Journal of Organometallic Chemistry, 370 (1989) 351–356
Elsevier Sequoia S.A., Lausanne – Printed in The Netherlands
JOM 09648

Homogeneous asymmetric catalysis by means of chiral metal complexes of 2,3-bis(dimenthylphosphino)maleic anhydride and of 2,3-bis(dimenthylphosphino)maleimide derivatives

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(Received November 16th, 1988)

Abstract

2,3-Bis(dimenthylphosphino)maleic anhydride and also 2,3-bis(dimenthylphosphino)maleimide derivatives have been prepared from 2,3-dichloromaleic anhydride, 2,3-dichloro-*N*-phenylmaleimide and 2,3-dichloro-*N*-methylmaleimide, respectively, and dimenthyl(trimethylsilyl)phosphine. These compounds have been used as ligands for Rh complexes in the asymmetric hydrogenation and hydrosilylation. Ni and Pd complexes of these ligands were tested in the Grignard cross-coupling reaction.

The hydrogenation of α-acetamido cinnamic acid gave 70% enantiomeric excess (ee) and hydrogenation of acetophenone up to 47% ee. Hydrosilylation of acetophenone led to 42% ee.

Attempts to asymmetric cross-coupling reactions resulted in very low enantiomeric excess.

Introduction

In 1986 we reported asymmetric hydrogenation of α,β-unsaturated amino acids catalyzed by Rh complexes of 2,3-bis(dimenthylphosphino)maleic anhydride and 2,3-bis(dimenthylphosphino)-*N*-phenylmaleimide [1]. For further studies of this type of ligand in asymmetric synthesis, we investigated their effectiveness in rhodium-catalyzed hydrogenation and hydrosilylation of ketones and in nickel and palladium catalyzed cross-coupling reactions.

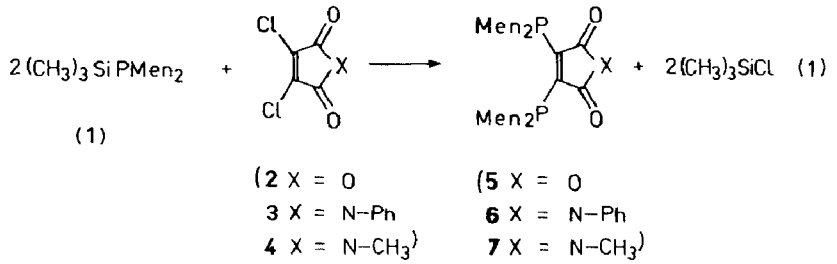
Results and discussion

Synthesis of ligands and metal complexes

Dimenthyl(trimethylsilyl)phosphine was heated with 2,3-dichloromaleic anhydride, 2,3-dichloro-*N*-phenylmaleimide and 2,3-dichloro-*N*-methylmaleimide, result-

0022-328X/89/$03.50

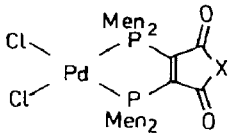
ing in the syntheses of respectively, compounds **5**, **6** and **7** according to eq. 1.



(Men = (-) - (1R, 3R, 4S) - menthyl)

All diphosphines were obtained as dark red crystals. The rhodium complexes, active in the asymmetric hydrogenation and hydrosilylation, were generated from $(Rh(COD)Cl)_2$ or $(Rh(NBD)_2)BF_4$ and ligands **5**, **6** or **7**. Nickel complexes for asymmetric cross-coupling reactions were prepared in situ by mixing nickel chloride and the ligand in a 1/1 ratio.

Crystalline palladium chloride complexes $(lig)PdCl_2$ were prepared by ligand exchange reaction in benzene solution starting from dichlorobis(benzonitrile)palladium(II).



5 - $PdCl_2$ (X=O)
6 - $PdCl_2$ (X=N-Ph)
7 - $PdCl_2$ ($X=N-CH_3$)

Asymmetric hydrogenation

Ligands **5**, **6** and **7** have been used in the hydrogenation of *Z*-α-acetamidocinnamic acid, its methyl ester and acetonphenone under mild conditions (25 °C, 0.1 MPa) with catalysts generated in situ. The results are summarized in Tables 1 and 2. Although methanol is the most suitable solvent for the hydrogenation of α,β-unsaturated acid [1] THF was added to increase the solubility of the ligands. However, the amount of THF added was small because the use of THF as a solvent decreases

Table 1

Asymmetric hydrogenation of 1 mmol of substrate in 15 ml of solvent at room temperature, $P(H_2)$ 0.1 MPa and substrate/catalyst = 100

Run	Substrate [a]	Catalyst [b]	Solvent [c]	Time (h)	Conversion (%)	Optical yield (%)	Configuration
1	A	**5**+$(Rh(NBD)_2)BF_4$	CH_3OH/THF	8	100	70	*R*
2	A	**6**+$(Rh(NBD)_2)BF_4$	CH_3OH/THF	22	100	57	*R*
3	A	**7**+$(Rh(NBD)_2)BF_4$	CH_3OH/THF	23	100	43	*R*
4	B	**5**+$(Rh(NBD)_2)BF_4$	CH_3OH/THF	2.5	100	41	*R*
5	B	**6**+$(Rh(NBD)_2)BF_4$	CH_3OH/THF	23	97	41	*R*
6	B	**7**+$(Rh(NBD)_2)BF_4$	CH_3OH/THF	3.5	100	37	*R*

[a] A = α-acetamidocinnamic acid, B = methyl-α-acetamidocinnamate. [b] Prepared in situ, Rh/L = 1/1. [c] CH_3OH/THF = 14 ml/1 ml.

Table 2

Asymmetric hydrogenation of acetophenone in 15 ml of solvent at room temperature, $P(H_2)$ 0.1 MPa and substrate/catalyst = 100

Run	Catalyst [a]	Solvent [b]	Time (h)	Conversion (%)	Optical yield (%)	Configuration
1	**5**+$(Rh(NBD)_2)BF_4$	CH_3OH/THF	84	81	47	*S*
2	**6**+$(Rh(NBD)_2)BF_4$	CH_3OH/THF	50	56	9	*R*
3	**6**+$(Rh(NBD)_2)BF_4$	CH_3OH	72	42	7	*R*
4	**7**+$(Rh(NBD)_2)BF_4$	CH_3OH/THF	100	41	9	*R*

[a] Prepared in situ, Rh/L = 1/1. [b] CH_3OH/THF = 14 ml/1 ml.

the optical and chemical yield. Ligand **5** gave the best results as well in the hydrogenation of α-acetamidocinnamic acid (Tab. 1, run 1), as of acetophenone (Tab. 2, run 1).

Changing the substrate from α-acetamidocinnamic acid to its methyl ester led to lower optical yields but higher activities (Tab. 1, run 4 and 6).

It was surprising, that ligand **5** gave relatively high optical yields of (*S*)-1-phenylethanol in the hydrogenation of acetophenone, whereas the ligands **6** and **7** led to (*R*)-1-phenylethanol (Tab. 2, run 1, 2 and 4).

An increase of the pressure to 1 MPa and addition of Et_3N decreased the optical yield, because higher pressure and longer reaction time promoted the formation of 1-cyclohexylethanol. In these cases the catalyst solutions became black, perhaps because of decomposition to metallic rhodium.

Asymmetric hydrosilylation

The results of this reaction are given in Tab. 3. The highest optical yield was obtained with ligand **5** in THF (run 4). In toluene all catalysts investigated gave about the same optical yield of carbinol. The ligand excess affects the asymmetric induction only insignificantly. Different results were observed with respect to conversion. In the case of ligand **6** the extent of conversion increases with increasing

Table 3

Asymmetric hydrosilylation of acetophenone with diphenylsilane at room temperature, $P(H_2)$ 0.1 MPa, time 48 h and substrate/catalyst = 250

Run	Catalyst [a]	Rh/L	Solvent	Conversion (%)	Optical yield (%ee)	Configuration
1	**5**+$(Rh(COD)Cl)_2$	1/1	toluene	78	28	*R*
2	**5**+$(Rh(COD)Cl)_2$	1/2.5	toluene	83	31	*R*
3	**5**+$(Rh(COD)Cl)_2$	1/5	toluene	79	33	*R*
4	**5**+$(Rh(COD)Cl)_2$	1/2.5	THF	46	42	*R*
5	**5**+$(Rh(COD)Cl)_2$	1/2.5	–	48	37	*R*
6	**6**+$(Rh(COD)Cl)_2$	1/1	toluene	52	24	*R*
7	**6**+$(Rh(COD)Cl)_2$	1/2.5	toluene	74	31	*R*
8	**7**+$(Rh(COD)Cl)_2$	1/1	toluene	74	31	*R*
9	**7**+$(Rh(COD)Cl)_2$	1/2.5	toluene	62	27	*R*

[a] Prepared in situ.

Table 4

Asymmetric Grignard cross-coupling of 1-phenylethylmagnesium chloride with (*E*)-β-bromostyrene at room temperature, time 20 h

Catalyst [a]	Chemical yield (%)	Optical yield (%)	Catalyst [a,b]	Chemical yield (%)	Optical yield (%ee) (configuration)
5-$PdCl_2$	9	–	**5**+$NiCl_2$	33	6 (*S*)
6-$PdCl_2$	33	–	**6**+$NiCl_2$	36	4 (*S*)
7-$PdCl_2$	15	–	**7**+$NiCl_2$	33	6 (*S*)

[a] Catalyst/bromostyrene/Grignard reagent 1/200/400. [b] Prepared in situ, Ni/L 1/1.

L/Rh molar ratio (run 6 and 7) contrary to ligand **7**, which gave less conversion with increasing molar ratio (run 8 and 9) and to ligand **5**, which had no effect at all.

Asymmetric Grignard cross-coupling reaction

The isolated Pd complexes of the ligands **5**–**7** and the Ni complexes prepared in situ have been used as catalysts in an asymmetric Grignard cross-coupling reaction between (*E*)-β-bromostyrene and 1-phenylethylmagnesium chloride. The values given in Table 4 represent the calculated averages of four independent runs.

The Pd complexes proved to be unsuitable for the asymmetric cross-coupling reaction. Under our conditions we obtained optically inactive coupling products and the chemical yields were very low, with exception of **6**-$PdCl_2$.

The Ni complexes induced a low stereoselectivity. After comparing several ligands with respect to their activity and optical induction we can state that a variation of X in the rigid backbone has no significant influence.

Experimental

Chemicals and apparatus

All reactions were carried out under argon, using freshly distilled dry solvents.

Dimenthyl(trimethylsilyl)phosphine, 2,3-bis(dimenthylphosphino)maleic anhydride and 2,3-bis(dimenthylphosphino)-N-phenylmaleimide were prepared by procedures reported in [1]

Diphenylsilane was prepared from chlorosilane by standard methods [2]. Acetophenone is commerically available and was purified by distillation. The optical yields were determined with a POLAMAT A polarimeter (Carl Zeiss, Jena) or by GLC on a HP-5880 A chromatograph using *N*-stearoyl-L-valin-t-butylamide in a fused silica capillary column (6.2 m) after transformation of the amino acid into the corresponding methyl ester. Alcohols were converted with isopropylisocyanate into carbamates and determined using a glass capillary column (18 m) coated with 0.3% XE-GO-L-valin-t-butylamide [3].

For the GLC analysis of (*E*)-1,3-diphenyl-1-butene, toluene was used as an internal standard, and gas chromatographic data were obtained using a HP 5880 A chromatograph, equipped with a 12 m OV-101 fused silica capillary.

Preparations

2,3-Bis(dimentylphosphino)-N-methylmaleimide (7). To a solution of 0.017 mol of 2,3-dichloro-*N*-methylmaleimide in 85 ml of ether at 0°C, 0.04 mol of dimenthyl(trimethylsilyl)phosphine in 50 ml of ether was added dropwise over a period of 3 h. The solution immediately turned to an intensive yellow colour and afterwards to a red-brown colour. After addition of 1, the solution was heated under reflux for 4 h and concentrated. At 0–5°C a dark-red substance was precipitated, which was filtered. Further product was isolated after concentration of the solution and addition of methanol. The crude product was recrystallized from ether, giving a 20% yield, m.p. 232–234°C. Anal. Found: C, 73.97 H, 10.74; N, 2.22. $C_{45}H_{79}NO_2P_2$ (728.0) calcd.: C, 74.23; H, 10.94; N, 1.92%.

Dichloro-[2,3-bis(dimenthylphosphino)maleic anhydride]palladium(II) (5-PdCl$_2$). To a suspension of 80 mg (0.21 mmol) of dichlorobis(benzonitrile)palladium in 5 ml of dry benzene under argon, a solution of 150 mg (0.21 mmol) of 2,3-bis(dimenthylphosphino)maleic anhydride in 8 ml of benzene was added with stirring. After 10 h stirring at room temperature the solvent was evaporated. The residue was recrystallized from ether/pentane, giving 150 mg (80%) of orange-yellow complex. Anal. Found: C, 59.44; H, 8.67; Cl, 7.80; P, 6.64; Pd, 11.51. $C_{44}H_{76}Cl_2O_3P_2Pd$ (892.3) calcd.: C, 59.22; H, 8.58; Cl, 7.95; P, 6.94; Pd, 11.92%.

Dichloro-[2,3-bis(dimenthylphosphino)-N-phenylmaleimide]palladium(II) (6-PdCl$_2$). To a suspension of 80 mg (0.21 mmol) of dichlorobis(benzonitrile)palladium in 5 ml of dry benzene under argon, a solution of 166 mg (0.21 mmol) of 2,3-bis(dimenthylphosphino)-*N*-phenylmaleimide in 8 ml of benzene was added with stirring. The mixture was stirred for 10 h at room temperature. Then the solution was reduced to a volume of 1 ml and 15 ml of pentane was added, which caused precipitation of a yellow complex. The precipitate was filtered, washed with pentane and dried in vacuum, giving 152 mg (75%) yellow complex. Anal. Found: C, 62.35; H, 8.37; Cl, 7.40; N, 1.59; P, 6.1; Pd, 11.3. $C_{50}H_{81}Cl_2NO_2P_2Pd$ (967.5) calcd.: C, 62.07; H, 8.44; Cl, 7.33; N, 1.45; P, 6.40; Pd, 11.00%.

Dichloro-[2,3-bis(dimenthylphosphino)-N-methylmaleimide]palladium(II) (7-PdCl$_2$). To a suspension of 80 mg (0.21 mmol) of dichlorobis(benzonitrile)palladium) in 5 ml of dry benzene under argon, a solution of 153 mg (0.21 mmol) of 2,3-bis(dimenthylphosphino)-*N*-methylmaleimide was added with stirring. After isolation, as described above had been carried out, 156 mg (82%) of a yellow complex were obtained. Anal. Found: C, 59.32; H, 8.53; Cl, 8.00; N, 1.59; P, 6.48; Pd, 11.40. $C_{45}H_{79}Cl_2NO_2P_2Pd$ (905.4) calcd.: C, 59.69; H, 8.80; Cl, 7.83; N, 1.55; P, 6.84; Pd, 11.75%.

Hydrogenation experiments

Hydrogenation of α-acetamidocinnamic acid and methyl-α-acetamidocinnamate under normal conditions was carried out as described in the literature [1].

Hydrosilylation experiments

The catalyst was prepared in situ by treating 0.02 mmol of $(Rh(COD)Cl)_2$ and the corresponding ligand in a molar ratio (see table 3) in 4 ml of solvent at ambient temperature. After stirring for 10 min diphenylsilane (12 mmol) was added and the mixture was stirred for a further 10 min. Then the solution was cooled to −2 to

0 °C and after 10 min acetophenone (10 mmol) was added. The reaction mixture was allowed to warm up to 25 °C (10 min).

When the hydrosilylation was carried out without solvent the catalyst solution was prepared in diphenylsilane. The hydrolysis was carried out as reported in the literature [4]. Chemical and optical yields were determined by GLC.

Cross-coupling experiments

After mixing the catalyst (0.0125 mmol) with (*E*)-β-bromostyrene (2.48 mmol) and Grignard reagent (5 mmol) in 12 ml of ether under argon at −45 °C the mixture was stirred for 20 h at 20 °C. The reaction was stopped by addition of 5 ml of 10% hydrochloric acid. The reaction products were isolated and the chemical and optical yields were determined by GLC and by optical rotation, respectively. Details of the analysis of the reaction products have been published previously [5].

Acknowledgement

The authors thank Prof. Dr. G. Oehme for fruitful discussions and Mrs. H. Groth, Mrs. K. Kortus and Mrs. I. Stahr for help in the experimental work.

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