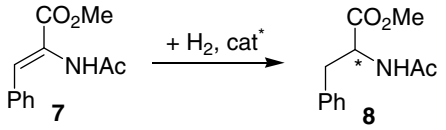
Contrary, the use of the complex **6** dramatically improved the enantioselectivity and gave product **8** in 91% ee (Table 2, entry 3). The result indicated that the bulky electron-donating ligand **4** tended to increase enantiomeric excess for the product **8**. However, the nature of the solvents showed no less important effect, changing the solvent from CH_2Cl_2 to EtOAc reduced the ee value of the product **8** from 91% to 27%. Closer effect was published by Hua and van den Berg for bulky phosphites and phosphoramidites [16,17].



Scheme 3. Complexation of the ligand with Rh(I).

Table 1
Selected spectroscopic data for compounds **3**–**6**

Compound	IR, ν(CO), cm^{-1} ($CHCl_3$)	^{31}P NMR, δ_P ($CDCl_3$)
3	2028, 1944	137.7
4	1940, 1872	142.9, 91.1
5	2024, 1940	125.3 ($^1J_{(P,Rh)}$, 241.9 Hz)
6	1932, 1864	125.4 ($^1J_{(P,Rh)}$, 243.5 Hz), 91.85

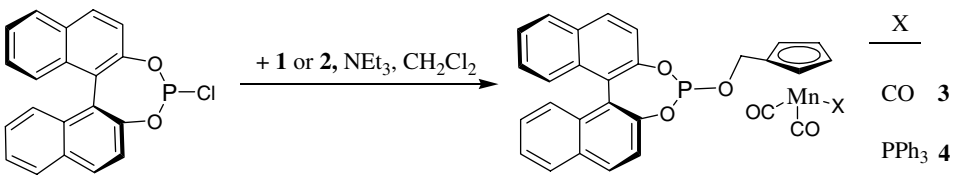


Scheme 4. Hydrogenation of (*Z*)-methyl 2-acetamido-3-phenylacrylate.

Influence of ligand structure on the enantioselectivity and chemical yield was also examined in hydrogenation of less sterical hindered substrate – dimethyl itaconate (**9**) (Scheme 5).

In this case, moderate enantioselectivities were obtained for both complexes **5** and **6**. The use of complex **6** with bulky phosphite **4** led to a completely different behavior during hydrogenation of **9**. In this case not only conversion was lower, but the enantioselectivity was decreased due to increased steric demands of ligand **4** as compared with **3** (Table 3). Solvent effect is also important, complex **6** showed only 30% conversion in CH_2Cl_2 (Table 3, entry 3), however EtOAc as solvent afforded product **10** with excellent chemical yield, but lower ees (Table 3, entry 4).

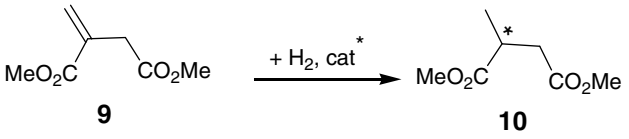
In summary, we have synthesized novel and easily prepared cymantrene-derived monodentate phosphites. It has been found that the more sterically hindered and better electron-donating phoshite **4** with a $P(Ph)_3$ group as ligand in cymantrene was a better asymmetric catalyst in hydrogenation of a dehydroamino acid ester (up to 91% ee), but less effective in hydrogenation of dimethyl itaconate. Further modification of cymantrene part, for example, substitution of second CO ligand by $P(Ph)_3$, may improve enatioselectivity. Such experiments are in progress.



Scheme 2. Synthesis of ligands **3** and **4**.

Table 2
Hydrogenation of (*Z*)-methyl 2-acetamido-3-phenylacrylate (20 h, 5 atm H_2, 20 °C)

Entry	Catalyst	Solvent	ee, %	Conversion, %
1	5	CH_2Cl_2	25 (*R*)	100
2	5	EtOAc	20 (*R*)	100
3	6	CH_2Cl_2	**91** (*R*)	100
4	6	EtOAc	27 (*R*)	97



Scheme 5. Hydrogenation of dimethyl itaconate.

Table 3
Hydrogenation of dimethyl itaconate (20 h, 5 atm H_2, 20 °C)

Entry	Catalyst	Solvent	ee, %	Conversion, %
1	5	CH_2Cl_2	83 (*S*)	100
2	5	EtOAc	80 (*S*)	100
3	6	CH_2Cl_2	70 (*S*)	30
4	6	EtOAc	61 (*S*)	93

3. Experimental

IR spectra were recorded on a Specord M80 instrument. ^{31}P, ^{13}C and ^{1}H NMR spectra were recorder with a Bruker AMX 400 instrument (162.0 MHz for ^{31}P, 100.6 MHz for ^{13}C and 400.13 MHz for ^{1}H). Complete assignment of all the resonances in ^{13}C NMR spectra was achieved by the use of DEPT techniques. Chemical shifts (ppm) are given relative to Me_4Si (^{1}H and ^{13}C) and 85% H_3PO_4 (^{31}P NMR). Mass spectra were recorded with a Varian MAT 311 spectrometer (EI) and a Finnigan LCQ Advantage spectrometer (electrospray ionization technique, ESI). Elemental analyses were performed at the Laboratory of Microanalysis (Institute of Organoelement Compounds, Moscow). The photochemical substitution of a CO-ligand by PPh_3 was carried out for **1** using the immersed ultraviolet lamp NORMAG TQ 150.

All reactions were carried out under a dry argon atmosphere in freshly dried and distilled solvents; phosphorylating reagent (S_{ax})-2-chloro-dinaphtho[2,1-d:1′,2′-f][1,3,2] dioxaphosphepine was prepared as published [18]. $[Rh(COD)_2]BF_4$ was synthesised using literature procedures [19]. The syntheses of rhodium(I) complexes (**5** and **6**) were performed by techniques similar to that reported [11–14].

3.1. Hydroxymethylcyclopentadienyl(dicarbonyl) (triphenylphosphine)manganese (*2*)

A solution of 0.7 g (3 mmol) of **1** and 0.84 g (3.2 mmol) PPh_3 in 250 ml dried benzene was irradiated at 5 °C for 1.5 h in the Ar stream. Then the solvent was removed and residue was crystallized from hexane to obtain 0.81 g (60%) of **2**, mp 119–120 °C. ^{1}H NMR (acetone-d_6): 4.03 (t, 1H, $^{2}J_{H,H} = 6.1$, OH), 4.16 (m, 2H, $J_{PH} = 3.2$, $^{3}J + {}^{4}J = 4$, βCp), 4.22 (d, 2H, $^{2}J = 6.1$, CH_2OH), 4.52 (dd, 2H, $^{3}J + {}^{4}J = 4$, αCp), 7.47–7.64 (m, 15H, Ph). IR, ν(CO), ($CHCl_3$), cm^{-1}: 1875, 1942. Anal. Calc. for $C_{26}H_{22}PO_3Mn$ (%): C, 66.68; H, 4.73; Found: C, 66.79; H, 4.71%.

3.2. Preparation of ligands *3,4* (general technique)

A solution of the phosphorylating reagent [18] 0.74 g (2.1 mmol) in CH_2Cl_2 (15 ml) was added to a vigorously stirred solution of **1** or **2** (2.1 mmol) and NEt_3 0.28 ml (2.1 mmol) in CH_2Cl_2 (10 ml). The mixture was stirred for additional 1 h. Obtained solution was washed with water (80 ml), dried over Na_2SO_4, filtered, and concentrated. The residues were purified by flash column chromatography (silica gel, CH_2Cl_2) to give the desired products as yellow powders. Yields – (65% for **3** and 72% for **4**).

3.3. (S_{ax})-*2*-(cymantrenylmethyloxy)-dinaphtho [2,1-d:1′,2′-f] [1–3] dioxaphosphepine (*3*)

^{13}C NMR ($CDCl_3$): δ_C: 66.3, 82.0, 82.6, 83.1, 84,0, 100.7, 117.8–152.7 (arryl), 224.5 (broad (CO)). MS (EI), *m*/*z* (*I*, %): 548 (2, $[M]^+$), 365 (90), 286 (100), 217 (20), 120 (18). Anal. Calc. for $C_{29}H_{18}O_6PMn$ (%): C 63.52, H 3.31; Found: C 63.61, H 3.41%.

3.4. (S_{ax})-(*2*-(dinaphto [2,1-d:1′,2′-f] [1,3,2] dioxaphosphepine) oxymethyl)cyclopentadienyl-(dicarbonyl) (triphenylphosphine)manganese (*4*)

^{13}C NMR ($CDCl_3$): δ_C, ($J_{C,P}$, Hz): 61.57 (d, $^{2}J_{C,P} = 39.1$), 82.7, 82.5, 83.7, 83.9, 95.6, 119.9–148.2 (arryl), 231.9, 231.6. MS (EI), *m*/*z* (*I*, %): 782 (1, $[M]^+$), 396 (10), 262 (70), 183 (70), 83.0 (100). Anal. Calc. for $C_{46}H_{33}O_5P_2Mn$ (%): C 70.59, H 4.25; Found: C 70.67, H 4.36%.

3.5. Cationic rhodium complex

$[Rh(COD)(3)_2]^+BF_4^-$ (**5**). Yellow solid. MS (ESI), *m*/*z* (*I*, %): 1397 (10%, $[M-BF_4]^+$), 1202 (100%, $[M-BF_4^-, -COD)]^+$. Anal. Calc. for $C_{66}H_{51}BF_4Mn_2O_{12}P_2Rh$ (%): C 56.72, H 3.68; Found: C 56.84, H 3.79%.

$[Rh(COD)(4)_2]^+BF_4^-$ (**6**). Yellow solid. MS (ESI), *m*/*z* (*I*, %): 1778 (5%, $[M-BF_4]^+$), 1670 (100%, $[M-BF_4^-, -COD)]^+$. Anal. Calc. for $C_{100}H_{80}BF_4Mn_2O_{10}P_4Rh$ (%): C 64.39, H 4.32; Found: C 64.48, H 4.48%.

3.6. Hydrogenation procedure (general technique)

A 25 ml stainless steel autoclave was charged open to air with Rh-complexes **5** or **6** (0.006 mmol) and substrates **7** or **9** (0.6 mmol). Solvent was added (5 ml) and the system was

closed. After repetitive purging with Ar (4×2 bar) the autoclave was pressurized with hydrogen (5 bar) and the reactions were stirred at 20 °C for 20 h. After the hydrogen was released, the mixture was filtered through a shot silica gel column to remove the catalyst; the filtrate was concentrated in vacuo. Optical yields of products **8** and **10** were determined using HPLC (Chiralcel OD-H column) according to the literature [20]. Conversion of the reactions was determined according to ^{1}H NMR [21].

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