EFFECTS OF THE DIARYLPHOSPHINO GROUPS OF MODIFIED DIOPS ON THE ENANTIOSELECTIVITY AND THE CATALYTIC ACTIVITY OF THEIR RHODIUM(I) COMPLEXES IN THE CATALYTIC ASYMMETRIC HYDROGENATIONS OF ENAMIDES[1)]

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Remarkable effects of the substituted diphenylphosphino groups of modified DIOPs on the enantioselectivity and the catalytic activity were observed in the asymmetric hydrogenation of an electron-rich olefin such as enamide using their rhodium(I) complexes as the catalyst. The cationic rhodium(I) complexes of modified DIOPs bearing electron-donating groups showed higher catalytic activities than that of original DIOP, and the cationic complexes showed better enantioselectivities than the corresponding neutral ones. The cationic rhodium(I) complex of *p*-methoxy-substituted DIOP was found to be the most efficient catalyst.

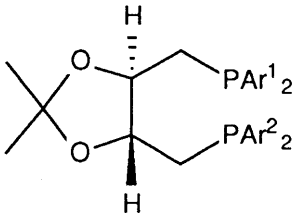
KEYWORDS chiral bisphosphine ligand; DIOP; asymmetric hydrogenation; rhodium(I) complex; enamide; acetamidocinnamic acid; enantioselectivity; catalytic activity

In our recent studies on the development of efficient chiral bisphosphine ligands for asymmetric hydrogenations,[2)] we proposed a design concept, "Respective Control Concept", and prepared several efficient ligands, such as BCPMs,[3)] DIOCP,[4)] modified DIOPs,[5)] modified BPPMs,[6)] and modified Degphos.[7)] Each ligand has at least one electron-rich phosphino group which is considered to be essential for exhibiting not only higher catalytic activity but higher enantioselectivity of the rhodium(I) complex catalysts. In most cases, prochiral substrates that can be hydrogenated in high enantiomeric excess were electron-deficient olefins or ketones bearing hetero atoms at their α or β positions for forming rigid chelation rings with the catalyst.[8)]

In connection with the asymmetric hydrogenations of electron-deficient olefins, further interest in proving the general utility of the design concept has led us to the examination of the asymmetric hydrogenation of electron-rich olefins[9)] using modified DIOPs-rhodium(I) complexes as the catalysts. Although the asymmetric hydrogenations of electron-rich olefins such as enamides (or enol esters) catalyzed by rhodium(I)-DIOP (**1**) complexes (substrate/catalyst = 100) have been reported by Kagan[10)] and Koenig,[11)] the steric and the electronic effects of the diphenylphosphino group on the enantioselectivity and the catalytic activity have not been clarified.

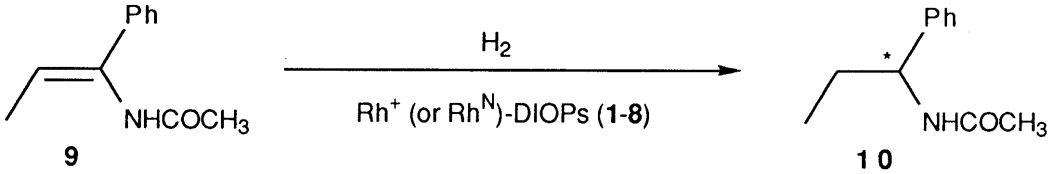
This communication describes the electronic and steric influences of the diarylphosphino groups of modified DIOPs on the enantioselectivity as well as the catalytic activity in the asymmetric hydrogenation of enamides.

Asymmetric hydrogenation of an enamide, (*Z*)-*N*-(1-phenylpropenyl)acetamide (**9**), was carried out in ethanol in the presence of cationic or neutral rhodium(I) complexes (substrate/catalyst = 1000) of (4*R*,5*R*)-DIOP (**1**) and modified (4*R*,5*R*)-DIOPs (**2**-**8**) bearing various substituents on the phenyl groups. The results are summarized in Table I. Under a standard condition (5 atm, 50

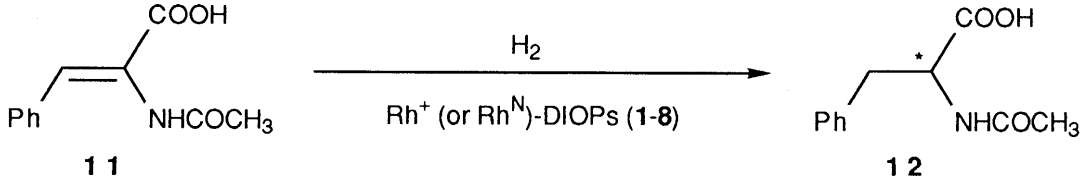


(4*R*,5*R*)-DIOPs

1: Ar^1=Ph, Ar^2=Ph
2: Ar^1=*p*-$Me_2NC_6H_4$, Ar^2=Ph
3: Ar^1=*p*-$Me_2NC_6H_4$, Ar^2=*p*-$Me_2NC_6H_4$
4: Ar^1=*p*-$MeOC_6H_4$, Ar^2=*p*-$MeOC_6H_4$
5: Ar^1=*p*-$MeOC_6H_4$, Ar^2=Ph
6: Ar^1=*m*-MeC_6H_4, Ar^2=*m*-MeC_6H_4
7: Ar^1=*p*-MeO-*m*,*m*'-$Me_2C_6H_2$, Ar^2=*p*-MeO-*m*,*m*'-$Me_2C_6H_2$
8: Ar^1=*p*-ClC_6H_4, Ar^2=*p*-$Me_2NC_6H_4$

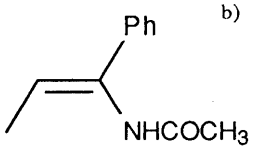
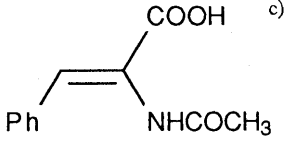


9 **10**



11 **12**

Table I. Asymmetric Hydrogenations[a] of (Z)-*N*-(1-Phenylpropenyl)acetamide (**9**) and (Z)-α-(Acetamido)cinnamic Acid (**11**)

	Ligand			Substrate			
				 [b]		 [c]	
	Ar^1	Ar^2	Rh	**9**		**11**	
				Convn[d] (%)	Opt.Y.[e] (%)	Convn[d] (%)	Opt.Y.[f] (%)
1	Ph	Ph	Rh^+	30	60 (69)	47	75
				(100	68 (70))[g]		
				(0	---)[h]		
			Rh^N	(87	39 (40))[i]	100	71
2	*p*-$Me_2NC_6H_4$	Ph	Rh^+	89	50 (50)	92	79
			Rh^N			100	75
3	*p*-$Me_2NC_6H_4$	*p*-$Me_2NC_6H_4$	Rh^+	100	24 (22)	94	77
				(100	10 (9))[g]		
				(72	25 (36))[h]		
			Rh^N			100	44
4	*p*-$MeOC_6H_4$	*p*-$MeOC_6H_4$	Rh^+	100	71 (72)	100	79
			Rh^N	100	66	100	65
5	*p*-$MeOC_6H_4$	Ph	Rh^+	73	72 (73)		
			Rh^N	65	47 (55)	100	71
6	*m*-MeC_6H_4	*m*-MeC_6H_4	Rh^+	83	49 (58)		
			Rh^N	(100	36 (37))[g]		
7	*p*-MeO-*m*,*m*'-$Me_2C_6H_2$	*p*-MeO-*m*,*m*'-$Me_2C_6H_2$	Rh^+	90	9 (6)[j]	94	80
			Rh^N			100	62
8	*p*-ClC_6H_4	*p*-$Me_2NC_6H_4$	Rh^+	40	41 (46)		
			Rh^N	(79	(43))[i]	100	57

a) All hydrogenations were carried out in EtOH (0.33M) in the presence of 0.1 mol % of cationic rhodium(I) catalyst (Rh^+=[ligand·Rh^+(cod)]·BF_4^-) prepared by a similar method reported previously or neutral rhodium(I) catalyst (Rh^N) prepared just prior to use by mixing $[Rh(cod)Cl]_2$ and the ligand in a molar ratio of 1:2.4 under an argon atmosphere. b) 5 atm, 50 °C, 4 h. c) 1 atm, 30 °C, 40 h (Rh^+) or 20 atm, 50 °C, 20 h (Rh^N); $[NEt_3]/[Rh]$ = 50. d) Determined by ^{1}H-NMR analysis or HPLC analysis. e) Determined by HPLC analysis with a chiral column of Chiralcel OD (hexane:isopropyl alcohol = 30:1). The values in parentheses are those estimated by using the reported value $[\alpha]_D^{20}$-134.8° (*c* 2.4, MeOH) for pure (*S*)-*N*-(α-ethylbenzyl)acetamide (**10**).[12] Configuration of all the products was *S* except the product using the ligand **7**. f) Calculated on the basis of the reported value $[\alpha]_D^{25}$+46.0° (*c* 1, EtOH) for pure (*S*)-*N*-acetylphenylalanine (**12**).[13] Configuration of all the products was *R*. g) 20 atm, 50 °C, 4 h. h) 1 atm, 30 °C, 40 h. i) 5 atm, 50 °C, 20 h. j) Configuration was *R*.

°C, 4 h) using the cationic rhodium(I) complexes, modified DIOPs (**2**-**8**) bearing electron-donating groups (*p*-dimethylamino, *p*-methoxy, or *m*-methyl groups) showed higher catalytic activities than DIOP (**1**). However, the enantioselectivities of **2** and **3** bearing *p*-dimethylamino groups were considerably lower than those of DIOP (**1**) and *p*-methoxy-substituted DIOPs (**4**, **5**). MOD-DIOP (**7**) bearing both a *p*-methoxy group and *m*,*m*'-dimethyl groups was much less effective for the enantioselection, and *m*-methyl-substituted DIOP (**6**) was also less effective. The enantioselectivities of modified DIOPs (Rh^+, 5 atm) were approximately in the following order: *p*-MeO > H > *m*-Me > *p*-Me_2N > *p*-MeO-*m*,*m*'-Me_2. In contrast to these results, we have already shown that **3** and **7** have much higher enantioselectivities than **1** in the hydrogenations of electron-deficient olefins such as itaconic acid

and its derivatives.[5] In general, the cationic complexes showed somewhat higher catalytic activities and better enantioselectivities than the corresponding neutral ones. The effect of changing the hydrogen pressure (1-20 atm) on the enantioselectivity of **3** was observed.

Further, we carried out the hydrogenation of a relatively electron-deficient enamide, (*Z*)-α-(acetamido)cinnamic acid (**11**), using the modified DIOPs (**2**-**8**)-rhodium(I) complexes in order to compare the effects of the phosphino groups on the enantioselectivity and the catalytic activity with the above results. The enantioselectivities of the cationic complexes under atmospheric hydrogen pressure were little affected by changing the ligands in comparison with the above results, while appreciable decrease of the enantioselectivity was observed in the use of neutral rhodium complexes of **3**, **4**, **7** and **8** under hydrogen pressure of 20 atm. In these cases, electron-rich phosphines also showed somewhat higher catalytic activities.

Thus the remarkable electronic and steric influences of the modified DIOPs on the enantioselectivity and the catalytic activity were observed in the asymmetric hydrogenation of an enamide **9**, and the cationic rhodium(I) complex of *p*-methoxy-substituted DIOP (**4**) was found to be the most efficient catalyst for the hydrogenations of enamides (**9**,**11**). The pressure effect on the enantioselectivity of **3** can be explained by Halpern's mechanism.[14] *m*-Methyl groups were regarded as having unfavorable steric effects on the enantioselection of the asymmetric hydrogenation of **9**. On the other hand, in the hydrogenation of the relatively electron-deficient enamide **11**, both electron-donating groups and *m*-methyl groups gave somewhat higher catalytic activities and better enantioselectivities to the cationic rhodium(I) complexes.

Since not only the steric effects but the electronic effects of the substituents of modified DIOPs were observed on the enantioselectivities and the catalytic activities of their rhodium(I) complexes, it is worth noting for the design of modified bisphosphine ligands that 1) the introduction of appropriate electron-donating groups on each phenyl group of DIOP is favorable to obtaining higher enantioselectivities and catalytic activities in the hydrogenations of various types of prochiral groups, 2) electron-rich phosphino groups are essential for exhibiting higher catalytic activities in the rhodium(I)-catalyzed hydrogenations, and 3) the *m*-methyl groups show significant steric effects on the enantioselectivities.

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