# Asymmetric Activation/Deactivation of Racemic Ru Catalysts for Highly Enantioselective Hydrogenation Irrespective of Ketonic Substrates: Molecular Design of Dimethylbinaphthylamine for Enantiomeric Catalysts Discrimination

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Received: July 15, 2002; Accepted: August 21, 2002

Dedicated to Prof. Noyori in honor of being awarded the Nobel Prize in Chemistry and for his excellent contribution to catalytic asymmetric hydrogenation.

**Abstract:** Asymmetric activation and deactivation of racemic catalysts are two extremes in asymmetric catalysis. In a combination of these two protocols, higher enantioselectivity can be achieved by maximizing the difference in catalytic activity between the enantiomers of racemic catalysts through selective activation and deactivation of enantiomeric catalysts. 3,3′-Dimethyl-2,2′-diamino-1,1′-binaphthyl (DM-DABN) is thus designed as a chiral poison (deactivator) for complete enantiomer resolution of racemic BINAP-Ru(II) catalysts. The catalyst system of DM-DABN, 1,2-diphenylethylenediamine (DPEN), and racemic BINAP-Ru(II) led to great success in highly enantioselective hydrogenation irrespective of the ketonic substrates. The lower catalytic activity of the BINAP-Ru(II)/DM-DABN complex stems from the electron delocalization from the Ru center to the diamine moiety in contrast to the BINAP-Ru(II)/DPEN complex where the highest electron densities are localized on the Ru-N region. The present 'asymmetric activation/deactivation protocol' can provide a guiding principle for the rational design of a molecule for enantiomeric discrimination between racemic catalysts.

**Keywords:** asymmetric activation; asymmetric deactivation; 3,3′-dimethyl-2,2′-diamino-1,1′-binaphthyl; hydrogenation; ruthenium(II) complex

## Introduction

Asymmetric catalysis of organic reactions is an important subject in modern science and technology.[1] Asymmetric catalysis enjoys this stature because it affords large amounts of enantioenriched products, while producing only a small amount of waste material, through the action of a chiral catalyst. Highly promising candidates for such asymmetric catalysts are metal complexes bearing chiral but usually non-racemic ligands. In homogeneous asymmetric catalysis, Sharpless et al. have emphasized the importance of "chiral ligand acceleration".[2] Here, an asymmetric catalyst is formed from a 'pre-catalyst' *via* ligand exchange with an added chiral ligand. The term 'asymmetric activation' may be proposed for this process in analogy to the activation process of an achiral reagent or catalyst, which provides an activated but achiral one (shown as "Achiral-Act" in Figure 1). The asymmetric catalysts thus prepared can be further transformed into highly activated catalysts by association with chiral activators (shown as "Act*" in Figure 1). This asymmetric activation process is particularly useful in racemic catalysis, as it can allow the selective activation of one enantiomer of racemic catalysts.[3]

In asymmetric catalytic reactions,[1] non-racemic catalysts thus prepared *via* chiral ligand exchange can generate non-racemic products with or without a non-linear relationship in enantiomeric excesses between catalysts and products.[4] However, racemic catalysts inherently give only a racemic mixture of chiral products. Recently, a strategy was reported whereby racemic catalysts could be used in catalytic asymmetric synthesis in different manners (Figure 2a and b).[5,6] An enan-

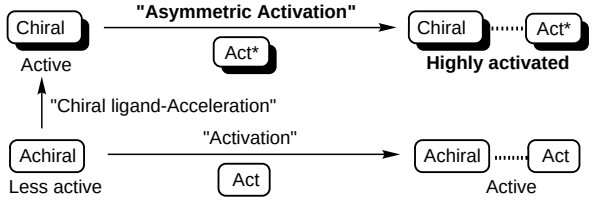


**Figure 1.** The concept of asymmetric activation.

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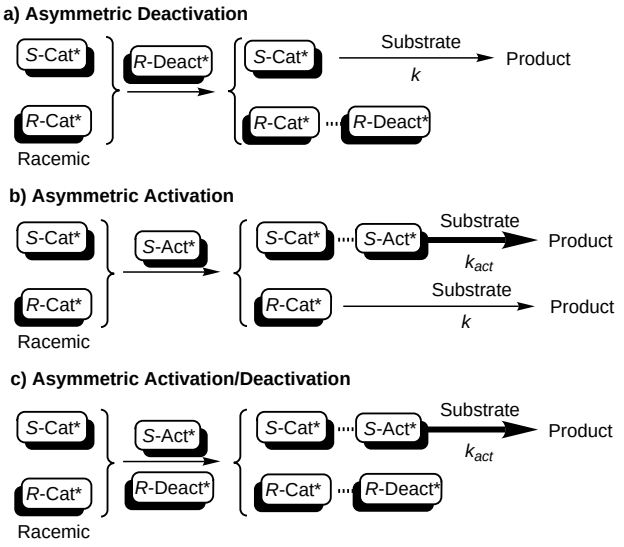



**Figure 2.** Strategies of asymmetric catalysis using a racemic catalyst.

tiomer-selective deactivation strategy for racemic catalysis has been reported, wherein a chiral poison (shown as "Deact*" in Figure 2a) selectively complexes with one enantiomer of a racemic catalyst and the non-complexed enantiomer performs the asymmetric catalysis (Figure 2a). However, exclusive complexation of one enantiomer of racemic catalysts with chiral poisons found to be a difficult task.[5] In fact, the chiral poisons have to be used in excess amounts[7] to the catalyst enantiomers because of an inherently ineffective discrimination. In contrast, we have recently reported that a chiral activator (shown as "Act*" in Figure 2b) both selectively complexes and activates rather than deactivates one enantiomer of a racemic catalyst (Figure 2b). The enantioselectivity can be higher than that achieved with enantiopure catalyst due to a higher efficiency of the catalyst ($k_{act} \gg k$). However, when a chiral activator non-selectively complexes with a racemic catalyst, the difference in catalytic activities between the activated diastereomers (e.g., "*S*-Cat*/*S*-Act*" and "*R*-Cat*/*S*-Act*") critically depends on the substrates.[6d] Thus, the asymmetric activation protocol in combination with the asymmetric deactivation protocol, namely 'asymmetric activation/deactivation', can achieve higher enantioselectivity regardless of the substrates by maximizing the difference in catalytic activity between enantiomeric catalysts in the racemic mixture (Figure 2c).

In the enantioselective hydrogenation of ketones using the racemic TolBINAP-Ru(II) complex and 1,2-diphenylethylenediamine (DPEN), the suitable molecular association of catalysts as well as the degree of asymmetric induction highly depends on the ketonic substrates.[6d] We report herein a molecular design of 3,3′-dimethyl-2,2′-diamino-1,1′-binaphthyl (DM-DABN)[8] as a chiral poison (deactivator) for complete

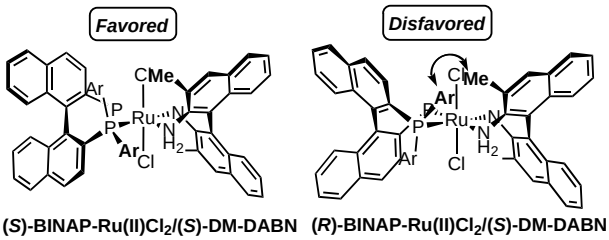



**Figure 3.** Rational design of a chiral deactivator for enantiomer discrimination of racemic BINAPs-Ru(II) complexes.

enantiomer discrimination[9] of racemic BINAP-Ru(II) catalysts in highly enantioselective hydrogenation. The combination of DM-DABN deactivating one enantiomer of a racemic BINAP-Ru(II) complex and DPEN activating the other enantiomer achieved highly enantioselective hydrogenation regardless of ketonic substrates.[10] Furthermore, we theoretically illustrated the reasons why DM-DABN and DPEN can act as a chiral deactivator and activator, respectively.

## Results and Discussions

Complexation of $RuCl_2(binaps)(dmf)_n$[11] [**1a**: BINAP-Ru(II)$Cl_2$, **1b**: XylBINAP-Ru(II)$Cl_2$] with chiral diamines has been reported to give stable *trans*-$RuCl_2$(binaps)(diamine) complexes[12b] which catalyze hydrogenation of simple ketones in the presence of KOH.[12] However, DPEN (**3**) as a chiral activator forms both diastereomeric complexes with racemic BINAPs-Ru(II)$Cl_2$ complex (**1**) in an equal amount.[6d] It is inevitable that the degree of asymmetric induction highly depends on substrates by the non-selective complexation of DPEN with racemic BINAPs-Ru(II)$Cl_2$. Therefore, it is essential to design a poisonous diamine to discriminate and maximize catalytic activities between the two enantiomers of racemic BINAPs-Ru(II)$Cl_2$ (**1**). (*S*)-DM-DABN (**2**) was thus designed as a deactivator by formation of the $RuCl_2$(binaps)(dm-x. As shown in Figure 3, DM-DABN has been rationally designed as a deactivator according to the enantiomer-selective steric repulsion of (*S*)-DM-DABN with the (*R*)-BINAPs-Ru(II)$Cl_2$ and the selective complexation of (*S*)-DM-DABN with (*S*)-BINAPs-$RuCl_2$.

Racemic DM-DABN (**2**) was synthesized by a coupling reaction of 3-methyl-2-aminonaphthalene, which was derived from commercially available 3-amino-2-naphthoic acid (Figure 4), since methylation of commercially available DABN through *ortho*-functionalization of aromatic amines[13] was unsuccessful. The resolution of DM-DABN was first attempted by using chiral resolving acids but failed and was finally established by employing (*S*)-BINAP-$RuCl_2$ (**1a**) (0.7 molar amount) under an argon atmosphere (Figure 4). (*R*)-**2** with 98% ee ($>99\%$ ee[14] after one recrystallization)

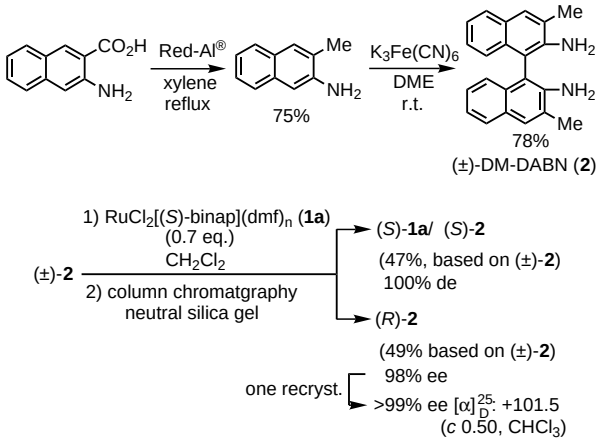



**Figure 4.** Synthesis of racemic DM-DABN **2** and enantiomer resolution with enantiopure BINAP-Ru(II) **1**.

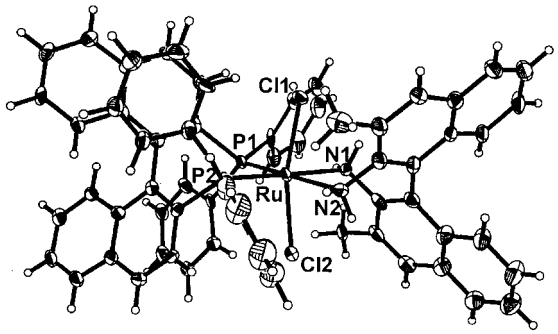
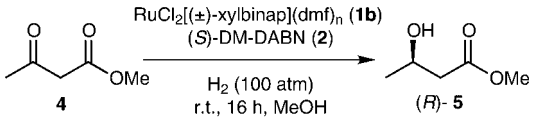



**Figure 5.** X-ray analysis of $RuCl_2$[(*S*)-binap][(*S*)-dmdabn]. Selective bond lengths [Å] and bond angles [°]: Ru – Cl1 2.418(4), Ru – Cl2 2.401(3), Ru – P1 2.273(3), Ru – P2 2.270(4), Ru – N1 2.228(9), Ru – N2 2.263(10); Cl1 – Ru – Cl2 165.34(11), P1 – Ru – P2 89.80(12), N1 – Ru – N2 80.1(4).

and pure (*S*)-BINAP-Ru(II)/(*S*)-DM-DABN [(*S*)-**1a**/(*S*)-**2**] were separated almost quantitatively after purification by neutral silica gel column chromatography. The slight decrease in the enantiomer excess of (*R*)-**2** is due to decomposition of (*S*)-**1a**/(*S*)-**2** through silica gel column, since (*R*)-**2** with 53% ee was obtained in the earliest fraction after outflow of (*S*)-**1a**/(*S*)-**2**. This result clearly shows that DM-DABN (**2**) can completely discriminate the enantiomers of the racemic BINAP-Ru(II)$Cl_2$ complex (**1a**). The (*S*)/(*S*) configuration of a BINAP-Ru(II)/DM-DABN diastereomer was confirmed by X-ray analysis of the single-crystal obtained from dichloromethane/ether/hexane (Figure 5). In turn, addition of racemic BINAP-$RuCl_2$ complex (**1a**) to the 0.5 molar amount of (*S*)-DM-DABN (**2**), obtained by the resolution described above, resulted in selective formation of the single diastereomeric (*S*)-**1a**/(*S*)-**2** complex. While no complex was formed between (*R*)-**1a** and (*S*)-**2**, as was confirmed in a separate run, the uncomplexed (*R*)-**1a** enantiomer gave an activated catalyst upon addition of enantiopure (*S*,*S*)- or (*R*,*R*)-DPEN.[15]

**Table 1.** Hydrogenation of methyl 3-oxobutanoate (**4**) by racemic BINAP-Ru(II) catalysts through chiral poisoning.




| Entry | Cat. | Deact* | Yield[a] [%] | ee[b] [%] |
|---|---|---|---|---|
| 1[c] | (±)-**1b** | 0.5 eq | 100 | 99.3 |
| 2[d] | (*R*)-**1b** | none | 100 | 99.9 |

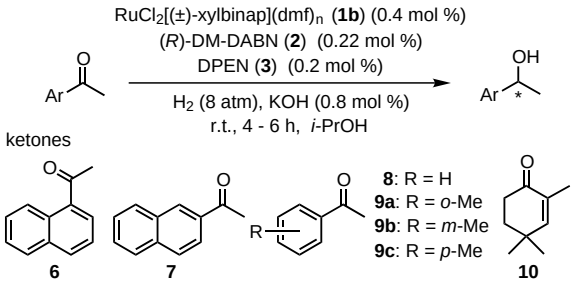
[a] Determined by GC analysis (TC-1701).
[b] Determined by chiral HPLC analysis (CHIRALCEL OB-H) after conversion to methyl 3-benzoyloxybutanoate.
[c] S/C (substrate to catalyst molar ratio) = 750.
[d] S/C = 1500.

Complete enantiomer recognition of the racemic BINAPs-$RuCl_2$ (**1**) was found to be effective for enantioselective hydrogenation of β-keto esters[16] using enantiopure DM-DABN (**2**) as the chiral poison (Table 1). Hydrogenation of methyl 3-oxobutanoate (**4**) by (±)-XylBINAP-$RuCl_2$ (**1b**) with (*S*)-**2** gave (*R*)-methyl 3-hydroxybutanoate (**5**) with 92.4% ee in quantitative yield. XylBINAP[17] was thus employed as a more efficient chiral ligand to give the more stable (S)-XylBINAP-$RuCl_2$/(*S*)-DM-DABN complex [(*S*)-**1b**/(*S*)-**2**].[18] A 0.5 molar amount of (*S*)-**2** was added to (±)-**1b** in $CH_2Cl_2$ and then stirred for 1 h. Methyl 3-oxobutanoate (**4**), MeOH and $H_2$ were subsequently introduced after removal of $CH_2Cl_2$. The reaction mixture was stirred at room temperature for 16 h to give (*R*)-methyl 3-hydroxybutanoate (**5**) with 99.3% ee in quantitative yield (Run 1). The enantioselectivity (99.3% ee) thus obtained was equally high to that (99.9% ee) obtained in our hands by the enantiopure (*R*)-**1b** catalyst (Run 1 *vs.* 2). Thus, asymmetric deactivation of racemic catalysts (chiral poisoning strategy) is successful in the case of highly selective complexation and deactivation with a well-designed chiral poison.

By using two different types of chiral diamines as an activator and deactivator, the racemic XylBINAP-$RuCl_2$ (**1b**) catalyst achieves higher enantioselectivities than those attained by simple activation. Addition of first DM-DABN (**2**) and then DPEN (**3**) should lead to the two different ruthenium dichloro complexes and further to the mono- or dihydrido Ru species under hydrogenation conditions. The DM-DABN complex is far less catalytically active than the DPEN complex for hydrogenation.

The mixture of (±)-**1b** and a 0.5 molar amount of (*R*)-**2** was stirred for 30 min at room temperature in dichloromethane. A 0.5 molar amount of (*S*,*S*)-**3** in 2-propanol was added to give selectively the two complexes $RuCl_2$[(*R*)-xylbinap][(*R*)-dmdabn] and $RuCl_2$[(*S*)-xylbinap][(*S*,*S*)-dpen] complexes. Enantioselective hydrogenation was performed by the mixture

**Table 2.** Hydrogenation of ketones by the racemic [$RuCl_2$(xylbinap)] complex through asymmetric activation/deactivation.




| Ketones | (*R*)-**2**[a] | **3** | Yield[a] [%] | ee[b] [%] |
|---|---|---|---|---|
| **6** | + | (*S*,*S*) | >99 | 96 (*R*) |
| **6** | - | (*S*,*S*) | >99 | 80 (*R*) |
| **7** | + | (*S*,*S*) | >99 | 91 (*R*) |
| **7** | - | (*S*,*S*) | >99 | 45 (*R*) |
| **8** | + | (*S*,*S*) | >99 | 95 (*R*) |
| **8** | - | (*S*,*S*) | >99 | 70 (*R*) |
| **9a** | + | (*S*,*S*) | >99 | 95 (*R*) |
| **9a** | - | (*S*,*S*) | >99 | 82 (*R*) |
| **9b** | + | (*S*,*S*) | >99 | 95 (*R*) |
| **9b** | - | (*S*,*S*) | >99 | 60 (*R*) |
| **9c** | + | (*S*,*S*) | >99 | 93 (*R*) |
| **9c** | - | (*S*,*S*) | >99 | 60 (*R*) |
| **10** | + | (*R*,*R*) | >99[b] | 92 (*R*) |
| **10** | - | (*R*,*R*) | >99[b] | 84 (*R*) |

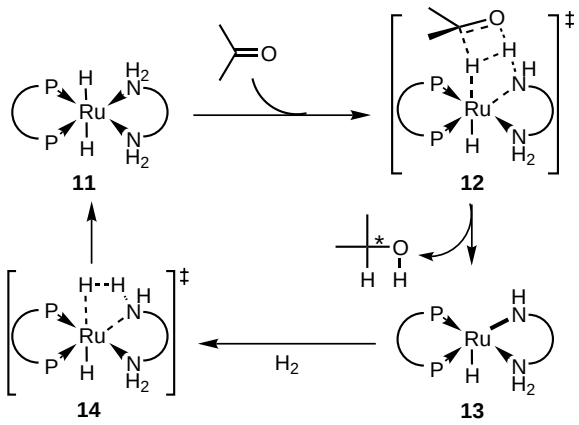
[a] "+" denotes the presence of (*R*)-**2**.

[b] Racemic [$RuCl_2$(tolbinap)] was used;

TolBINAP = 2,2'-bis(di-4-tolylphosphanyl)-1,1'-binaphthyl.

after the addition of KOH and different types of ketones (**6 – 10**) to the mixture. The efficiency of this asymmetric activation/deactivation protocol was reflected, regardless of the ketonic substrates, in the high enantioselectivity in the asymmetric hydrogenation (Table 2). All ketones employed can be hydrogenated at room temperature with enantiomeric excesses higher than 90% ee in the same quantitative yield. The asymmetric activation/deactivation protocol achieved a higher level of enantioselectivity than those obtained using the (±)-XylBINAP-$RuCl_2$/(*S,S*)-DPEN complexes at the same temperature and pressure. A superiority of the asymmetric activation/deactivation protocol is significantly shown in the case of 2-naphthyl methyl ketone (**7**), where the enantioselectivity of (*R*)-1-(2-naphthyl)-ethanol using (*R*)-**2** is increased up to 91% ee in contrast to only 45% ee without (*R*)-**2**. 2,2,4,4-Trimethyl-2-cyclohexenone (**10**) was also hydrogenated in high enantioselectivity (92% ee) by changing the chirality of DPEN from *S* to *R*.

To clarify the reasons why DM-DABN and DPEN can act as a deactivator and activator, respectively, we carried out a density functional calculation[19] for the hydrogen-splitting step of amide complex **13** in a heterolytic manner *via* transition state **14** (Scheme 1).

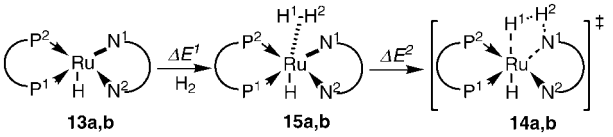


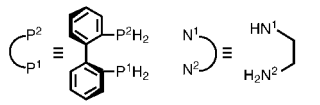
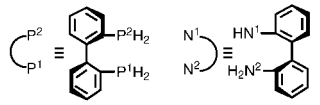

**Scheme 1.** The catalytic mechanism of asymmetric hydrogenation of ketones.

The catalytic mechanism of hydrogenation of ketones has been proposed in the closely related Ru(II)-catalyzed transfer hydrogenation (Scheme 1).[12a,20] In terms of the reduction process of ketones, which has been studied in detail, the reactivity of the coordinatively saturated complex **11** originates from the dipolar $H^{\delta-}$-$Ru^{\delta+}$-$N^{\delta-}$-$H^{\delta+}$ arrangement fitting well with the carbonyl dipole and stabilizing the pericyclic transition state **12**. On the other hand, less attention has been devoted to the hydrogen-splitting step although the reaction rate is highly sensitive to the pressure of hydrogen and becomes rapid under high pressure. The dependency of the rate on the hydrogen pressure indicates the cleavage of hydrogen (**13** → **14**) would be the turnover-limiting step. From views of the difference of the catalytic activity between the ruthenium complexes bearing the two different types of diamines, much attention should be devoted to the cleavage of hydrogen forming the active ruthenium hydride **11**.

Thus, the present theoretical study focused on the hydrogen-splitting step of amide complex **13.** The hydrogen molecule coordinates on the 16-electron Ru center of the amide complex **13** to form the initial coordination complex **15** followed by the cleavage of hydrogen *via* transition state **14** (Table 3 and Figure 6). The amide complexes **13a** and **13b** as the models of (*S*)-BINAP-Ru(II)/(*S,S*)-DPEN and (*R*)-BINAP-Ru(II)/(R)-DM-DABN were stabilized by 3.2 and 1.7 kcal/mol, respectively, through coordination of hydrogen molecule on the Ru center. The activation energy of the hydrogen-cleavage in the series **a** (+11.2 kcal/mol; DPEN model) is 4.0 kcal/mol smaller than that in the series **b** (+15.2 kcal/mol; DM-DABN model). This activation energy difference clearly indicates that the amide complex bearing DPEN preferentially forms the reactive ruthenium hydride species in comparison with that bearing DM-DABN. What is the origin of the 4.0 kcal/mol difference between the series **a** and **b**? As

**Table 3.** The stabilization energies ($\Delta E^1$) through coordination of hydrogen molecule and the activation energies ($\Delta E^2$) of hydrogen-cleavage.




| | | $\Delta E^1/\Delta E^2$ [kcal/mol] |
|---|---|---|
| a |  | –3.2/+11.2 |
| b |  | –1.7/+15.2 |

shown in Figure 6, the series **a** and **b** show almost the same structural feature in the amide complex **13**, where the Ru-$P^2$ coordination (**a**: 2.31 Å, **b**: 2.30 Å) is weaker than Ru-$P^1$ coordination (**a**: 2.26 Å, **b**: 2.27 Å) due to the *trans* influence of the dipolar Ru-$N^1$ bond (**a**: 2.01 Å, **b**: 2.09 Å). In the transition structures of **14a** and **14b**, the cleaving Ru-$N^1$ and H-H bonds in **14b** are 0.1 Å and 0.04 Å longer than in **14b** and the forming Ru-H and $N^1$-H bonds in **14a** are 0.04 Å and 0.06 Å shorter than in **14b**. These structural features illustrate that **14a** is an earlier transition state in comparison with **14b** and give a good account for the larger activation energy of the hydrogen-cleavage of **13b**.

Furthermore, examination of the natural population for the Ru, phosphorus, and nitrogen atoms revealed an interesting tendency of charge distribution in the series **a** and **b** (Table 4). The negative charge on the Ru center in the amide complex **13a** ( – 0.28) is larger than that in **13b** ( – 0.25), while the negative charges become the same value in the transition states of **14a** and **14b** ( – 0.37). Two nitrogen atoms $N^1$ and $N^2$ in the series **a** are more negative than those in the series **b**, while the diamine moieties in the series **a** are less negatively charged than in the series **b.** The tendency of the nitrogen charge is not changed through the cleavage of the hydrogen molecule. The charge distributions of the phosphorus atoms are comparable in both series **a** and **b**. It is noted that the electron population is highly localized on the ruthenium and nitrogen atoms in the series **a** and is delocalized from the ruthenium to the diamine region in the series **b** due to electron-withdrawing aryl groups attached to the nitrogen atoms. Thus, the lower activity of the amide complex bearing DM-DABN for hydrogen-splitting originates from electron delocalization from the ruthenium to the diamine region. In the amide complex bearing DPEN, the highest energy electrons localized on the Ru-$N^1$ region readily donate to the H-H σ*-

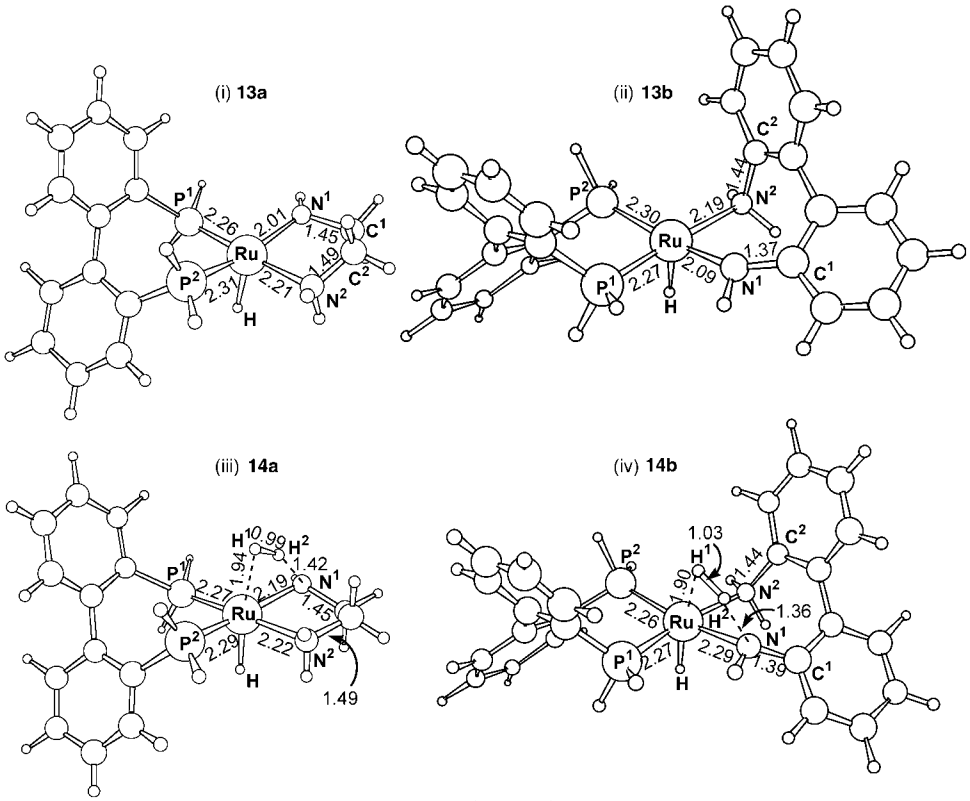



**Figure 6.** 3D structures of the amide complexes **13a** and **13b** (i and ii) and the hydrogen-splitting transition states **14a** and **14b** (iii and iv) at the B3LYP/631SDD level. Bond lengths are shown in Å.

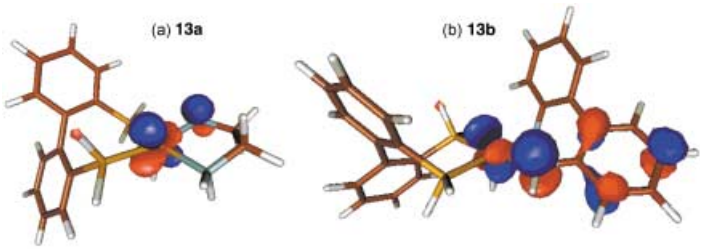



**Figure 7.** The highest occupied Kohn–Sham orbitals of **13a** and **13b**.

**Table 4.** The natural population analysis of the amide complex **13** and the transition state **15** at the B3LYP/631SDD level.

| | Ru | $H^1$ | $H^2$ | $P^1$ | $P^2$ | $N^1$ | $N^2$ | $N^1$ $N^2$ |
|---|---|---|---|---|---|---|---|---|
| **13a** | −0.28 | - | - | +0.64 | +0.55 | −0.88 | −0.84 | −0.19 |
| **14a** | −0.37 | −0.20 | +0.22 | +0.66 | +0.61 | −0.91 | −0.83 | −0.17 |
| **13b** | −0.25 | - | - | +0.64 | +0.57 | −0.84 | −0.81 | −0.33 |
| **14b** | −0.37 | −0.20 | +0.26 | +0.66 | +0.65 | −0.87 | −0.81 | −0.26 |

orbital to cleave hydrogen molecule and form the active ruthenium hydride species. The natural charges of cleaving hydrogen atoms, $H^1$ and $H^2$ in **14**, which are highly polarized, show that hydrogen-splitting step proceeds in a heterolytic manner.

The highest occupied Kohn–Sham orbitals (HO) of **13a** and **13b** at the B3LYP/631SDD level support the tendency of charge distribution. As shown in Figure 7, the HOs in the series **a** and **b** are recognized as an out-of phase interaction between the Ru d-orbital and the $N^1$ lone pair orbital. Although the energy levels of the HOs are almost same (**a**: − 4.2 eV, **b**: − 4.1 eV), the highest energy electrons are delocalized in **13b** because the HO extended from the Ru center to the diamine region (Figure 7). Indeed, the $N^1$-$C^1$ bond lengths (**13b**: 1.37 Å, **14b**: 1.39 Å) are shorter than the $N^2$-$C^2$ bond lengths (1.44 Å) in **13b** and **14b** due to conjugation between $N^1$ lone pair orbital and π-orbital (Figure 6, ii and iv).

In conclusion, the racemic BINAP-$RuCl_2$ catalysts (**1**) can be completely discriminated with the designed DM-DABN (**2**) and used as an equally effective catalyst to the enantiopure **1** for asymmetric hydrogenation. The success in DM-DABN thus provides a guiding principle for rational design of a molecule for enantiomeric catalysts discrimination. Furthermore, this 'asymmetric activation/deactivation' strategy leads to highly enantioselective hydrogenation regardless of the ketonic substrates by maximizing the difference in catalytic activity between the enantiomeric catalysts in the racemic mixture. The present 'asymmetric activation/deactivation protocol' can be regarded as a paradigm shift in racemic catalysis.

# Experimental Section

## General

$^1$H NMR and $^{13}$C NMR were measured on a Varian Gemini 300 (300 MHz) spectrometer and $^{31}$P NMR was measured on a GX-500 (500 MHz) spectrometer. Chemical shifts of $^1$H NMR are expressed in parts per million downfield from tetramethylsilane as internal standard ($\delta = 0$) in $CDCl_3$. Significant $^1$H NMR data are tabulated in following order: multiplicity (s: singlet; d: doublet; t: triplet; q: quartet; sept: septet; bs: broad singlet; bd: broad doublet; m: multiplet) and coupling constants ($J$) are reported (Hz). Chemical shifts of $^{13}$C NMR are expressed in parts per million downfield from $CDCl_3$ as internal standard ($\delta = 77.0$) in $CDCl_3$. Chemical shifts of $^{31}$P NMR are expressed in parts per million downfield from 85% $H_3PO_4$ as an external standard ($\delta = 0$) in $CDCl_3$. Optical rotations were measured on a JASCO DIP-370. Liquid chromatographic analysis (LC) was conducted on JASCO PU-980, LG-980-02, DG-980-50 and CO-966 instruments equipped with model UV-975 spectrometers as an ultra-violet light detector. Capillary gas chromatographic analysis (GC) was conducted on a Shimadzu GC-14B instrument equipped with FID detector and capillary column coated with PEG-20M, using He as a carrier gas. Peak areas were calculated by Shimadzu C-R6A.

## Computational Methods

All calculations were performed with a Gaussian 98 package. The B3LYP functional was employed with the basis set denoted 631SDD consisting of the SDD basis set including Stuttgart effective core potential for Ru atom and 6-31G(d) basis set for the rest. The chemical models consisted of simple diphosphine and diamine ligands, where hydrogen atoms were used instead of phenyl rings.

## Preparation of (±)-DM-DABN

**3-Methyl-2-naphthylamine:** To a mixture of 3-amino-2-naphthoic acid (80% purity, 12.1 g, 52 mmol) and xylene (350 mL) was added Red-Al® (117 mL, 390 mmol) at room temperature under argon atmosphere. After stirring for 6 h at 150 °C, the reaction mixture was cooled and a second portion of Red-Al® (39 mL, 130 mmol) was added. After stirring for 18 h at 150 °C, 20% KOH was carefully added at 0 °C. The crude mixture was filtered over Celite®, and the filtrate was washed with 1 N KOH. After concentration of the organic layer under reduced

pressure, the residue was purified by silica-gel chromatography (hexane/ethyl acetate = 4:1 to 3:1) followed by recrystallization from hexane and ethyl acetate to give 3-methyl-2-naphthylamine; yield: 6.1 g (75%). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta = 2.36$ (s, 3H), 3.79 (br, 2H), 7.01 (s, 1H), 7.22 (t, $J = 7.5$ Hz, 1H), 7.33 (t, $J = 7.5$ Hz, 1H), 7.55 (s, 1H), 7.59 (d, $J = 8.1$ Hz, 1H), 7.65 (d, $J = 8.1$ Hz, 1H); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta = 17.9, 108.6, 122.4, 125.3, 125.4, 127.0, 128.2, 128.7, 133.7, 143.4, 161.0$.

**3,3′-Dimethyl-2,2′-diamino-1,1′-binaphthyl [(±)-DM-DABN] (on a 1 mmol scale):** To a solution of 157 mg (1 mmol) of 3-methyl-2-naphthylamine in 30 mL of dimethoxyethane was added 1.32 g (4 mmol) of $K_3Fe(CN)_6$ dissolved in 60 mL of 0.5 N NaOH solution. The mixture was stirred at 0 °C for 1 h. Dichloromethane (10 mL) was added and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 10 mL) and dried over $MgSO_4$. After removal of the solvent under reduced pressure, the residue was purified by Florisil chromatography (dichloromethane), and then by silica-gel chromatography (hexane/ethyl acetate = 4:1 to 3:1) to give racemic 3,3′-dimethyl-2,2′-diamino-1,1′-binaphthyl; yield: 79.6 mg (51%). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta = 2.45$ (s, 6H), 3.45 (br, 4H), 7.01 (d, $J = 8.1$ Hz, 2H), 7.15 (t, $J = 7.5$ Hz, 2H), 7.22 (t, $J = 7.5$ Hz, 2H), 7.70 (s, 2H), 7.75 (d, $J = 8.1$ Hz, 2H); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta = 18.4$, 112.8, 122.4, 123.8, 125.2, 125.8, 127.3, 128.4, 128.9, 132.5, 142.1.

## Resolution of (±)-DM-DABN with BINAP-Ru(II) Complex

To a mixture of racemic 3,3′-dimethyl-2,2′-diamino-1,1′-binaphthyl (0.73 g, 2.3 mmol) and $RuCl_2$[(*S*)-binap](dmf)$_2$ (1.6 g, 1.7 mmol) was added dichloromethane (70 mL) at room temperature under argon atmosphere. After stirring for 2 h at room temperature, dichloromethane was removed under reduced pressure. The residue was purified by neutral silica-gel chromatography (dichloromethane) to give 0.36 g [49%, based on (±)-DM-DABN] of (*R*)-DM-DABN and 1.2 g [47%, based on (±)-DM-DABN] of (*S*)-BINAP-Ru(II)/(*S*)-DM-DABN complex. (*R*)-DM-DABN was recrystallized from dichloromethane, diethyl ether and hexane to give 99.5% ee of (*R*)-DM-DABN. HPLC analysis of (*R*)-DM-DABN: HPLC (CHIRALCEL OD-H column, hexane/2-propanol = 80:20, flow rate 0.7 mL/min, detection UV = 254 nm): $t_R$ of *R*-isomer 12.7 min, $t_R$ of *S*-isomer 20.3 min. $[\alpha]_D^{25}$: +101.5 (*c* 0.50, $CHCl_3$).

The single crystal growth was carried out from a dichloromethane/ether/hexane mixture at room temperature. X-ray crystallographic analysis was performed on a Bruker SMART 1000 diffractometer (graphite monochromator, Mokα radiation, $\lambda = 0.71073$ Å). The structure was solved by direct methods and expanded using Fourier techniques. Crystal data for $RuCl_2$[(*S*)-binap][(*S*)-dmdabn]: $C_{66}H_{52}Cl_2N_2P_2Ru$, reddish-orange, crystal dimensions 0.07 × 0.17 × 0.22 mm, orthorhombic, space group *P*21212 (No.18), $a = 20.822(3)$, $b = 22.130(3)$, $c = 13.1320(18)$ Å, $V = 6051.2(14)$ Å$^3$, $Z = 4$, $\rho$calc = 1.215 g cm$^{-3}$, ($\mu$Mokα) = 1.43 cm$^{-1}$, $T = 103$ K, 10304 reflections were independent and unique, and 6256 with $I > 2\sigma(I)$ ($2\theta_{max} = 24.7°$) were used for the resolution of the structure. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. $R = 0.095$, w$R2 = 0.2116$. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited at the Cambridge Crystallographic Data Center as supplementary publication no. CCDC-144099. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB@ 1EZ, UK (fax:(+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

## Catalytic Hydrogenation of Methyl 3-Oxobutanoate by Racemic XylBINAP-Ru(II) Catalyst (1b) with DM-DABN (2)

To the mixture of $RuCl_2$[(±)-xylbinap](dmf)$_n$ complex (14.0 mg, 0.0133 mmol) and (*S*)-DM-DABN (2.2 mg, 0.0069 mmol) in a 100-mL autoclave was added dichloromethane (2.0 mL) under argon atmosphere. After stirring for 1 h at room temperature, dichloromethane was removed under reduced pressure. Methanol (1.2 mL) and methyl 3-oxobutanoate (1.1 mL, 10 mmol) were then added to the autoclave under a stream of argon. Hydrogen was introduced at a pressure of 100 atm. The solution was stirred for 16 h at room temperature. After concentration under reduced pressure, the residue was filtered through a short column of silica gel to give methyl 3-hydroxybutanoate. Chemical yield of methyl 3-hydroxybutanoate was calculated by GC analysis. The crude 3-hydroxybutanoate was distilled to give 1.0 g of methyl 3-hydroxybutanoate. $^1$H NMR ($CDCl_3$, 300 MHz): $\delta = 1.23$ (d, $J = 6.3$ Hz, 3H), 2.43 (dd, $J = 8.4, 16.5$ Hz, 1H), 2.53 (dd, $J = 4.2$, 16.5 Hz, 1H), 3.00 (br, s, 1H), 3.72 (s, 3H), 4.22 (m, 1H). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta = 22.4$, 42.6, 51.6, 64.2, 173.2. GC analysis: column, CP-Chirasil-Dex-CB, i.d. 0.25 mm × 25 m, CHROMPACK; carrier gas, nitrogen (75 kPa); column temp, 75 °C; injection temp, 105 °C; split ratio, 100:1, $t_R$ of methyl 3-oxobutanoate 6.3 min (0%), $t_R$ of methyl 3-hydroxybutanoate 8.3 min (100%) (*R*- and *S*-isomers were not separated under these conditions). The enantioselectivity was determined by HPLC analysis after converting to the methyl 3-benzoyloxybutanoate by benzoyl chloride and pyridine. HPLC analysis: HPLC (CHIRALCEL OB-H column, hexane/2-propanol = 90:10, flow rate 0.5 mL/min, detection UV = 240 nm): $t_R$ of *R*-isomer 18.2 min (99.65%), $t_R$ of *S*-isomer 24.2 min (0.35%). The absolute configuration was determined by comparison of (*S*)- and (*R*)-methyl 3-benzoyloxybutanoates derived from enantiopure methyl 3-hydroxybutanoate which was synthesized according to the reported procedure.[16a]

## Hydrogenation of 1′-Acetonaphthone through Asymmetric Activation/Deactivation of Racemic Xyl-BINAP-Ru(II) Catalyst (1b)

$RuCl_2$[(±)-xylbinap](dmf)$_n$ (10.5 mg, 0.010 mmol) and (*R*)-DM-DABN (1.9 mg, 0.0050 mmol) were added to an autoclave. Dichloromethane (3.3 mL) was added to the autoclave under a stream of argon. After stirring at room temperature for 30 min, dichloromethane was removed under reduced pressure. Air present in the autoclave was replaced by argon after addition of (*S*,*S*)-DPEN (1.0 mg, 0.0045 mmol). 2-Propanol (2.8 mL) was added to the autoclave under a stream of argon, followed by the addition of KOH/2-propanol (0.5 M, 40 μL,

0.02 mmol) with stirring for 30 min. 1′-Acetonaphthone (0.38 mL, 2.5 mmol) was added to the autoclave under a stream of argon, and then hydrogen was introduced at a pressure of 8 atm. After vigorous stirring for 4 h at room temperature, the solvent was removed under reduced pressure. The residue was filtered through a short column of silica gel. Chemical yield and enantiomeric ratio of 1-(1-naphthyl)ethanol were calculated by chiral GC [ > 99%, 96% ee (*R*)]. The product can also be isolated by silica gel column chromatography (eluent, hexane/EtOAc, 5:1) to give 426 mg (99%) of alcohol. $[\alpha]_D^{28}$: +75.5 (*c* 1.0, $CHCl_3$) {lit.[12] $[\alpha]_D^{25}$: +78.9 (*c* 1, $CHCl_3$), (*R*)-isomer}. $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 1.59$ (d, $J = 6.6$ Hz, 3H, $CH_3$), 1.90 (d, $J = 3.6$ Hz, 1H, HO), 5.59 (dq, $J =$ 3.6, 6.6 Hz, 1H, CH), 7.37 – 7.51 (m, 3H, aromatic), 7.60 (d, $J =$ 6.6 Hz, 1H, aromatic), 7.70 (d, $J = 8.1$ Hz, 1H, aromatic), 7.78 – 7.81 (m, 1H, aromatic), 8.02-8.05 (m, 1H, aromatic).GC (column CP-Cyclodextrin-ß-2,3,6-M-19, i.d. 0.25 mm × 25 m, CHROMPACK; carrier gas, nitrogen (75 KPa); column temp, 160 °C; injection temp, 190 °C; split ratio, 100:1), retention time ($t_R$); (*R*)-(+)-isomer: 32.7 min (98.1%), (*S*)-(−)- isomer: 31.6 min (1.9%), 1′-acetonaphthone: 21.3 min (0%).

## Acknowledgements

*We are grateful to Profs. R. Noyori and T. Okumura for their continuous encouragement and useful discussion of our results and Drs. H. Kumobayashi and N. Sayo of Takasago International Corp. for providing BINAP ligands. This work was financially supported by the Ministry of Education, Science, Sports and Culture of Japan (Nos. 07CE2004, 09238209 and 10208204) and the Research Fellowships of the Japan Society for the Promotion of Science for Dr. T. Korenaga.*

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