Catalytic Asymmetric Hydroformylation by the Use of Rhodium-complexes of Chiral Bidentate Phosphorus Ligands Bearing Saturated Ring Skeletons

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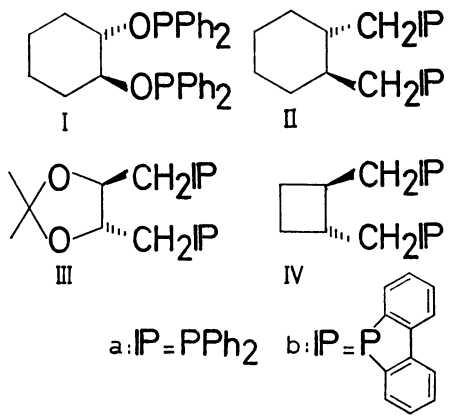
(1*S*,2*S*)-1,2-Bis(diphenylphosphinoxy)cyclohexane, (1*S*,2*S*)-1,2-bis(phosphinomethyl)cyclohexanes, (2*R*,3*R*)-2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(phosphino)butanes, and (1*R*,2*R*)-1,2-bis(phosphinomethyl)cyclobutanes, whose phosphino groups were diphenylphosphino or 5*H*-dibenzophosphol-5-yl groups where the rotation of phenyl–P bonds is impossible, were used as chiral ligands in rhodium-catalyzed asymmetric hydroformylation. The highest stereoselectivity was attained by the use of (1*R*,2*R*)-1,2-bis(5*H*-dibenzophosphol-5-ylmethyl)cyclobutane or (2*R*,3*R*)-2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(5*H*-dibenzophosphol-5-yl)butane.

The asymmetric hydroformylation reaction[1–4] of olefins by the use of chiral rhodium-complex catalysts is a promising method for synthesizing optically active aldehydes which allow numerous transformations to the final products. However, when compared with the hydrogenation of olefinic double bonds or the hydrosilylation of ketones,[5] the optical yields obtained so far in hydroformylation are relatively low and far from having any practical meaning. The difficulty lies in the fact that the reaction is effected at a higher temperature and consists of more steps, such as carbon monoxide insertion, than hydrogenation or hydrosilylation. In addition, a reactant carbon monoxide of a strong coordination power may compete with the chiral ligands in coordinating with rhodium; this complicates the situation as well.

In order to overcome these difficulties, although there is no doubt that the development of more active catalyst systems[6] which would allow the reaction to be carried out at a lower temperature is of primary importance, the breakthrough may come in the use of a chiral bidentate ligand,[3,4,7] which can be expected to chelate the central rhodium atom to make a more rigid and, therefore, more reliable asymmetric catalyst than a monodentate ligand.

In this paper, several kinds of bidentate chiral ligands, (1*S*,2*S*)-1,2-bis(diphenylphosphinoxy)cyclohexane (I),[8] (1*S*,2*S*)-1,2-bis(diphenylphosphinomethyl)-cyclohexane (IIa),[9,10] (1*S*,2*S*)-1,2-bis(5*H*-dibenzophosphol-5-ylmethyl)cyclohexane (IIb),[10] (2*R*,3*R*)-2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane (IIIa),[11] (2*R*,3*R*)-2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(5*H*-dibenzophosphol-5-yl)butane (IIIb),[7] (1*R*,2*R*)-1,2-bis(diphenylphosphinomethyl)-cyclobutane (IVa),[12,13] and (1*R*,2*R*)-1,2-bis(5*H*-dibenzophosphol-5-ylmethyl)cyclobutane (IVb),[13] were prepared and used for the rhodium-catalyzed hydroformylation of four typical kinds of olefins. The results were then compared with those of asymmetric hydrogenation.



Experimental

All the manipulations of organophosphorus compounds were carried out under a pure nitrogen atmosphere. I (85.5% optical purity),[8] (+)-(1*S*,2*S*)-1,2-bis(hydroxymethyl)cyclohexane ditosylate,[14,15] (+)-(1*R*,2*R*)-1,2-bis(hydroxymethyl)cyclobutane ditosylate,[12] (−)-Diop (IIIa),[11] 2-phenyl-1-butene,[16] and α-acetamidocinnamic acid[17] were prepared as has been described in the literature.

Chiral Bisphosphines. Method A (IIa): Eighty mmol of Na and 20 mmol of Ph_2PCl in 20 ml of dioxane were stirred for 6 h at 110 °C. To the cooled solution, THF (15 ml) was added, and then the ditosylate ($[\alpha]_D$+25.5° (benzene, *c* 3.16), lit,[14] +25.0° (benzene, *c* 5)) (6.7 mmol) in THF (12 ml) was added over 10 min at room temperature. Then the solution was refluxed for 2 h and cooled. After filtration, the filtrate was concentrated, water (10 ml) was added, and the product was extracted with benzene. The organic layer was washed and concentrated, and the residue was subjected to molecular distillation.

Method B (IIb, IIIb, IVa, and IVb): Seven mmol of a phenylphosphine (5-phenyl-5*H*-dibenzophosphole or triphenylphosphine) and 16 mmol of Li wire in 16 ml of THF were stirred for 2 h at room temperature and then refluxed for 10 min. After the excess Li wire had been removed, a 7 mmol portion of *t*-butyl chloride was added and the solution was refluxed for 15 min. To the solution, a THF (8 ml) solution of a ditosylate (3.5 mmol) was added over 7 min at room temperature, after which the mixture was stirred for an additional 2 h, refluxed, and worked up as above (liquid) or finally recrystallized (solid).

The properties of the chiral bisphosphines are listed in Table 1.

Catalytic Hydroformylation Procedure. A rhodium complex (1.35×10^{-2} mmol-Rh), a bisphosphine or diphosphinite (2.7×10^{-2} mmol or 5.4×10^{-2} mmol), a solvent (6 ml), and a substrate (3 ml) were placed in a 50-ml Schlenk-type autoclave (SUS 316) under a pure N_2 atmosphere, and 50 kgw/cm² (at 0 °C) of CO and then the same amount of H_2 were pressurized. The sealed reactor was immersed in a temperature-controlled oil bath, and the reaction solution was magnetically stirred.

Table 1. Properties of the chiral bisphosphine used

Bisphosphine	Purification	Yield/%	$[\alpha]_D$/°	Found (Calcd), %
IIa	Molecular distillation bp 200—210 °C (bath) ($2—4\times10^{-4}$ mmHg)	80	+50.0[a] (toluene, *c* 2.58)	C 79.52 (79.98) H 7.06 (7.13)
IIb	Recrystallization from toluene-MeOH mp 163.9—165.0 °C	21	−30.4 (toluene, *c* 2.54)	C 80.60 (80.65) H 6.54 (6.35)
IIIa			−12.6[b] (benzene, *c* 1.48)	
IIIb	Recrystallization from benzene-EtOH mp 188.0—189.2 °C	69	−63.2[c] (benzene, *c* 1.05)	
IVa	Recrystallization from EtOH mp 106.2—107.2 °C[d]	73	−15.7[d] (benzene, *c* 1.22)	C 79.23 (79.63) H 6.63 (6.68)
IVb	Molecular distillation bp 215—220 °C (bath) (1.0×10^{-3} mmHg)	49	−5.9 (benzene, *c* 1.21)	C 80.28 (80.34) H 5.99 (5.84)

a) Ref. 12 +52.7° (*c* 1.0, benzene). b) Ref. 11 −12.3° (*c* 4.57, benzene). c) Ref. 21 −65.5° (*c* 2, benzene), mp 188—190 °C. d) Ref. 12 −18.6° (*c* 1.0, benzene), mp 107 °C.

Table 2. Optical purities[a] (and prevailing configurations) of products in asymmetric hydroformylation and hydrogenation

Chiral ligand	Hydroformylation[b]				Hydrogenation	
	Styrene[e]	1-Butene	*cis*-2-Butene	2-Phenylpropene	α-Acetamidocinnamic acid[c]	2-Phenyl-1-butene[d]
	Temp 80 °C	90 °C	120 °C	150 °C	25 °C	50 °C
I	0.8(*S*)[f]	2.2(*S*)[g]	0 (*R*)[g]	0.3(*R*)	51.2(*S*)	28.3(*R*)
IIa	15.1(*S*)[h] 12.1(*S*)	9.4(*S*)[g] 11.5(*S*)	3.9(*R*)[g] 3.1(*R*)	0.1(*S*)	24.5(*S*)	4.0(*R*)
IIb	0.6(*R*)	4.8(*S*)	10.7(*R*)	2.7(*R*)	25.7(*R*)	3.2(*S*)
IIIa	18.3(*R*)	6.8(*R*)	9.5(*S*)	1.7(*R*)	77.8(*R*)	24.5(*S*)
IIIb	37.0(*S*)	16.2(*S*)	16.6(*R*)	1.6(*R*)	23.2(*S*)	1.1(*S*)
IVa[i]	4.2(*R*)	1.5(*R*)	8.0(*S*)	0.5(*S*)	52.7(*R*)	22.2(*S*)
IVb[i]	40.3(*S*)	16.2(*S*)	16.8(*R*)	2.5(*R*)	25.5(*S*)	0.1(*R*)

a) The optical purities were calculated on the following bases: *N*-acetyl-(*R*)-phenylalanine: $[\alpha]_D$ −51.8 (*c* 1, EtOH),[25] (*S*)-2-phenylbutane: $[\alpha]_D$ +27.31° (neat),[26] (*S*)-2-phenylpropanal: $[\alpha]_D$ +160° (neat)[23] (Pino, *et al.* claim +238°,[27] (*S*)-2-methylbutanal: $[\alpha]_D$ +31.2° (neat),[28] (*R*)-3-phenylbutanal: $[\alpha]_D$ −31.3° (neat).[29] b) Rh: $[RhCl(CO)_2]_2$, P/Rh=8 (atom ratio), solvent: benzene for styrene and 2-phenylpropene, or ethylbenzene for butenes. c) Substrate: 0.5 g, solvent: EtOH+benzene (1:1) 3.5 ml. d) Sudstrate: 1 ml, solvent: benzene 3 ml. e) P/Rh=4. f) At 110 °C. g) At 130 °C. h) At 90 °C. i) Rh: $[Rh(CO)_3]_4$.

Catalytic Hydrogenation Procedure. $[RhCl(1,5\text{-hexadiene})]_2$ (1.9×10^{-2} mmol), a bisphosphine or diphosphinite (4.0×10^{-2} mmol), a solvent, and a substrate were placed in a 25-ml Schlenk-type autoclave (SUS 316) under a pure N_2 atmosphere, and then the reactor was immersed in a bath of a designated temperature. H_2 was pressurized up to 50 kgw/cm² at that temperature, and the reaction solution was magnetically stirred.

Product Analysis. An aliquot of the reaction solution was analyzed by GLC (DEGS), and the remainder was distilled to afford an optically active product whose $[\alpha]_D$ was measured on a JASCO DIP-180 digital polarimeter. In the case of the hydrogenation of α-acetamidocinnamic acid, the reaction solution was worked up according to the literature.[11]

Results and Discussion

The optical purities were calculated through the optical rotation of isolated products; they are listed in Table 2.

A diphosphinite, I, although it resulted in fairly high optical yields in asymmetric hydrogenation,[8] caused a low asymmetric induction in the hydroformylation of any kind of olefins applied. The methylene-bridged analogue of I, a bisphosphine IIa, whose molecular structure is similar to that of I, brought about a much higher stereoselectivity than I.

On the other hand, IIa, with a saturated six-membered ring, was compared with Diop (IIIa), which has a five-membered dioxolane ring and with the IVa of a cyclobutane ring.[13,18] IIIa showed a certain asymmetric induction ability for each of the four olefins, while those of IIa or IVa depended on the structures of the olefins. That is, the ability decreased in the order of IIIa>IIa>IVa for styrene, in that of IIa>IIIa>IVa for 1-butene, and in that of IIIa>IVa>IIa for *cis*-2-butene. In the reaction of styrene or butenes, IIa of the configuration opposite to that of IIIa or IVa gave the antipode opposite to those given by IIIa and IVa; *i.e.*, the prevailing absolute configurations of the products from styrene or butenes were independent of the skeletal ring sizes of the bisphosphines, IIa—IVa.

The bidentate ligands mentioned above have Ph_2P

Table 3. Relative rates[a] (and product linearities (%)[b]) in catalytic hydroformylation[c]

Chiral bisphosphine	Styrene	1-Butene	*cis*-2-Butene	2-Phenylpropene
Temp	80 °C	90 °C	120 °C	150 °C
IIa	0.16 (17)	0.31 (72)	0.21 (0)	0.23 (85)
IIb	0.70 (9)	0.90 (60)	0.50 (1)	0.71 (72)
IIIa	0.47 (35)	2.8 (89)	0.65 (2)	1.3 (86)
IIIb	1.9 (10)	3.5 (68)	0.77 (5)	1.6 (79)
IVa[d]	8.2 (29)	6.4 (90)	0.76 (2)	2.3 (78)
IVb[d]	14 (14)	12 (72)	3.9 (6)	20 (76)

a) Maximum pressure drop, kgw/cm² in 1 h. b) Linear aldehyde/(linear aldehyde + branched aldehyde) × 100. c) Rh: $[RhCl(CO)_2]_2$. d) Rh: $[Rh(CO)_3]_4$.

groups. Upon chelating coordination, the four phenyl groups may protrude toward the coordination sites for a substrate and others, and they are considered to be responsible for the steric regulation. The phenyl group will take various conformations. In contrast to this, in the case of bisphosphines with 5*H*-dibenzophosphol-5-yl (DBP) groups which correspond to the planar Ph_2P groups whose phenyl groups are linked together at the *ortho*-positions, the influence of the rotation of the phenyl group can be excluded.

From this point of view, IIa, IIIa, and IVa, all with Ph_2P groups, were compared with IIb, IIIb, IVb, which have DBP ones. The substitution of DBP groups for Ph_2P ones always brought about a rate enhancement,[19] as is shown in Table 3. Moreover, Table 2 shows that the optical yields in the hydroformylation of styrene and butenes increased in the cases of III and IV upon DBP substitution. The orders of the asymmetric induction abilities among IIb≈IVb were IVb>IIIb>IIb for styrene and IVb—IIIb>IIb for butenes. Thus, IIIb and IVb were the most effective among the bidentate chiral ligands prepared in this study; this is in remarkable contrast to their lower stereoselectivity than IIIa and IVa in asymmetric hydrogenation. On the other hand, the prevailing configuration of the hydrogenation product from α-acetamidocinnamic acid was reversed through the substitution of DBP groups for Ph_2P ones, as is shown in Table 2.[20] In the hydroformylation of styrene and butenes also, IIIb or IVb prefered the opposite antipode to that IIIa or IVa prefered, respectively.

However, by the use of the II of a cyclohexane-ring skeleton, DBP-substitution for Ph_2P groups decreased the optical yields in the hydroformylation of styrene and 1-butene. In addition, the prevailing absolute configuration of the products was not reversed for all the olefins. Thus, the results with II were different from those with III or IV, which has a five- or four-membered ring skeleton, respectively. Furthermore, in the hydroformylation of styrene by the use of IIb, as the reaction temperature rose, the prevailing enantiomer was reversed at around 100 °C, and the optical purity of the product increased with an increase in the temperature up to about 160 °C, as is shown in Fig. 1.[22] This is in contrast with the behavior of IIIb or IVb, which invariably gave prevailing enantiomer

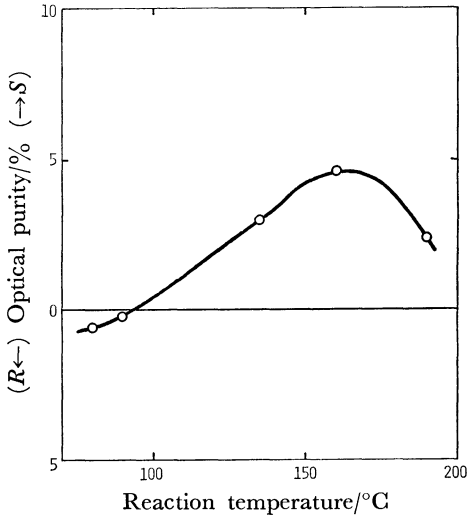


Fig. 1. Effect of reaction temperature on the optical purity of 2-phenylpropanal produced in the hydroformylation of styrene catalyzed by Rh-IIb system. (Other conditions are the same as in Table 2).

with a decrease in the stereoselectivity when the reaction temperature was raised in this range.

The present authors previously reported that the asymmetric induction abilities of IIIb and IVb were fairly high to a vinylidene-type olefin, 2-phenylpropene (V), in hydroesterification.[24] However, it is noteworthy that the abilities of I—IV remained low in the hydroformylation of V (Table 2). This is partly because the low reactivity of V requires a high reaction temperature (150 °C).

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