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Asymmetric hydrogenation of prochiral carboxylic acids and functionalized carbonyl compounds catalysed by ruthenium(II)–binap complexes with aryl nitriles (binap = (*R*)- or (*S*)-2,2′-bis(diphenylphosphino)-1,1′-binaphthyl)

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Abstract

Complexes $RuCl_2(ArCN)_2$(binap), II (binap = (*R*)- or (*S*)-2,2′-bis(diphenylphosphino)-1,1′-binaphthyl; ArCN = benzonitrile, a; 2-furancarbonitrile, b; pentafluorobenzonitrile, c) were prepared, and their solution properties were investigated by ^{31}P NMR measurements. The catalytic activities and enantioselectivities for IIa–c catalysed hydrogenation of some prochiral acids were very similar to those provided by $Ru_2Cl_4(binap)_2(NEt_3)$, I. In the hydrogenation of β-functionalized carbonyl compounds, however, IIa–c showed considerably lower activities and/or selectivities, compared with complex I. The differences in IIa–c catalysed reactions are discussed in relation to the coordinating abilities of ArCN in II.

Introduction

Ruthenium(II) complexes coordinated with the chiral diphosphine, binap (binap = (*R*)- or (*S*)-2,2′-bis(diphenylphosphino)-1,1′-binaphthyl) [1], have attracted considerable attention recently, because they present powerful catalytic activities for asymmetric hydrogenation of a wide variety of substrates [2]. We have disclosed that the complex having the formula $Ru_2Cl_4(binap)_2(NEt_3)$ (I), which is the first Ru^{II}–binap complex employed as a hydrogenation catalyst [3a], is markedly effective for asymmetric hydrogenation with high enantiomeric purities not only of prochiral carboxylic acids [3] but also of functionalized carbonyl compounds [4]. We have supposed that I assumes a chloride-bridged dinuclear structure [5],

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although the exact structure of I has not been clarified owing to non-availability of single crystals suitable for X-ray crystallography.

We presumed, further, that I dissociates in a reaction mixture to generate a mononuclear species with coordinating solvent molecules as shown in eq. 1, and that this solvent-coordinated mononuclear complex should work as the precursor of catalytically active species in actual reaction mixtures. We considered it possible that, by treatment of complex I with a solvent having enough coordinating ability, a binap complex with the composition $RuCl_2(L)_2$(binap) (L = ligating solvent) would be obtained as a crystalline product as shown in eq. 2. It has been found that a similar reaction of $RuCl_2(PPh_3)_3$ with benzonitrile gives rise to a nitrile-coordinated complex $RuCl_2(PhCN)_2(PPh_3)_2$ [6].

$$Ru_2Cl_4(binap)_2(NEt_3) \longrightarrow 2\ RuCl_2(S)_2(binap) \quad (1)$$

(I) (S = solvent)

$$Ru_2Cl_4(binap)_2(NEt_3) \xrightarrow[(L=ligand)]{L,\ heat} 2\ RuCl_2(L)_2(binap) \quad (2)$$

(I) (II)

$$RuCl_2(L)_2(binap) \xrightarrow{S\ (large\ excess)} RuCl_2(S)_2(binap) \quad (3)$$

II

a L = PhCN b L = FrCN c L = C_6F_5CN

Indeed, a benzonitrile complex $RuCl_2(PhCN)_2$(binap) (IIa) could be prepared by heating I in PhCN at an elevated temperature (eq. 2). If the coordinating PhCN molecules are readily replaced with solvent molecules to generate the solvent coordinating species as indicated in eq. 3, complex IIa will be able to act as an effective catalyst for asymmetric hydrogenation in a similar manner to complex I. In this respect, we examined the catalytic activity and enantioselectivity of IIa-catalysed asymmetric hydrogenation of unsaturated carboxylic acids and β-functionalized carbonyl compounds.

In addition, analogous complexes, $RuCl_2(FrCN)_2$(binap), IIb and $RuCl_2(C_6F_5CN)_2$(binap), IIc, which contain 2-furancarbonitrile (FrCN) and pentafluorobenzonitrile (C_6F_5CN) respectively, as a ligand in place of PhCN in IIa, were also prepared according to eq. 2. Compared with the phenyl group of PhCN, the aromatic substituents of these nitriles belong to stronger electron withdrawing groups, so that the nitriles in IIb and IIc would be replaced more readily than PhCN in complex IIa. Thus, we also tested the catalytic activities of IIb and IIc for asymmetric hydrogenation. The profiles of the activities and selectivities provided by complexes IIa–c will be discussed in relation to the ^{31}P NMR features of these complexes.

Results and discussion

^{31}P NMR investigations of $RuCl_2(ArCN)_2$(binap)

Reactions of $Ru_2Cl_4(binap)_2(NEt_3)$, I with aryl nitriles at elevated temperatures afforded yellow or yellow brown complexes having the expected formula $RuCl_2(ArCN)_2$(binap) (see Experimental section). It is probable that these com-

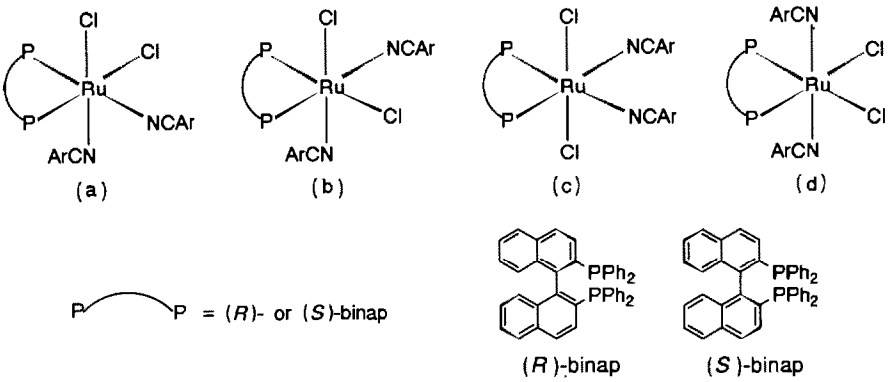


Fig. 1. Possible diastereoisomers of $RuCl_2(ArCN)_2$(binap): *cis* isomers, a and b; *trans* isomers, c and d.

plexes exist as a mixture of possible stereoisomers, as depicted in Fig. 1: four diastereomers, two *cis* and two *trans* forms respectively, for (*R*)- and (*S*)-binap complexes. In order to see whether the crystalline products of $RuCl_2(ArCN)_2$(binap) consist of a single diastereomer or involve two or more possible isomers, we conveniently monitored the ^{31}P NMR spectra of the respective complexes. It is expected that, assuming no rapid ligand exchange took place for these complexes, the *cis* isomers, having molecular dissymmetry, should reveal an AB quartet, while the *trans* isomers, which have C_2 symmetry, should show simply a singlet as the phosphorus resonances of coordinating binap.

The ^{31}P NMR spectrum of $RuCl_2(PhCN)_2$(binap), IIa in CH_2Cl_2 solution exhibited a typical AB quartet (δ 52.99 and 51.22, J(P,P) = 34.9 Hz) at 303 K (see Fig. 2(a)). The spectrum showed no significant changes in the temperature range 233–303 K, although several small peaks could be observed in the higher field region. The spectral patterns of $RuCl_2(FrCN)_2$(binap), IIb and $RuCl_2(C_6F_5)_2$(binap), IIc obtained in CH_2Cl_2 were very similar to that of IIa. The representative ^{31}P NMR data are summarized in Table 1.

The above-mentioned spectral features in CH_2Cl_2 solutions seem to coincide with the fact that the complexes IIa–c take either of the possible *cis* structures almost exclusively. However, we reached the conclusion that the ruthenium species in CH_2Cl_2 is not the six-coordinate complex $RuCl_2(ArCN)_2$(binap), but the five-coordinate complex represented as $RuCl_2(ArCN)$(binap) or solvent-coordinated $RuCl_2$(S)(ArCN)(binap) ((S) = solvent), which should be derived from IIa–c by dissociating a coordinating nitrile. This assumption was reached using the ^{31}P NMR measurements of these complexes in the presence of respective nitriles.

As a representative, the spectral features of complex IIa will be discussed in detail. Thus, the spectrum of IIa in PhCN solution exhibited a singlet (δ 48.64) and an AB quartet (δ 47.03, 43.32, J(P,P) = 34.9 Hz) at 303 K (see Fig. 2(b)). The singlet can be assigned to either of the *trans* isomers, and the second AB signal to one of the *cis* isomers of the six-coordinate complex $RuCl_2(PhCN)_2$(binap). In accordance with these assignments, we observed that the same singlet and AB quartet appeared by adding PhCN to a CH_2Cl_2 solution of IIa, at the expense of the initially observed AB signals. The original AB quartet (δ *ca.* 53 and 51) could

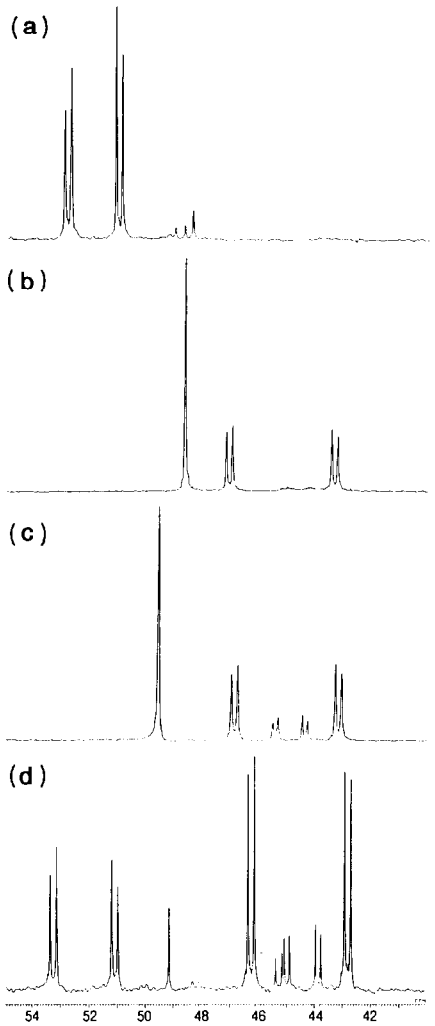


Fig. 2. ^{31}P NMR spectra of $Ru_2Cl_4(PhCN)_2(binap)$: a, in CH_2Cl_2 at 303 K; b, in PhCN at 303 K; c, in PhCN at 233 K; d, in a mixture of CH_2Cl_2 and PhCN (1:1) at 233 K.

be observed just after adding PhCN (see Fig. 2(d)), but it disappeared completely after standing the solution for several hours. However, the lower field AB quartet did not appear with appreciable intensity with the addition of CH_2Cl_2 to a PhCN solution of IIa. These findings strongly suggest that the Ru–binap species in CH_2Cl_2 are the five-coordinate $RuCl_2(PhCN)(binap)$ or solvent-coordinated $RuCl_2(S)(PhCN)(binap)$, and it readily converts into the isomers of six-coordinate $RuCl_2(PhCN)_2(binap)$ in the presence of excess PhCN (see Scheme 1).

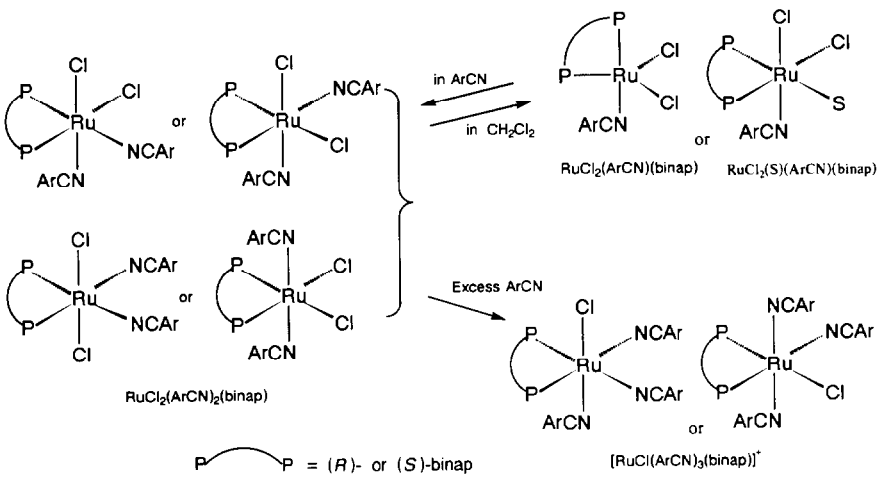
The ^{31}P NMR pattern of the five-coordinate complex $RuCl_2(ArCN)(binap)$ (or solvent-coordinated $RuCl_2(S)(ArCN)(binap)$) shows the non-equivalence of two phosphorus atoms of binap. Several tetragonal-pyramidal or trigonal-bipyramidal structures are possible for such a non-symmetrical complex, but it is difficult to determine unequivocally the structure of $RuCl_2(ArCN)(binap)$ or $RuCl_2(S)$-

Table 1

^{31}P NMR spectral data of $RuCl_x(ArCN)_y(binap)$ in solutions

Nitrile	Solvent	T (K)	$RuCl_2(ArCN)(binap)$			$RuCl_2(ArCN)_2(binap)$				$RuCl(ArCN)_3(binap)$		
			δ_A	δ_B	J(P,P)	δ_S [a]	δ_A	δ_B	J(P,P)	δ_A	δ_B	J(P,P)
PhCN	CH_2Cl_2	303	52.99	51.22	34.9							
		233	53.28	51.30	35.0							
	PhCN	303				48.64	47.03	43.32	34.9		broad	
		233				49.51	46.82	43.13	35.0	45.39	44.33	29.4
	CH_2Cl_2 +	303				48.62	46.69	43.28	35.0		broad	
	PhCN	233	53.24	51.09	34.9	49.15	46.24	42.81	36.8	44.98	43.86	30.3
FrCN	CH_2Cl_2	303	51.87	50.20	34.9							
		233	52.08	50.38	34.0							
	FrCN	303				46.60	44.60	41.39	34.9		broad	
		233				47.46	44.25	41.27	35.0	42.84	41.53	30.3
	FrCN+	303	51.85	50.16	33.1	46.50	44.54	41.17	34.9		broad	
	CH_2Cl_2	233	52.13	50.40	33.1	47.32	44.23	41.04	34.9	42.59	41.43	29.5
C_6F_5CN	CH_2Cl_2	303	50.03	48.61	35.0							
		233	50.30	48.78	34.9							
	CH_2Cl_2 +	303	50.21	48.82	34.9							
	C_6F_5CN	273	50.37	48.94	34.9	(46.26)						

[a] The singlet of the *trans* isomer.



Scheme 1.

(ArCN)(binap). One of the trigonal-bipyramidal structures and a solvent-coordinated form are depicted in Scheme 1 as representatives of possible structures.

It was noticed, further, that as the temperature lowered, an additional AB quartet emerged in the spectrum of IIa in PhCN or in a mixture of PhCN and CH_2Cl_2 (see Figs. 2(c), and 2(d) and Table 1). The third AB signals (δ *ca.* 45 and 44), which could not be detected at 303 K owing to signal broadening (see Fig. 2(b)), were ascribed not to the other *cis* isomer of $RuCl_2(PhCN)_2(binap)$, but to a tri(nitrile) species $[RuCl(PhCN)_3(binap)]^+$ for the following reasons.

Firstly, the same AB quartet could be observed for a reaction product of IIa with $AgBF_4$ in the presence of PhCN. It is highly possible that this tri(nitrile) complex can be produced in PhCN solution by a reaction such as that shown by eq. 4, where a chloride ligand in IIa should be removed as AgCl and a PhCN molecule occupies the vacant coordination site to give $[RuCl(PhCN)_3(binap)]^+$. Indeed, a yellow–brown solution was obtained by adding 1 equivalent of $AgBF_4$ to IIa in PhCN and successive removal of AgCl. As expected, the ^{31}P NMR measurement of the sample solution at 233 K exhibited predominantly an AB quartet having the identical chemical shifts and J(P,P) values with the third AB signals in Fig. 2(c). It was recognized, further, that a remarkable signal broadening occurs even for the present system above 300 K, in a similar manner to that of the corresponding AB signals.

$$RuCl_2(PhCN)_2(binap) + AgBF_4 \xrightarrow{PhCN} [RuCl(PhCN)_3(binap)]BF_4 + AgCl \quad (4)$$

$$[RuCl(binap)(\eta^6\text{-}C_6H_6)]Cl + AgBF_4 \xrightarrow{PhCN,\ heat} [RuCl(PhCN)_3(binap)]BF_4 + AgCl \quad (5)$$

Furthermore, a reaction of $[RuCl(binap)(\eta^6\text{-}C_6H_6)]Cl$ [7] with $AgBF_4$ in PhCN at an elevated temperature (see eq. 5) gave rise to the same complex formed by eq. 4. Under the conditions employed here, the $\eta^6\text{-}C_6H_6$ group is expected to dissociate readily from the ruthenium atom, and to be replaced with three PhCN molecules.

It was demonstrated, therefore, that the $AgBF_4$ treatments of complex IIa and [RuCl(binap)(η^6-C_6H_6)]Cl gave rise to the same Ru–binap species in PhCN, that should be a cationic complex $[RuCl(PhCN)_3(binap)]^+$. The ^{31}P NMR characteristics of the third AB quartet recorded for a PhCN solution of IIa at lower temperatures (Fig. 2(c)) coincide well with those of the present cation under similar conditions. This strongly indicates that IIa tends to transform partly into the above tri(nitrile) complex in PhCN by an exchange of Cl^- with PhCN.

It was evident, therefore, that a PhCN solution of complex IIa contains not only a mixture of a *cis* and a *trans* isomer of six-coordinate species $RuCl_2(PhCN)_2$(binap), the configurations of which have not been specified, but also the cationic tri(nitrile) complex [RuCl(PhCN)$_3$(binap)]Cl (see Scheme 1). It should be pointed out, further, that the tri(nitrile) complex undergoes a ligand exchange at a rate comparable with the NMR time scale, so that the ^{31}P NMR signal broadening takes place at higher temperatures.

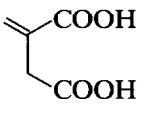
The ^{31}P NMR spectral features and their temperature dependence for $RuCl_2(FrCN)_2$(binap), IIb in FrCN or in a mixture of FrCN and CH_2Cl_2 are in accord with those of complex IIa in the presence of PhCN (see Table 1). It should be noted, however, that the lowest field AB quartet, assignable to the resonances of five-coordinate species $RuCl_2(FrCN)$(binap) or solvent-coordinated $RuCl_2(S)$-(FrCN)(binap), was detected in the ^{31}P NMR spectrum for a sample prepared by adding CH_2Cl_2 to an FrCN solution of IIb (CH_2Cl_2 : FrCN = 1 : 1), although the signal intensity was very small. This suggests that a small part of the six-coordinate $RuCl_2(FrCN)_2$(binap) changes into the five-coordinate species even in the presence of FrCN. It seems that IIb dissociates a nitrile ligand more readily than the corresponding PhCN complex, probably owing to a weaker coordinating ability of FrCN compared with PhCN.

It was impossible to obtain the ^{31}P NMR spectrum of $RuCl_2(C_6F_5CN)_2$(binap), IIc in C_6F_5CN, because of the low solubility of the complex in this nitrile. Further, the spectrum taken after adding C_6F_5CN to a CH_2Cl_2 solution of IIc showed no clear singlet and AB quartet assignable to the six-coordinate species $RuCl_2(C_6$-$F_5CN)_2$(binap) at 303 and 273 K. It is apparent that IIc is predominantly converted into the five-coordinate complex $RuCl_2(C_6F_5CN)$(binap) even in the presence of excess C_6F_5CN. We consider that such distinct behaviour of IIc can be ascribed to a significantly lower coordination ability of C_6F_5CN, compared with other nitriles.

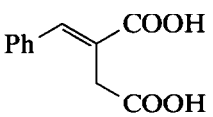
Thus, clear distinctions could be observed among the ^{31}P NMR behaviours of IIc and those of IIa and IIb in the presence of respective nitriles. Under these conditions, IIa and IIb exist principally as a mixture of *cis* and *trans* isomers of $RuCl_2(ArCN)_2$(binap) and of a tri(nitrile) species $RuCl(ArCN)_3$(binap), while IIc assumes predominantly the five-coordinated form $RuCl_2(C_6F_5CN)$(binap) (or solvent-coordinated $RuCl_2(S)(C_6F_5CN)$(binap)). In general, coordinatively unsaturated species such as $RuCl_2(ArCN)$(binap) are anticipated to give catalytically active species more readily than coordinatively saturated complexes such as $RuCl_2(ArCN)_2$(binap). It is of interest to investigate the effects of such differences in the solution properties of complexes IIa–c on their activities and selectivities as catalysts. Therefore, asymmetric hydrogenations of some prochiral carboxylic acids and β-functionalized carbonyl compounds were performed using IIa–c as the catalysts.

Asymmetric hydrogenation of prochiral carboxylic acids catalysed by $RuCl_2(ArCN)_2$-(binap)

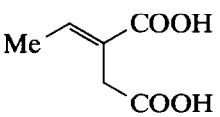
The asymmetric hydrogenation of prochiral carboxylic acids employing nitrile complexes IIa–c as the catalyst was performed under the usual conditions adopted for the complex I catalysed reaction [3b,c]. The hydrogenations of methylenesuccinic acid (**1**), (*E*)-benzylidenesuccinic acid (**2**), (*E*)-ethylidenesuccinic acid (**3**), and (*E*)-2-methyl-2-butenoic acid (**4**) were carried out under low H_2 pressure (5 atm), while for 2-phenyl-2-propenoic acid (**5**) a high initial H_2 pressure (100 atm) was applied. Triethylamine equimolar to the carboxyl group(s) of substrates was added (N/S = 2.2 for **1–3**, and 1.1 for **4** and **5**). As expected, the hydrogenations catalysed by IIa–c proceeded smoothly to give the saturated acids. The results of hydrogenations are summarized in Table 2, along with those for I.



(**1**)



(**2**)



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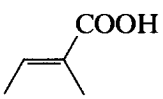

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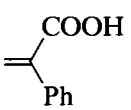


(**5**)

For methylenesuccinic acid and derivatives **1**, **2**, and **3**, the hydrogenation products using IIa–c mostly showed enantioselectivities in the range 85–90% e.e. Regardless of the catalyst used, the selectivities were slightly lower for **4** and considerably lower for **5**, compared with **1–3**. No obvious differences were found in the enantioselection effected by complexes I and IIa–c, except for IIa-catalysed hydrogenation of **2** and **5**.

It is remarkable that the enantioselectivities for complex IIa-catalysed reactions of substrates **2** and **5** were apparently lower than those given by I, IIb or IIc. In contrast, the e.e. values obtained using IIb and IIc as the catalyst were, in most instances, on the same level as those presented by complex I. These facts strongly suggest that, under hydrogenation conditions, IIb and IIc give rise to the catalytically active species practically identical with that derived from I. However, the active species derived from IIa should be considerably different from those from I, IIb or IIc at least in the case of hydrogenation of **2** and **5**.

Owing to the low solubilities in methanol, it was impossible to obtain the clear ^{31}P NMR spectra of IIa–c in methanol. We suppose that the solution behaviours of IIa–c in methanol are essentially similar to those in dichloromethane, and that one of two aryl nitriles dissociates from IIa–c to give the five-coordinated $RuCl_2$(ArCN)(binap) or methanol-coordinated species (see Scheme 2). Thus, the differences between IIa and IIb or IIc as the hydrogenation catalyst should be ascribed to the differences in the reactivities of these five-coordinate species.

Although the true catalytically active species has not been specified for Ru–binap catalysed hydrogenation, a hydride-containing species such as RuH(carboxy-

Table 2

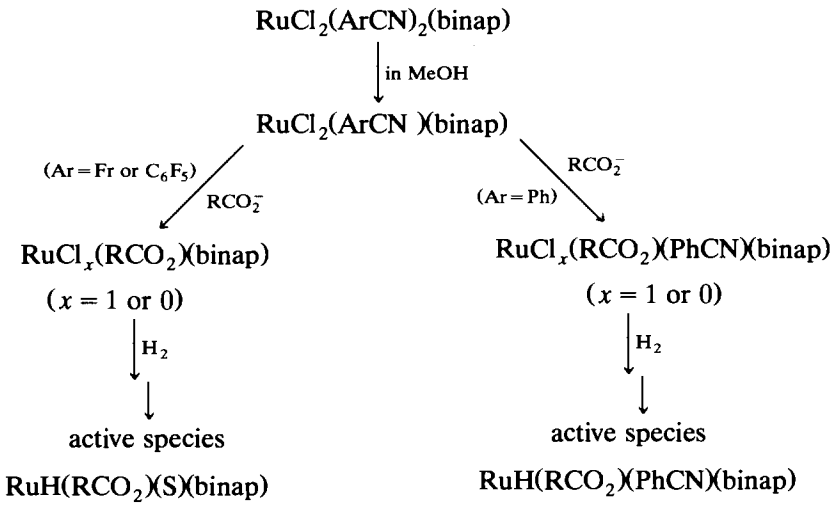
Asymmetric hydrogenation of prochiral carboxylic acids catalysed by $RuCl_2(ArCN)_2$(binap) [a]

Substrate	Catalyst [b]	Temperature (°C)	NEt_3/Substrate	e.e. (%)	*R* or *S* [c]
1	*R*-I	35	2.2	90	*S*
	S-IIa	35	2.2	86	*R*
	R-IIb	35	2.2	89	*S*
	S-IIc	35	2.2	86	*R*
2	*R*-I	50	2.2	90	*S*
	S-IIa	50	2.2	72	*R*
	R-IIb	50	2.2	88	*S*
	S-IIc	50	2.2	90	*R*
3	*R*-I	50	2.2	93	*S*
	S-IIa	50	2.2	89	*R*
	R-IIb	50	2.2	94	*S*
	S-IIc	50	2.2	93	*R*
	S-IIc	50	0	78	*R*
	S-III	50	0	87	*R*
4	*R*-I	35	1.1	85	*S*
	S-IIa	35	1.1	81	*R*
	R-IIb	35	1.1	84	*S*
	S-IIc	35	1.1	80	*R*
5 [d]	*R*-I	50	1.1	68	*R*
	R-I	50	0	72	*R*
	R-IIa	50	0	60	*R*
	R-IIb	50	0	66	*R*
	S-IIc	50	0	70	*S*

[a] Following reaction conditions were applied for hydrogenations unless otherwise noted: H_2 pressure, 5 atm; solvent, THF–EtOH (1:1) 10 cm^3; substrate, 1.0 mmol; catalyst, 0.01 mmol (as ruthenium). [b] I, Ru_2Cl_4(binap)$_2(NEt_3)$; IIa, $RuCl_2(PhCN)_2$(binap); IIb, $RuCl_2(FrCN)_2$(binap); IIc, $RuCl_2(C_6F_5CN)_2$-(binap); III, $Ru((CH_3)_3CCO_2)_2$(binap). *R* and *S* indicate the configuration of the binap. [c] *R* or *S* refers to the enantiomers preferentially formed. [d] Initial H_2 pressure, 100 atm; solvent, methanol.

late)(S)(binap) was adopted as a candidate for the active form in the hydrogenation of unsaturated carboxylic acids [3b,8]. We have supposed that, in actual reaction mixtures, complex I cleaves into mononuclear species, which subsequently react with carboxylic acid to initiate the catalytic cycle of hydrogenation [3b]. On the basis of the similar enantioselectivities effected by I, IIb and IIc, we assume that the nitrile ligand, FrCN or C_6F_5CN, in the five-coordinate species $RuCl_2$(ArCN)(binap) (or solvent-coordinated $RuCl_2$(S)(ArCN)(binap)) (ArCN = FrCN or C_6F_5CN) should be readily replaced with a carboxylic acid under the hydrogenation conditions to generate the same catalytically active species generated from I (Scheme 2).

In the case of the complex IIa-catalysed reaction, however, an Ru–binap species which holds a PhCN as the ligand may act as a catalytically active species (Scheme 2). It is possible that such an Ru–binap species containing PhCN (RuH(RCO_2)-(PhCN)(binap)) presents a poorer selectivity than those having no nitrile (RuH(RCO_2)(S)(binap)). We consider, therefore, that the much lower e.e. values presented by IIa for some unsaturated acids can be ascribed to the higher

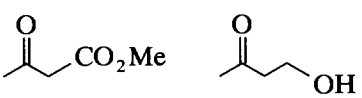


Scheme 2.

coordination ability of PhCN, in comparison with FrCN or C_6F_5CN.

Asymmetric hydrogenation of β-functionalized carbonyl compounds with $RuCl_2(ArCN)_2(binap)$

In order to investigate the effects of aryl nitriles of IIa–c on the catalytic activities and stereoselectivities in the hydrogenation of other types of substrates, we tested the asymmetric hydrogenations of methyl acetoacetate (**6**) and 4-hydroxy-2-butanone (**7**) promoted by these nitrile complexes, and the results are summarized in Table 3.



(**6**) (**7**)

As reported previously [9], methyl acetoacetate **6** was hydrogenated smoothly using complex I as the catalyst to give methyl 3-hydroxybutanoate (**8**) with high enantioselectivity (greater than 98% e.e.). In sharp constrast, no hydrogenation of **6** occurred under the same reaction conditions (temperature 35°C), when complexes IIa–c were employed as the catalyst (Table 3). Instead of hydrogenation, the acetalization of **6** took place to give methyl 3,3-di(methoxy)butanoate (**9**). The aryl nitriles affected considerably the conversion of **6** to **9**, and the following order, PhCN > FrCN > C_6F_5CN, was observed (Table 3).

As the reaction temperature rose to 50°C, the hydrogenation of **6** catalysed by IIb or IIc occurred along with the acetalization to give a mixture of the hydroxyester **8** and acetal **9** (Scheme 3). The ratio of the products **8**:**9** changes with the coordinating nitriles. Thus, at the ratio of substrate to catalyst (S/C) = 1000, the hydroxyester **8** was preferentially obtained in the presence of C_6F_5CN complex IIc, while the acetal **9** was predominantly formed with FrCN complex IIb. When the amount of catalyst was increased (S/C = 100), the hydrogenation proceeded highly

Table 3

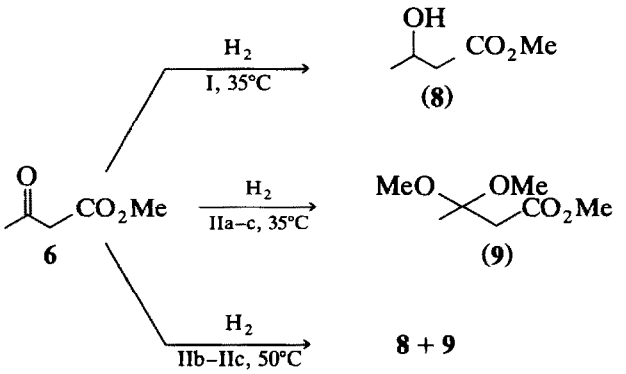
Asymmetric hydrogenation of β-functionalized carbonyl compounds catalysed by Ru–binap catalysts

Substrate	Catalyst [c]	S/C [d]	Temperature (°C)	Conversion (%) [e]	Yield (%)		e.e. (%) [f]	R or S
					8	9		
6 [a]	R-I	1000	35	100	100	0	98	R
	S-I	1000	35	100	100	0	98	S
	S-IIa	1000	35	88	0	100	–	–
	R-IIb	1000	35	15	0	100	–	–
	S-IIc	1000	35	13	0	100	–	–
	S-IIa	1000	50	91	0	100	–	–
	R-IIb	1000	50	100	40	60	92	R
	S-IIc	1000	50	100	62	38	95	S
	S-IIa	100	50	93	17	83	–	–
	R-IIb	100	50	100	30	70	94	R
	S-IIc	100	50	100	92	8	97	S
7 [b]	R-I	1000	50	100		–	98	R
	S-I	1000	50	100		–	97	S
	S-IIa	100	50	0		–	–	–
	R-IIb	100	50	4		–	–	–
	S-IIc	100	50	100		–	68	S

[a] Reaction conditions: initial H_2 pressure, 100 atm; solvent, methanol; 48 h. [b] Reaction conditions: initial H_2 pressure, 50 atm; solvent, methanol; 24 h. [c] **I**, $Ru_2cl_4(binap)_2(NEt_3)$; **IIa**, $RuCl_2(PhCN)_2(binap)$; **IIb**, $RuCl_2(2\text{-}FrCN)_2(binap)$; **IIc**, $RuCl_2(C_6F_5CN)_2(binap)$. [d] Substrate to catalyst ratio (as ruthenium). [e] Determined by GC. [f] Determined by HPLC; see experimental section.

preferentially (**8**:**9** = 92:8) by IIc. The e.e. values of the hydroxyester **8** produced by the use of IIb or IIc were slightly lower than those obtained using **I**. Even at this temperature and S/C = 100, the reaction in the presence of IIa afforded predominantly the acetal **9**.

A remarkable difference in catalytic activities of the nitrile complexes was also observed in the asymmetric hydrogenation of 4-hydroxy-2-butanone **7**, the hydrogenation of which was also performed by complex **I**. Under the same conditions employed for I, IIa and IIb revealed no or very poor activity. In contrast, **7** was completely hydrogenated using IIc as the catalyst, although the enantiomeric excess of the product was much lower (68%) than that produced using I (98%). It



Scheme 3.

excess of the product was much lower (68%) than that produced using I (98%). It is obvious that the order of catalytic activities of IIa–c for the hydrogenation of **7** coincide well with the order of easiness of dissociation of ArCN, established by ^{31}P NMR measurements (C_6F_5CN > FrCN > PhCN).

A distinct effect of nitrile on ruthenium complex catalysed reactions has been reported [10]. Thus, the lactonization of α,ω-diols catalysed by $RuH_2(PPh_3)_4$ was inhibited by the addition of acetonitrile in an equivalent amount to ruthenium [10]. The inhibition was considered to be due to the strong coordination of acetonitrile to the ruthenium complex in comparison with alcohols.

We assume that the ArCN ligands in IIa–c should be exchanged with substrates or solvent molecules to give rise to catalytically active species. It seems true that the ligating ability of an ester carbonyl or a hydroxy group is considerably lower than that of ArCN. When the exchange hardly takes place as in the case of PhCN, it is difficult for the ketoester **6** or hydroxyketone **7** to coordinate with the ruthenium centre to form an active species. Judging from ^{31}P NMR features, the diassociation of nitrile for the C_6F_5CN complex should occur to a considerable extent, resulting in the observed hydrogenation activities of IIc for **6** and **7**. The activities presented by IIb were similar to, but apparently lower, than that of IIc, reflecting the stronger ligating ability of FrCN compared with C_6F_5CN. It is uncertain, however, whether the active species derived from IIc or IIb in the hydrogenation of β-functionalized carbonyl compounds are entirely identical with that derived from I.

Experimental

General

All the solvents and triethylamine employed for preparing ruthenium complexes and for asymmetric hydrogenation were dried and distilled by conventional methods and stored under nitrogen. (*R*)- and (*S*)-binap were presented by Takasago Research Institute Inc. (*E*)-Benzylidenesuccinic acid was obtained by the Stobbe reaction [11]. (*E*)-Ethylidenesuccinic acid was prepared by reported methods [12]. 2-Phenylpropenoic acid was prepared by the following procedures. α-Phenylvinylmagnesium bromide, obtained from α-bromostyrene (14.5 g, 79 mmol) and magnesium (2.1 g, 87 mmol) in dry THF (100 ml), was poured onto a large excess of dry-ice. The reaction mixture was extracted with ethyl acetate, and the solvent was removed. The crude product was recrystallized from benzene–hexane to give the pure acid in 76% yield (8.9 g).

Gas chromatographic (GC) analysis was performed with a Shimadzu GC-14A instrument equipped with a fused silica capillary column (Shimadzu CBP10, 25 m) and a flame ionization detector. High performance liquid chromatography (HPLC) was carried out with a Shimadzu SPD-6 apparatus equipped with a Shimadzu SPC-7A UV spectrometric detector and a Shimadzu Chromatopac CR-5A, employing chiral stationary columns Daicel Chiralcel-OD. ^1H NMR (400 MHz) and ^{31}P NMR (167 MHz) spectra were measured with a JEOL JMN-GX 400 spectrometer.

Ru_2Cl_4((R)-binap)$_2$(NEt_3) (R)-I and Ru_2Cl_4((S)-binap)$_2$(NEt_3) (S)-I

These complexes were prepared by the reported method [3b,5].

$RuCl_2(PhCN)_2$((S)-binap) (S)-IIa

A suspension of complex (*S*)-I (550 mg, 0.65 mmol) in PhCN (8 cm^3) was heated to 150°C for 2 h under a nitrogen atmosphere. A deep red solution was obtained during heating. The solution was filtered and then evaporated under reduced pressure to remove excess PhCN. The residue was redissolved in PhCN (1.5 cm^3), and diethyl ether (2 cm^3) was added to give yellow fine needle crystals. The crystals were collected by filtration, washed with diethyl ether, and dried under vacuum. Analysis for $RuCl_2(PhCN)_2$((*S*)-binap). Found: C, 68.6; H, 4.1; N, 2.8. $C_{58}H_{42}Cl_2N_2P_2Ru$ calcd.: C, 69.6; H, 4.2; N, 2.8%.

$RuCl_2(FrCN)_2$((R)-binap) (R)-IIb

A suspension of complex (*R*)-I (550 mg, 0.65 mmol) in FrCN (8 cm^3) was heated under reflux for 24 h under a nitrogen atmosphere. An orange solution was obtained during the heating. The solution was evaporated under reduced pressure to a small volume, and to the concentrated solution diethyl ether was added. The yellow crystals thus obtained were collected by filtration, washed thoroughly with diethyl ether, and dried under vacuum. Analysis for $RuCl_2(FrCN)_2$((*R*)-binap). Found: C, 65.3; H, 4.1; N, 3.1. $C_{54}H_{38}Cl_2N_2O_2P_2Ru$ calcd.: C, 66.1; H, 3.9; N, 2.9%.

$RuCl_2(C_6F_5CN)_2$((S)-binap) (S)-IIc

A suspension of complex (*S*)-I (550 mg, 0.65 mmol) in C_6F_5CN (5 cm^3) was heated to 150°C for 24 h under a nitrogen atmosphere. No clear solution was obtained, but a yellow brown precipitate formed during the heating. The precipitate was collected by filtration, and washed thoroughly with diethyl ether. Analysis for $RuCl_2(C_6F_5CN)_2$(binap). Found: C, 58.3; H, 2.9; N, 2.1. $C_{58}H_{32}Cl_2F_{10}N_2P_2Ru$ calcd.: C, 59.0; H, 2.7; N, 2.4%.

Asymmetric hydrogenation of prochiral carboxylic acids

A mixture of carboxylic acid (**1–5**) (1 mmol), catalyst (I or IIa–c) (0.01 mmol as ruthenium atom), and triethylamine (1.1 equivalent for a carboxyl group) dissolved in a mixture of THF (5 cm^3) and ethanol (5 cm^3) was stirred under a hydrogen atmosphere for 24 h. The detailed reaction conditions are given in Table 2. The solvent was removed under reduced pressure, and 1 *M* aqueous NaOH (10 cm^3) was added. The filtered aqueous layer was washed with chloroform, and then acidified with 2 *M* HCl to pH 1. The acidic aqueous layer was extracted with chloroform (10 $cm^3 \times 3$), and the dried organic phase was evaporated to give the crude hydrogenation product. An aliquot of the crude product was dissolved in THF and then treated with diazomethane to convert the carboxylic acids into methyl or dimethyl esters, which were employed to determine the conversion of hydrogenation by means of GC analysis.

The dimethyl ester of the hydrogenation product of **2** was purified by a silica gel chromatography (eluent, diethyl ether), and subjected to the chiral HPLC analysis to determine the enantiomeric purity of the product.

Enantiomeric excesses of the products from **1**, **3**, **4**, and **5** were determined as follows. Another aliquot of the product (*ca.* 0.1 mmol) was dissolved in THF (2 cm^3), and aniline (1.1 equivalent per carboxyl group), *N,N'*-dicyclohexylcarbodiimide (1.1 equivalent per carboxyl group), and 4-dimethylaminopyridine (2 mg)

Table 4

Conditions and parameters of chiral HPLC analysis

Substrate	Derivatives [a]	Column [b]	Eluent [c]	*R* or *S* [d]	α [e]	K_1 [e]	R_S [e]
1	Dianilide	OD	95:5	*S*	2.56	0.36	1.07
2	Dimethyl ester	OD	9:1	*R*	1.31	1.32	1.28
3	Dianilide	OD	9:1	*S*	2.13	1.19	2.18
4	Anilide	OD	95:5	*R*	1.14	3.38	0.76
5	Anilide	OD	9:1	*S*	1.38	2.00	1.16
6	(*R*)-MTPA ester	Silica gel	99:1	*R*,*R*	1.16	0.88	0.84
7	Phenylcarbomate	OD	9:1	*R*	1.28	4.12	2.17

[a] The derivatives of the hydrogenation products applied for the chiral HPLC analysis. [b] OD refers to Chiralcel OD of Daicel Co. [c] The ratio of hexane to isopropyl alcohol. [d] The configuration of the faster eluted enantiomer. [e] For the definitions of parameters, see ref. 13.

were added. The mixture was stirred at room temperature for 20 h, the precipitate was filtered off, and the filtrate was evaporated. The residue was purified by short column chromatography on silica gel with diethyl ether as an eluent. The enantiomeric purities of the anilides were determined by chiral HPLC analyses. The conditions and parameters of chiral HPLC analysis [13] are listed in Table 4.

Asymmetric hydrogenation of methyl acetoacetate

A mixture of methyl acetoacetate (5 mmol), catalyst (I or IIa–c, 0.005 or 0.05 mmol as ruthenium) dissolved in methanol (10 cm^3) under a nitrogen atmosphere was placed in a 50 cm^3 stainless steel autoclave. After the atmosphere was replaced with hydrogen, hydrogen was pressurized to 100 atm, and the mixture was stirred at 30°C (or 50°C) for 48 h. The solvent was removed under reduced pressure, and the residue was distilled by bulb-to-bulb to give methyl 3-hydroxybutanoate. $[\alpha]_D^{26}$ −24.2° (neat) (catalysed by $Ru_2Cl_4((R)\text{-binap})_2(NEt_3)$).

The enantiomeric excess of methyl 3-hydroxybutanoate was determined by HPLC after converting an aliquot of the product to the (*R*)-MTPA (MTPA = α-methoxy-α-trifluoromethylphenyl acetic acid) ester. A mixture of methyl 3-hydroxy-butanoate (0.1 mmol), (*R*)-MTPA (0.1 mmol), DCC (0.11 mmol), and 4-dimethylaminopyridine (2 mg) dissolved in CH_2Cl_2 (5 cm^3) was stirred at room temperature for 20 h. The white precipitate was filtered, and the filtrate was washed with saturated aqueous $NaHCO_3$ solution and water, and dried over $MgSO_4$. After the solvent was removed, the crude residue was passed through a short column of silica gel (eluent, ether), and the ester-containing fractions were collected and concentrated. The sample solution containing an (*R*)-MTPA ester of methyl 3- hydroxybutanoate was analysed by an HPLC system equipped with a silica gel column, using hexane–isopropyl alcohol (99:1) as an eluent.

Asymmetric hydrogenation of 4-hydroxy-2-butanone

Under a nitrogen atmosphere 4-hydroxy-2-butanone (5 mmol) and catalyst (I 0.005 mmol, IIa–c 0.05 mmol as ruthenium atom) were dissolved in methanol (10 cm^3), and the solution was placed in a 50 cm^3 stainless steel autoclave. After the atmosphere was replaced with hydrogen, hydrogen was pressurized to 50 atm, and the mixture was stirred at 50°C for 24 h. The solvent was removed under reduced

pressure, and the residue was purified by a bulb-to-bulb distillation to give 1,3-butanediol. $[\alpha]_D^{22}$ −30.2 (neat) (catalysed by $Ru_2Cl_4((R)\text{-binap})_2(NEt_3)$).

The enantiomeric excess of 1,3-butanediol was determined as follows. 1,3-Butanediol (0.2 mmol) and phenyl isocyanate (0.6 mmol) were dissolved in THF (5 cm^3), and the mixture was stirred at 50°C for 12 h. The solvent was removed by evaporation, and the residue was purified by column chromatography on silica gel with ethyl acetate–hexane (2:3) as an eluent. The sample solution of dicarbamate was analysed by an HPLC system equipped with a chiral stationary phase column (Daicel Chiralcel OD) using hexane–isopropyl alcohol (9:1) as an eluent. The conditions and parameters of chiral HPLC analysis are listed in Table 4.

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