Double Stereoselection in Hydrogenation of Prochiral Dehydrocarboxylic Acids on Rh(*S*,*S*-DIODMA)$_2^+$TfO$^-$ Complex in the Presence of (+)-Neomenthyldiphenylphosphine

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Abstract

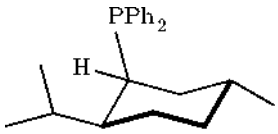
Enantioselective hydrogenation of α-acetamidocinnamic (AACA) and itaconic (IA) acids has been studied on rhodium complexes {[Rh(COD)$_2$]$^+$TfO$^-$ + *n*MDPP}COD = 1,5-cyclooctadiene, *n*MDPP = (1*S*,2*S*,5*R*)-(+)-neomenthyldiphenylphosphine)] and {[Rh(*S*,*S*-DIODMA)$_2$]$^+$ TfO$^-$ + *n*MDPP} [(*S*,*S*)-DIODMA = 4*S*,5*S*-(+)-N^4,N^4,N^5,N^5,2,2-hexamethyl-1,3-dioxolane-4,5-dimethaneamine]. Addition of *n*MDPP decreases the activity of the catalyst and increases the optical yield with retention of the direction of stereoselection. Optical yields for hydrogenation on {[Rh(*S*,*S*-DIODMA)$_2$]$^+$TfO$^-$ + *n*MDPP} exceed those obtained on the diamine complex in the presence of Ph$_3$P as well as those obtained on {[Rh(COD)$_2$]$^+$TfO$^-$ + *n*MDPP}. The result of combined action of two ligands may be considered as manifestation of 'matched' effect. Transformations of complexes have been studied by the use of ^{1}H and ^{31}P NMR spectroscopy. At least three complexes exist in the catalytic system, namely, diamine complex [Rh(*S*,*S*-DIODMA)$_2$]$^+$TfO$^-$, solvate complex [(*n*MDPP)$_2$Rh(solv)$_2$]$^+$ TfO$^-$ and diamine-phosphine complex [(*n*MDPP)$_2$Rh(*S*,*S*-DIODMA)]$^+$ TfO$^-$.

INTRODUCTION

The term 'double stereoselection' denotes symbate or antibate action of two chiral species in enantioselective reactions. The two chiral species may be a chiral ligand and a substrate possessing chiral center, or two different chiral ligands. Combination of chiral species resulting in a higher or lower enantioselectivity is designated as 'matched' or 'mismatched', respectively. Recently we have studied enantioselective hydrogenation of α-acetamidocinnamic (AACA) and itaconic (IA) acids on rhodium complex [Rh(*S*,*S*-DIODMA)$_2$]$^+$ TfO$^-$ **1**, where (*S*,*S*)-DIODMA is 4*S*,5*S*-(+)-N^4,N^4,N^5,N^5,2,2-hexamethyl-1,3-dioxolane-4,5-dimethaneamine [1]. Complex **1** is formed by replacement of both cyclooctadiene (COD) ligands from complex [Rh(COD)$_2$]$^+$ TfO$^-$ by two molecules of DIODMA. The reached optical yields are moderate (<30 %), which is not only due to the nature of the ligand but, probably, also because of reduction of rhodium(+1) to rhodium metal.

To prevent this reduction, we introduced an equivalent amount of triphenylphosphine (PPh$_3$/Rh = 1) into the catalytic system, that led to a decrease of chemical yields but increased optical yields. Effect of an achiral P-ligand may consist in stabilization of the diamine rhodium complex during the process of hydrogenation due to formation of a new complex possessing both ligands in the coordination sphere of the metal. Besides, we cannot rule out steric hindrances in the coordination sphere of rhodium arising from its coordination with Ph$_3$P. This must give rise to more rigid selection of the *re* or *si* side of the C = C double bond during formation of the substrate rhodium complex, that is, to an increase of free energy difference of the two diastereomeric rhodium olefin complexes.

Formation of the phosphine-diamine rhodium complex [(Ph$_3$P)$_2$Rh(DIODMA)]$^+$TfO$^-$ **2** by



3 (*n*MDPP)

Scheme 1.

the reaction of complex $[Rh(COD)_2]^+TfO^-$ with molecular hydrogen in the presence of two moles of triphenylphosphine was corroborated by ^1H and ^{31}P NMR studies [1].

HYDROGENATION OF PROCHIRAL SUBSTRATES ON RHODIUM COMPLEXES

Here we report on the results of enantioselective hydrogenation of AACA and IA on rhodium complex $[Rh(COD)_2]^+$ TfO^- in the presence of chiral phosphine **3**, (1*S*,2*S*,5*R*)-(+)-neomenthyldiphenylphosphine (*n*MDPP) and on rhodium diamine complex **1** also in the presence of *n*MDPP (Scheme 1).

Phosphine **3** was used by Morrison *et al.* in hydrogenation of prochiral acids, like atropic, *E*-α-methylcinnamic and *E*-β-methylcinnamic acids on the *in situ* formed rhodium complex $Rh[(+)nMDPP]_3Cl$ [2, 3]. The optical yields reached 28 % for (*S*)-2-phenylpropionic acid, 60 % for (*R*)-2-methyl-3-phenylpropionic acid, and 61 % for (*S*)-3-phenylbutanoic acid. Later on, Valentine *et al.* [4] succeeded in hydrogenation of 3,7-dimethyl-2, 6-octadienoic (geranic) acid to optically active (*R*)-3,7-dimethyl-6-octenoic (citronellic) acid under mild conditions on the dimeric complex $[Rh(COD)Cl]_2$ and (+)-*n*MDPP in the presence of MeONa in 65–70 % optical yield after 3 days. Less than moderate activity of the catalyst was observed for hydrogenation of α-(acetylamino)-6-methylindol-3-acrylic acid: the conversion after 7 days in the presence of triethylamine and with ratio substrate : Rh = 100 was as low as 29 %.

Neither optical yield nor configuration was determined.

The results on hydrogenation of IA and AACA under mild conditions in the catalytic system $[Rh(COD)_2]^+$ TfO^- + *n*MDPP are given in Table 1.

As follows from the results of Table 1, under mild conditions the catalyst is less active with respect to AACA than to IA since the C=C double bond in the former is less accessible for coordination. Both enantioselectivity of the process and the effect of the phosphine/Rh ratio on the rate of hydrogenation unequivocally point to the *in situ* formation of phosphine rhodium complexes and to the presence of chiral ligand in the rhodium coordination sphere in the rate- and enantioselectivity-determining stages. Hydrogenation of IA results predominantly in (*R*)-(+)-α-methylsuccinic acid whereas AACA gives mainly (*S*)-(+)-*N*-acetylphenylalanine.

Based on our previous results we could anticipate formation of phosphine-diamine rhodium complexes from $[Rh(DIODMA)_2]^+TfO^-$ **1** and *n*MDPP during hydrogenation of the substrates under consideration. Hydrogenation on rhodium complexes with diamine [1] and with *n*MDPP (see Table 1) displays the same direction of stereoselection. Therefore, it was of interest to shed a light on the question wheth-

TABLE 1

Hydrogenation of IA and AACA in the system $[Rh(COD)_2]^+$ TfO^- + *n*MDPP (C_6H_6 : MeOH = 1 : 2; C_{Rh} = 2 mmol/l, 24 h)

Entry	*n*MDPP : Rh	P_{H_2}, atm	*t*, °C	Substrate (substrate : Rh)	Chemical yield, %	Optical yield, %
1	1	1	20	IA (25)	100	27.6 (*R*)
2	2	1	20	IA (25)	25.0	44.7 (*R*)
3	1	1	20	AACA (50)	23.0	52.4 (*S*)
4	1.9	1	60	AACA (50)	7.0*	–
7**	*in situ* RhL_3Cl	20	60	Atropic acid	not given	28 (*S*)
	or RhL_2ClS			*E*-α-methylcinnamic acid	100	60 (*R*)
				E-β-methylcinnamic acid		61 (*S*)

*Catalysate contained 84 % of AACA and 9 % of its methyl ester.
**[2, 3].

TABLE 2

Hydrogenation of IA and AACA on complex **1** in the presence of *n*MDPP (C_6H_6 : MeOH = 3 : 7; C_{Rh} = 2 mmol/l, 5–24 h)

Entry	*n*MDPP : Rh	P_{H_2}, atm	*t*, °C	Substrate (substrate:Rh)	Chemical yield, %	Optical yield, %
1	1	1	20	IA (25)	34.6	62.2 (*R*)
2	1.2	1	60	IA (25)	100.0	48.3 (*R*)
3	1.9	1	20	IA (25)	8.3	74.3 (*R*)
4	2	1	60	IA (25)	21.2	65.3 (*R*)
5	1	1	60	AACA (50)	7.0*	
6	1	20	20	AACA (50)	25.0	32.7 (*S*)
7	–	35	20	AACA (40)	100	20.3 (*S*)

*Catalysate contained 73 % of AACA and 20 % of its methyl ester.

er two chiral ligands, namely, DIODMA and *n*MDPP, would demonstrate so called 'matched' effect in hydrogenation of IA and AACA. Table 2 shows the results obtained for hydrogenation on complex **1** with one or two equivalents of *n*MDPP added.

Indeed, as can be seen, addition of *n*MDPP to complex **1** gives rise to a decrease of activity of the catalyst and an increase of optical yield (up to 62–74 % for IA) with retention of the direction of stereoselection. These optical yields exceed those obtained on complex **1** in the presence of achiral phosphine Ph_3P [1] as well as those obtained on rhodium complex with *n*MDPP (see Table 1). This is true both for mild conditions and hydrogenation under high pressure of hydrogen. Consequently, we do observe a consistent action of the two chiral ligands in the coordination sphere, which may be considered as manifestation of 'matched' effect.

TRANSFORMATIONS OF RHODIUM(+1) COMPLEXES IN THE CATALYTIC SYSTEM

In spite of good results obtained for hydrogenation on rhodium complexes with *n*MDPP [2–4] their spectral characteristics were not studied. We made an attempt to fill in this gap by the use of ^1H and ^{31}P NMR spectroscopy. Addition of two equivalents of **3** to brick-red solution of complex $[Rh(COD)_2]^+TfO^-$ in acetone-d_6 changes the color to yellow-orange. Along with the singlet at −14.1 ppm belonging to **3**, a doublet at 26.42 ppm with $^1J_{P-Rh}$ 141.3 Hz appears in the ^{31}P NMR spectrum, and signals of free COD (5.50 and 2.32 ppm) appear in the proton spectrum. This testifies coordination of **3** to rhodium and formation of complex **4** (see the Scheme 2).

Addition of one equivalent of (*S*, *S*)-DIODMA with respect to rhodium results in changing the ratio of the signals of the coordinated and free *n*MDPP in favor of the latter. Simultaneous downfield shift of the signals of DIODMA ($\Delta\delta_{CH}$ 0.14, $\Delta\delta_{CH_A}$ 0.22, $\Delta\delta_{CH_B}$ 0.27, $\Delta\delta_{CH_3N}$ 0.20, $\Delta\delta_{CH_3C}$ 0.03) gives an indication of its coordination to rhodium with formation of complex **5**. On the contrary, on addition of phosphine **3** to complex **1** no signals of free DIODMA are observed, so *n*MDPP is unable to replace diamine from the rhodium coordination sphere.

Further treatment of complex **5** with molecular hydrogen during 20 min gives rise to disappearance of complex **4** and appearance of two new doublets in the ^{31}P NMR spectrum at 55.15 ppm ($^1J_{P-Rh}$ 204.2 Hz) (complex **6**) and 78.45 ppm ($^1J_{P-Rh}$ 190.4 Hz) (complex **7**) of similar intensity. Signals of DIODMA suffer further downfield shift in the ^1H NMR spectrum and approach the values characteristic of the ligand in complex **1**. Chemical shifts of DIODMA and COD in various complexes are given in Table 3.

Based on the literature data we assign complexes **6** and **7** the structure of the solvate and diamine complexes $[Rh(solv)_2\{(+)nMDPP\}_2]^+OTf^-$ (**6**) [5] and $[Rh(DIODMA)\{(+)nMDPP\}_2]^+OTf^-$ (**7**) [6].

Thus, the results of NMR monitoring of the catalytic system allow us to conclude that:

TABLE 3

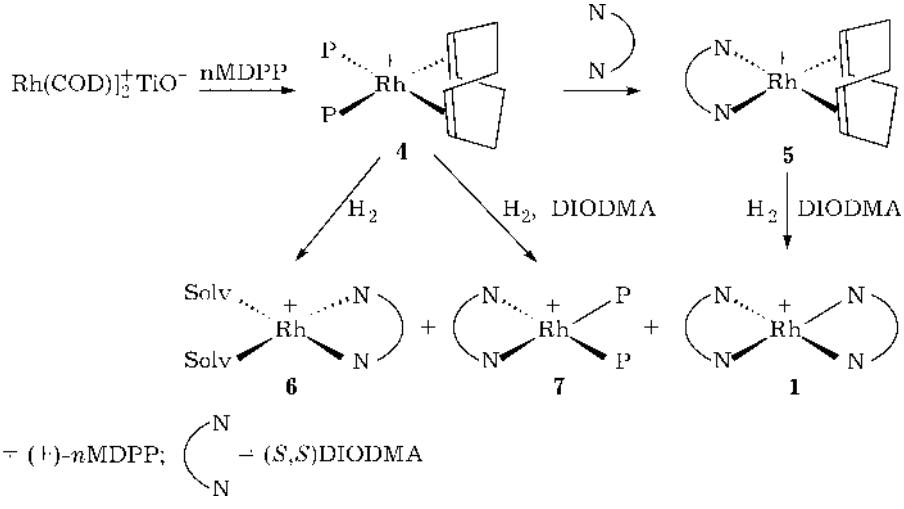
Chemical shifts of DIODMA and COD in rhodium(+1) complexes

Complex	CH	CH_A in CH_2	CH_B in CH_2	$N-CH_3$	$C-CH_3$
		DIOMA			
(*S*,*S*)-DIODMA	3.80	2.52	2.37	2.21	1.29
Complex **1**	4.06	2.97	2.89	2.61	1.36
4 + (*S*,*S*)-DIODMA (complex **5**)	3.94	2.74	2.63	2.41	1.32
4 + (*S*,*S*)DIODMA + H_2	4.05	2.94	2.86	2.60	1.35
$Rh(DIODMA)(IA)^+ TfO^-$ (complex **8**)	4.21	3.37	3.02	2.79	1.38
		COD			
$Rh(COD)_2^+ TfO^-$	4.15	2.50	1.77		
$Rh(COD)(PPh_3)_2^+ TfO^-$	4.70	2.58	2.28		
Complex **4**	5.12 br	2.50 m	2.50 m		
4 + (*S*,*S*)-DIODMA (complex **5**)	4.18 br	*	*		

* Overlapped with signals of DIODMA.

1) ligand **3** does not replace DIODMA in complex **1**, whereas substrate (IA) replaces one molecule of DIODMA to form olefin-diamine rhodium complex **8** [1]; 2) complex **4** reacts with DIODMA to afford the diamino-diene rhodium complex **5** which after treatment with molecular hydrogen liberates cyclooctane and is transformed to complex **1**; 3) complex **4** after treatment with molecular hydrogen also affords cyclooctane and complexes **6** and **7** possessing chiral phosphine **3**. With all this taken into account the tentative scheme can be suggested (Scheme 2).

Therefore, at least three complexes possessing chiral ligands in different combinations are formed in the catalytic system during hydrogenation, the concentration of complexes **1**, **6**, and **7** depending on the reaction conditions. Complex **1** with two bidentate diamine ligands reacts with IA to afford rather stable complex **8** which then slowly reacts with hydrogen [1]. According to Brown *et al.* [5], cationic complexes $[(PR_1R_2R_3)_2Rh(NBD)]^+BF_4^-$, where NBD stands for bicyclo-[2,2,1]-heptadiene form two types of complexes when treated with molecular hydrogen: bis-solvate rhodium rhodium(+1) complexes like **6** and dihydrido-bis-phosphine rhodium(+3) complexes with *trans* arrangement of the phosphine ligands, their ratio being very sensitive to the nature of a tertiary phosphine. In the present study we failed to detect the dihydride complex, apparently, due to its low



Scheme 2.

stability at room temperature. Apparently, it is complex **7** and its precursor, complex **6**, which are responsible for consistent action of chiral ligands in the catalytic system.

Catalytic hydrogenation is known to proceed via formation of an octahedral dihydrido-olefinic rhodium (+3) complex [7]. This requires six coordination sites for bidentate molecule of diamine, two hydrogen atoms, and a substrate (IA or AACA) coordinated to rhodium atom in bidentate mode. Hence, there is no free place for an additional ligand (in our case *n*MDPP). However, the results given in Table 2 unequivocally point to participation of phosphine **3** in the catalytic cycle, which is especially distinct for hydrogenation of IA where addition of two equivalents of phosphine **3** (cf. entries 1 *vs.* 3, and 2 *vs.* 4) gives rise to a sharp decrease of activity of the catalyst. Probably, coordination of chiral phosphine **3** is accompanied by monodentate coordination of the bidentate *N*,*N*-ligand to transition metal in the stage responsible for stereodifferentiation.

REFERENCES

1 L. O. Nindakova, B. A. Shainyan, A. I. Albanov, *Russ. Chem. Bull.*, 50 (2001) 1860.
2 J. D. Morrison, W. F. Master, *J. Org. Chem.*, 39 (1974) 270.
3 A. M. Aguar, C. J. Morrow, J. D. Morrison *et al.*, *J. Org. Chem.*, 41 (1976) 1545.
4 J. D. Valentine, K. K. Jonson, W. Priester *et al.*, *Ibid.*, 45 (1980) 3698.
5 J. M. Brown, P. A. Chaloner, P. N. Nicholson, *Chem. Comm.*, (1978) 646.
6 S. Inoue, H. Takaya, K. Tani *et al.*, *J. Amer. Chem. Soc.*, 112 (1990) 4897.
7 A. S. C. Chan, J. Halpern, *Ibid.*, 102 (1980) 838.