THE ORIGIN OF THE ENANTIOSELECTION IN THE RUTHENIUM(II)-CATALYZED ASYMMETRIC HYDROGENATION OF α,β-UNSATURATED CARBOXYLIC ACID[1)]

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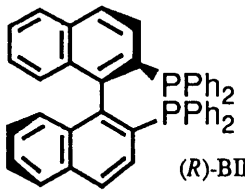
Using our chiral atropisomeric bisphosphines ruthenium(II) complexes, asymmetric hydrogenations of tiglic acid and its isomer were carried out. A possible enantioselective mechanism was considered on the basis of their different results on hydrogenation pressure effects.

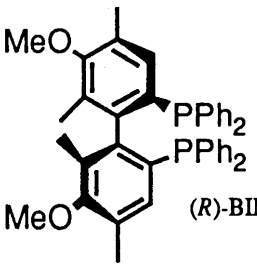
KEYWORDS atropisomeric biphenylbisphosphine; ruthenium(II) complex; asymmetric hydrogenation; pressure effect; tiglic acid; angelic acid

BINAP(1)-ruthenium(II) complex[2)] is an excellent catalyst for asymmetric hydrogenation of a series of functionalized olefins and ketones rather than that of rhodium(I) complex.[3)] On the other hand, almost all of the good ligands for rhodium(I)-based asymmetric hydrogenations were not well applied to ruthenium(II)-based ones.[4)] Previously, we prepared new atropisomeric biarylbisphosphines, BIMOP(2)[5)] and Cy-BIMOP(3),[6)] which were more electron-donative ligands than BINAP for the purpose of enhancing the catalytic activity. As we expected, the rhodium(I) complex of the electron-donative ligands has proved to have much better enantioselectivity and higher catalytic activity than that of BINAP. But the highly electron-donative ligand, Cy-BIMOP, was not suitable for the ruthenium(II)-promoted hydrogenation because this system was reported to be operated on the basis of monohydride mechanism,[7)] in contrast to the rhodium(I)-based dihydride mechanism.[8)]

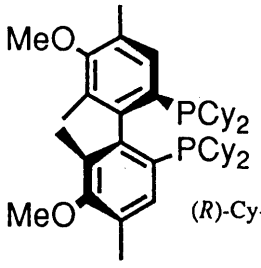
Chart 1. Atropisomeric Biarylbisphosphines



(*R*)-BINAP



(*R*)-BIMOP

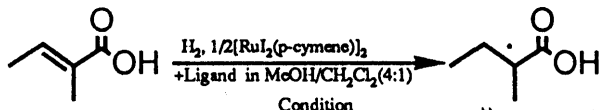


(*R*)-Cy-BIMOP

Asymmetric hydrogenations of α,β-unsaturated carboxylic acids, such as tiglic acid and its geometrical isomer, angelic acid, catalyzed by the ruthenium(II) complexes of these ligands were carried out, and the results are summarized in Tables I and II. The results for tiglic acid (Table I) show that the pressure effect of the hydrogen molecule was found to be the same as that for the rhodium(I)-based one in all cases. That is to say, the higher the pressure of the hydrogen molecule rose, the lower the enantiomeric excess of the product became. But, in contrast, in the asymmetric hydrogenation of angelic acid (Table II), the direction of the hydrogen pressure effect was reversed to that using tiglic acid as the substrate.

In order to explain such a phenomenon, we have presented *a new enantioselective mechanism* in the asymmetric hydrogenations of tiglic acid and angelic acid catalyzed by those ruthenium(II) complexes shown in Figures 1 and 2 on the

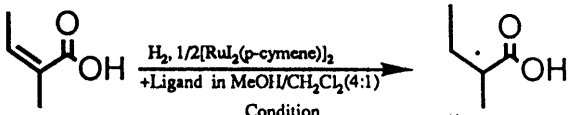
Table I. Asymmetric Hydrogenations[a] of Tiglic Acids Catalyzed by Ru(II) Complex of Chiral Atropisomeric Bisphosphines



Ligand	[Subst]/[Rh]	Condition atm/°C/h	Convn.(%)[b]	O.Y.(%)[c]
(*R*)-BINAP	1000	5/50-60/24	100	87(*R*)
		100/50-60/24	100	49(*R*)
(*R*)-BIMOP	1000	5/50-60/24	100	91(*R*)
		100/50-60/24	100	58(*R*)
(*R*)-Cy-BIMOP	100	5/50-60/24	10	60(*R*)
		100/50-60/24	94	27(*R*)

a) All hydrogenations were carried out in 0.5M solution of the substrate. b) Determined by NMR analysis. c) Determined by Chiral GLC analysis.

Table II. Asymmetric Hydrogenations[a] of Angelic Acids Catalyzed by Ru(II) Complex of Chiral Atropisomeric Bisphosphines



Ligand	[Subst]/[Rh]	Condition atm/°C/h	Convn.(%)[b]	O.Y.(%)[c]
(*R*)-BINAP	1000	25/50-60/24	100	21(*S*)
		100/50-60/24	100	45(*S*)
(*R*)-BIMOP	1000	25/50-60/24	100	15(*S*)
		100/50-60/24	100	33(*S*)
(*R*)-Cy-BIMOP	100	25/50-60/24	15	37(*R*)
		100/50-60/24	76	10(*R*)

a) All hydrogenations were carried out in 0.5M solution of the substrate. b) Determined by NMR analysis. c) Determined by Chiral GLC analysis.

basis of the reported monohydride mechanism.[7c] Regard[illegible] sults on, especially, the hydrogen pressure effect, we considered that each hydrogenation step should play an [illegible] ective role. The first step is the state of the substrate's coordination to the catalyst; there exist two diastereom[illegible] ct-(A) and adduct-(B), whose stabilities are different on the basis of the catalyst's chirality.[8, 9] It is thought th[illegible] does not determine the rate of the oxidative addition of the hydrogen molecule. After the rearrangement of th[illegible] there are still two diastereomers, adduct-(C) and adduct-(D), either of which should predominantly undergo the oxi[illegible] ition of the hydrogen molecule also on the basis of the catalyst's chirality.[9] In the asymmetric hydrogenation [illegible] id, adduct-(A) and -(C) are less stable than adduct-(B) and -(D). So it is considered that predominantly produced e[illegible] is derived from the minor (or less stable) diastereomer (adduct-(A)), similar to the case of the dihydride syste[illegible] um catalysts.[8] On the other hand, in the asymmetric hydrogenation of its geometrical isomer, angelic acid, addu[illegible] ess stable than adduct-(B') on the basis of the catalyst's chirality at the first step. But at the second step (rate-deter[illegible] ep), it is considered that the minor diastereomer (adduct-(A')) becomes the more stable diastereomer (adduct-(C')) rather than the other (adduct-(D'); derived from the adduct-(B')) on the basis of the catalyst's chirality.

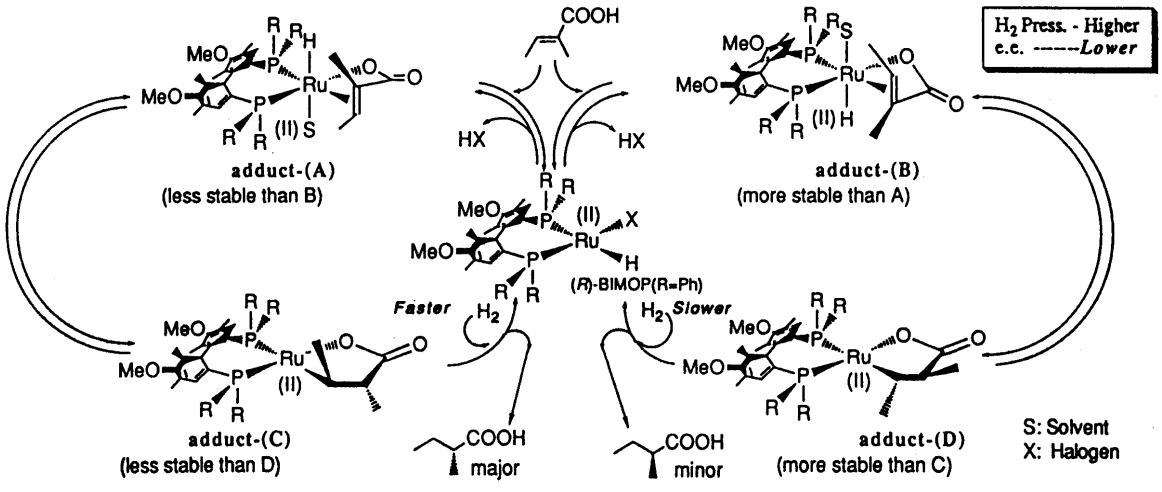


Fig.1. A Possible Enantioselective Mechanism for Ruthenium(II)-catalyzed Asymmetric Hydrogenation of Tiglic Acid

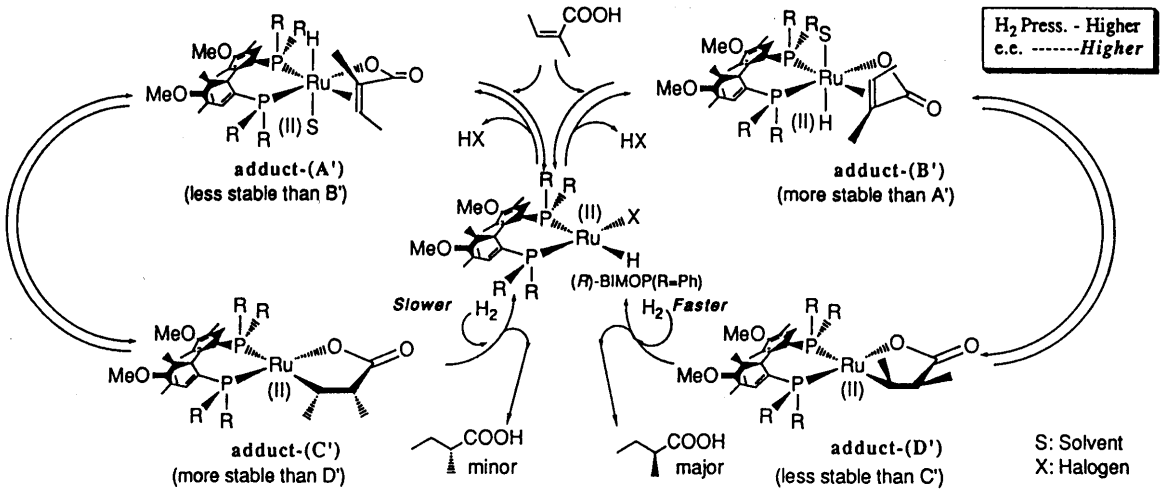


Fig.2. A Possible Enantioselective Mechanism for Ruthenium(II)-catalyzed Asymmetric Hydrogenation of Angelic Acid

Since the equilibrium between adduct-(A') and -(B') should come to play a major role with the increase of hydrogen pressure, the higher the hydrogen pressure rises, the higher the enantiomeric excess becomes, in the opposite manner to the rhodium catalyst. In addition, the direction of the selectivity of the product catalyzed by ruthenium(II)-(*R*)-Cy-BIMOP complex was reversed to that catalyzed by ruthenium(II)-(*R*)-BIMOP complex in the asymmetric hydrogenation of angelic acid. From the analysis using gas chromatography of the total product derived from the asymmetric hydrogenation catalyzed by ruthenium(II)-(*R*)-Cy-BIMOP complex, the peak of tiglic acid in the hydrogenated product appeared large. It is considered that partial isomerization of angelic acid occurred in the process of hydrogen elimination *in situ* in the asymmetric hydrogenation of angelic acid catalyzed by ruthenium(II)-(*R*)-Cy-BIMOP (bearing electron-donating groups) complex. So it can be explained that its hydrogenation rate is relatively very slow. Consequently, it is likely that tiglic acid isomerized from angelic acid underwent the oxidative addition of hydrogen molecules to reverse the direction of enantioselection to that using ruthenium(II)-(*R*)-BIMOP complex.

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