Synthesis and use of bisoxazolinyl-phenyl pincers

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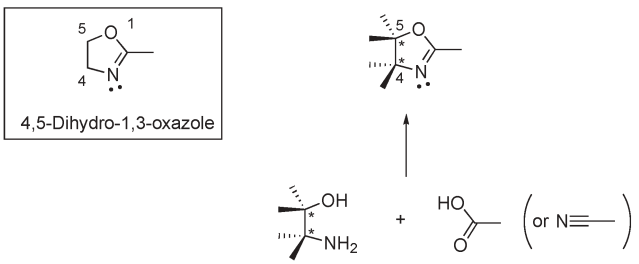
The bisoxazolinyl-phenyl (Phebox) ligand is an example of an N,C,N tridentate (pincer type) ligand, which has a central carbon–metal covalent bond and two oxazolines. In this *tutorial review*, synthetic methods to prepare bisoxazolinyl-phenyl derivatives and their transition-metal complexes including rhodium, iridium, platinum, palladium, nickel and copper, are summarized. In addition, several applications to homogeneous and asymmetric catalysis with chiral bisoxazolinyl-phenyl metal complexes have been reviewed.

1 Introduction

Construction of ligands for transition-metal complexes is a very important subject especially in the field of molecular catalysis and organic synthesis, because the ligands can provide appropriate stereochemical and electronic environments around active metal centers controlling catalysis. We have adopted the heterocyclic oxazoline skeleton, 4,5-dihydro-1,3-oxazole, as a modular unit of multidentate ligands, since the oxazoline can supply sufficient substituent diversity including chiral centers at 4- and 5-positions by use of a variety of β-aminoalcohols (Scheme 1).[1–5]

We first reported pyridine-bisoxazoline (abbreviated as Pybox) as a tridentate oxazoline-based ligand for rhodium-catalyzed asymmetric hydrosilylation of ketones.[6] Despite its tridentate nature, Pybox dissociation from the rhodium atom was observed, and extra ligand was necessary for operation. This fact prompted us to come up with new tridentate chiral ligands, bis(oxazolinyl)phenyl ligands (abbreviated as Phebox), which adopt a C_2-symmetric and meridional configuration, but which also show a central covalent bond to the metal (Fig. 1).



Scheme 1

In this context, the pioneering organo-transition metal chemistry with tridentate meridional design of N,C,N ligands, so called N,C,N-pincers, displaying a central carbon–metal bond with two amine groups, has been intensively investigated by van Koten's group.[7] In this review, a special attention to tridentate oxazoline-based ligands, Phebox, their complexes, and catalysis is focused on in terms of organometallic chemistry, coordination chemistry, and homogeneous and asymmetric catalysis (Fig. 2).

2 Ligand synthesis

Ligand precursors were synthesized from isophthalic acid or 2-bromoisophthalic acid. For example, the corresponding acid chlorides were treated with optically active valinol followed by

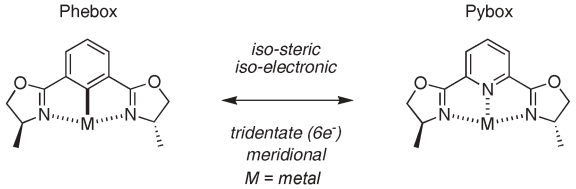


Fig. 1

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Prof. Dr Hisao Nishiyama was born in Mie-prefecture, in 1951. He received his degrees of B.Tech. and Ms.Tech. at Nagoya University (Yoshio Ishii's Laboratory), and Dr.Sci. from Tokyo Institute of Technology in 1980. He worked at Research Center of Toray Industries Inc., in 1975–1980. From 1980–2002, he worked at Toyohashi University of Technology, where he was associate professor from 1985 to 1996 and full professor from 1996 to 2002. Since 2002 (September), he has been a professor of Nagoya University. His main research interests are homogeneous catalysis, asymmetric catalysis with late transition-metal complexes bearing nitrogen based ligands, and organometallic chemistry. He has received the Progressive Award of Young Chemists (1984, Chem. Soc. Jpn.) and Award of Organic Synthetic Chemistry of Japan (1996, Org. Synth. Chem. Jpn.).

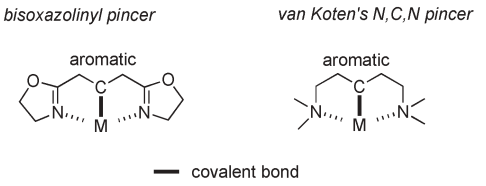
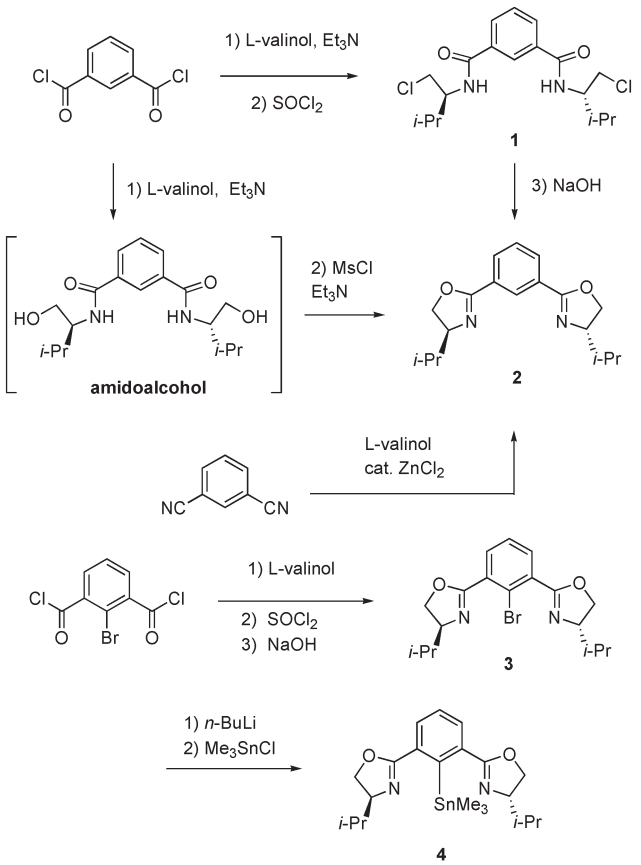


Fig. 2



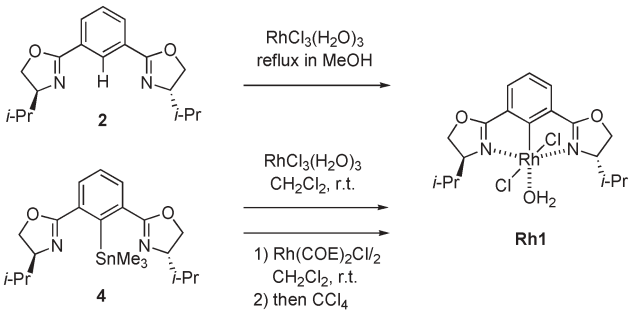
Scheme 2

the treatment with thionyl chloride to give bis(amido chloride) **1** (Scheme 2). Finally, oxazoline formation was completed with NaOH to give *ip*-Phebox-H and -Br, **2** and **3**, respectively. Alternatively, the intermediate amido alcohol can be treated with MsCl and triethylamine to directly give the bis(oxazoline)benzene **2**. Bolm *et al.* originally reported a synthetic method of bis(oxazolinyl)benzene derivatives including **2** by direct reaction of nitriles and amino alcohols in the presence of $ZnCl_2$.[8] Stannyl derivative **4** was synthesized by lithiation of the bromide followed by treatment with Me_3SnCl.[9]

3 Complex synthesis and reactivity

3.1 Rh

There are several ways to access the Phebox metal complexes by making carbon–metal bonds. C–H bond activation is an easy way to prepare the complexes simply by heating of the ligands and rhodium chloride. For example, reaction of *ip*-Phebox-H **2** and $RhCl_3 \cdot 3H_2O$ in refluxing methanol gives the



Scheme 3

desired complex Rh(*ip*-Phebox)$Cl_2(H_2O)$ **Rh1** in 56% yield (Scheme 3).[9] Formation of a similar Rh(III) aqua complex *via* C–H bond activation and *ortho*-metallation, was reported by van Koten and co-workers in the case of the 1,3-bis(aminomethyl)benzene derivative.[10] A simple alternative route is transmetallation with stannane derivatives. The stannyl derivative **4** could be subjected to the reaction with $RhCl_3 \cdot 3H_2O$ to produce the same complex in 45% yield. This was a little increased to 67% with $\{Rh(I)(COE)_2\}_2$ (COE = cyclooctene) and CCl_4 *via* probably a transmetallation and oxidation sequence. As an oxidant, $CuCl_2$ was employed to give 75% yield. On the basis of NMR and X-ray analysis, Rh(Phebox) aqua complexes proved to be C_2-symmetric with one water molecule in equatorial position. The angle of N–Rh–N is *ca.* 158°.

We observed that carbonyl compounds such as acetone, benzaldehyde and cinnamaldehyde, 4-dimethylaminopyridine, and *tert*-butyl isocyanide could exchange with the water molecule. Indeed we could isolate a stable acetone complex **Rh2** and confirmed the structure by X-ray analysis.[9] This fact implied that Rh(Phebox) complex may act as a Lewis acid catalyst (Fig. 3). Moreover, the coordinatively vacant site has a C_2-symmetric chiral environment.

Similarly, isocyanide derivatives can form complexes with an Rh(Phebox)Cl_2 fragment. The catalytic coupling reaction of methyl cyanoacetate and benzaldehyde with the benzyl complex **Rh3** was examined, but resulted in failure, leading only to form the isocyanide complex Rh(*bn*-Phebox)$Cl_2(CNCH_2CO_2Me)$ **Rh4** in quantitative yield (Scheme 4).[11] Treatment of the isocyanide complex **Rh4** with *tert*-BuOK in THF at 0 °C followed by addition of aldehydes could form the corresponding carbon–carbon bond forming product on the rhodium atom. Interestingly, the obtained complex **Rh5** proved to be the corresponding carbene complex, which was confirmed by NMR and X-ray analysis. After the condensation reaction with the carbanion species to the aldehyde, the intramolecular

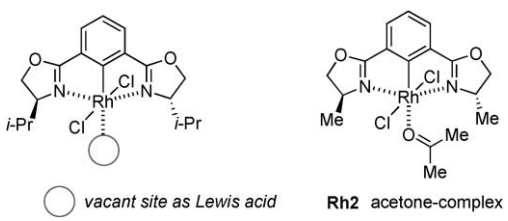
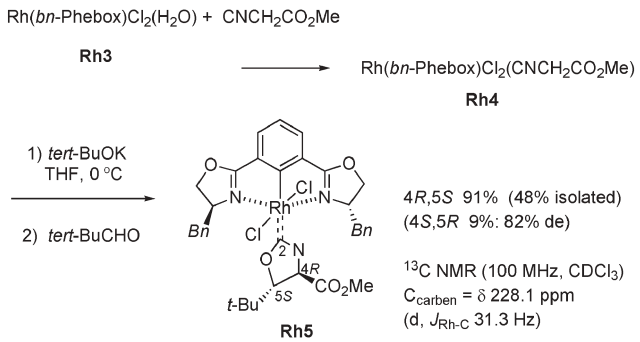
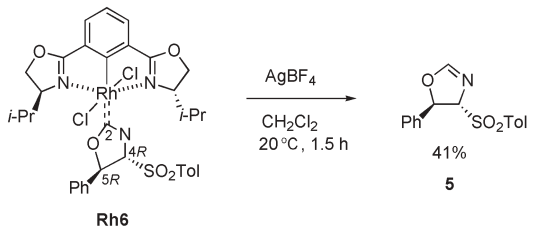


Fig. 3



Scheme 4



Scheme 5

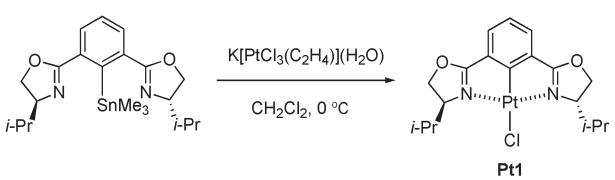
cyclization of the oxide ion to the carbene center occurred to form the carbene complex. The *trans*-isomer predominantly formed with high diastereoselectivity.

For isolation of the organic fragment, silver tetrafluoroborate was successfully employed to give optically pure *trans*-(4*R*,5*R*) oxazoline **5** in the case of the carbene complex **Rh6** derived from benzaldehyde and *p*-tolylsulfonylmethyl isocyanide (Scheme 5).[11]

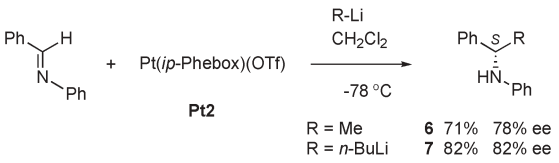
3.2 Pt

Pt(II)(*ip*-Phebox)Cl (**Pt1**) was synthesized at 0 °C in 88% by the transmetallation of *ip*-Pheobx-SnMe$_3$ **4** and K[PtCl$_3$(C$_2$H$_4$)]·H$_2$O (Scheme 6).[12] The coordination geometry is almost planar with a N–Pt–N angle of 158.6° and a Pt–C bond length of 1.928 Å. The complex **Pt1** could be converted to Pt(II)(*ip*-Phebox)(OTf) **Pt2** and [Pt(II)(*ip*-Phebox)(H$_2$O)][BF$_4$] **Pt3**. Furthermore, the divalent platinum complex **Pt1** was oxidized to the tetravalent Pt(IV) trichloride with CuCl$_2$.

The platinum triflate and tetrafluoroborate complexes did not catalyze the allylation of benzaldehyde and allylstannanes, because the complexes could not capture the aldehyde. However, the reaction with benzaldimine spontaneously produced the corresponding aldimine-complex **Pt4**, the formation of which could be confirmed by NMR study. The direct alkylation toward these complexes was carried out so that the magnitude of enantioselection around the prochiral faces of



Scheme 6



Scheme 7

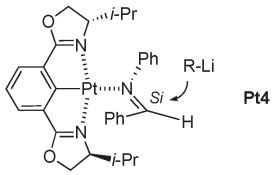


Fig. 4

the coordinating aldimine skeleton could be estimated. Addition of MeLi and *n*-BuLi at −78 °C resulted in formation of the secondary amines **6** and **7** in 78% ee and 82% ee, respectively (Scheme 7). Judging from the *S*-absolute configuration of the major products, alkyl anions should attack on the *Si*-face of the coordinating aldimines (Fig. 4). On the other hand, Pt(IV) complexes did not give the aldimine complexes.

3.3 Pd

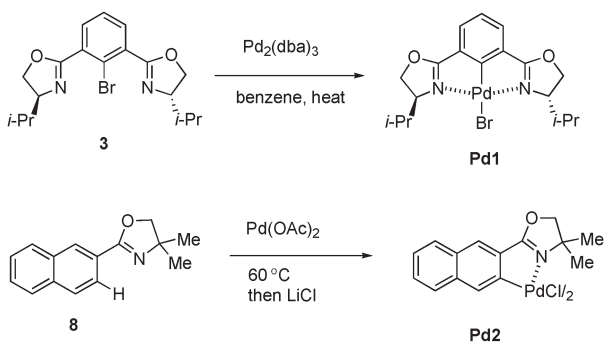
Oxidative addition to low-valent metal complexes with bromo- or iodo-substituted aryl oxazoline derivatives also can efficiently provide pincer type complexes such as **Pd1** (Scheme 8).[13] In this context, C–H bond activation with oxazolinylnaphthalene **8** and palladium acetate gave the corresponding bidentate oxazolinylphenyl complex **Pd2**.[14]

3.4 Ni

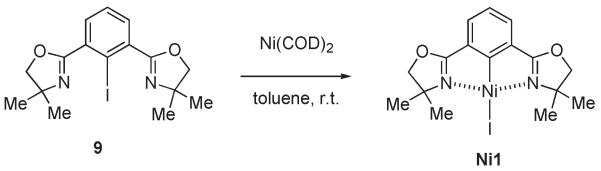
The oxidative addition method is convenient for the preparation of nickel complex **Ni1** by using Phebox iodide **9** with Ni(COD) complex (Scheme 9).[15] The cationic complex generated from **Ni1** with silver triflate exhibited Lewis acidity.

3.5 Cu

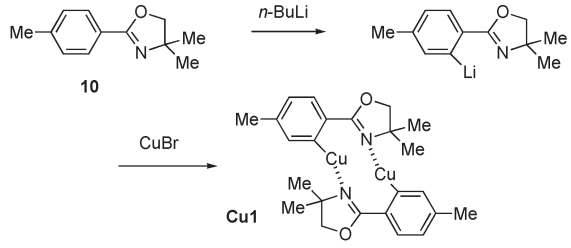
A facile *ortho*-lithiation of oxazolinyl benzene **10** with *n*-butyllithium and subsequent treatment with copper bromide leads to the corresponding bidentate oxazolinylphenyl Cu complex **Cu1** (Scheme 10).[16]



Scheme 8



Scheme 9



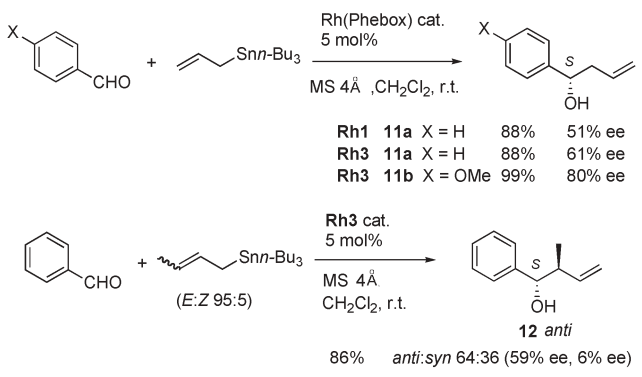
Scheme 10

4 Catalytic applications

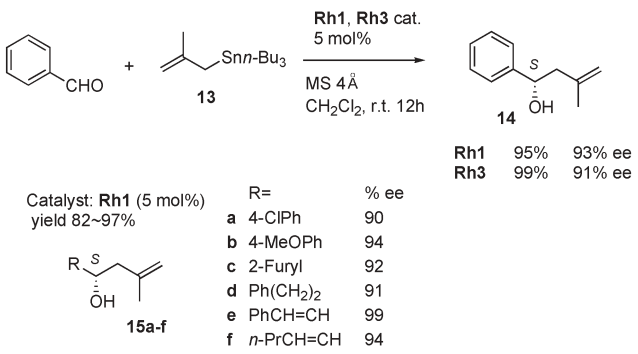
4.1 Asymmetric allylation

Rh(Phebox) complexes can act as efficient Lewis acid catalysts. Reaction of allyltributylstannane and benzaldehyde can be carried out with 5 mol% of Rh(*ip*-Phebox)$Cl_2(H_2O)$ **Rh1** in CH_2Cl_2 at room temperature for 7 h to give the corresponding allylated products **11** in 88% yield and 51% ee (Scheme 11).[9] The enantioselectivity increased up to 61% ee by use of the benzyl-substituted catalyst **Rh3** in place of the isopropyl one. *p*-Methoxybenzaldehyde and cinnamaldehyde resulted in 80% ee and 77% ee, respectively. Crotyl stannane was examined, and found to give *anti*-selectivity with a middle range of ee for **12**. The *E* and *Z* ratio of the crotyl stannane did not influence the *anti* selectivity.

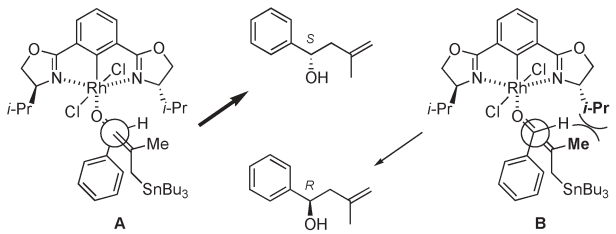
Enantioselectivity was dramatically improved to over 90% ee with methallylstannane **13** (Scheme 12).[17] Not only several aromatic aldehydes but also dihydrocinnamaldehyde were methallylated with 5 mol% of isopropyl catalyst **Rh1** to give high ee values (up to 99% ee for **15e** with cinnamaldehyde). Molecular sieves need not always have to be added, and the reaction proceeds smoothly under aerobic condition. Moreover, the catalyst can be recovered during the last run of chromatographic purification of the product alcohols.



Scheme 11



Scheme 12



Scheme 13

A hypothetical consideration is that a steric repulsion between the isopropyl groups of **Rh1** and the methyl group of the methallylstannane largely occurs for one of the transition states giving a minor *R*-product (Scheme 13). Therefore, the *S*-product homoallylic alcohol was preferably produced *via* transition state **A**, where the *Si*-face of benzaldehyde was attacked.

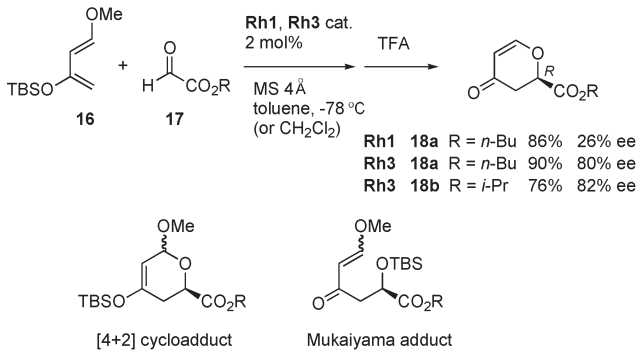
Recently, Weissberg and Portnoy reported the synthesis of the polymer supported Phebox unit and the corresponding rhodium complexes, which promoted enantioselective allylation of aldehydes with allylstannane in up to 48% ee.[18]

4.2 Asymmetric hetero-Diels–Alder reaction

The above catalytic system condition for the allylation was applied to asymmetric hetero Diels–Alder reaction with Danishefsky's diene **16** and glyoxylates **17**.[19] The benzyl catalyst **Rh3** exhibited high efficiency to attain high ee values up to 82% of **18b** in the reaction of *tert*-butyldimethylsilyloxy (TBSO)-diene and isopropyl glyoxylate (Scheme 14). The reaction took place at −78 °C for 1 h with 2 mol% of **Rh3** followed by acid treatment with trifluoroacetic acid (TFA) to give the corresponding dihydropyran derivative. NMR spectroscopy at low temperature revealed that the adduct is a [4 + 2] cycloadduct, rather than a Mukaiyama aldol type. In this catalysis, the *Re* face of the aldehyde moiety was attacked to produce the *R* absolute configuration. A fluoride-substituted complex Rh(*bn*-Phebox)$F_2(H_2O)$ was applied to increase the ee from 80% for *n*-butyl glyoxylate **18a** to 84%.

4.3 Michael addition

The efficient Lewis acidity of Rh(Phebox) complexes was then examined for promotion of Michael addition of α-cyanocarboxylates **19** and acrolein. However, Rh aqua complexes **Rh1**



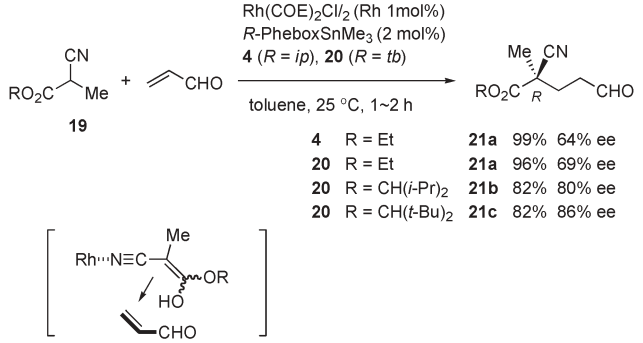
Scheme 14

or **Rh3** showed no catalytic activity.[20] In the presence of trialkylamines the aqua complexes promote the reaction but resulted in lower enantioselectivity below 30%. A rather simple catalyst system was found for this purpose. The *in situ* catalyst prepared by a mixing Phebox-$SnMe_3$ **4** or **20** and Rh(I) complex $\{Rh(COE)_2Cl\}_2$ exhibited higher efficiency to give the desired Michael adducts **21** in high yields with up to 86% ee for **21c** (Scheme 15). Bulky substituents of the ester and *tert*-butyl catalyst derived from **20** afforded relatively higher enantioselectivity. On the basis of NMR study, Rh(III)(Phebox)-($SnMe_3$)Cl generated from Phebox-$SnMe_3$ and the Rh(I) complex was postulated as an active catalyst, which might produce the *N*-bonded enol by coordination of α-cyanoester. At the Michael addition stage, the *Si* face attacks on acrolein to give an *R*-quaternary carbon center.

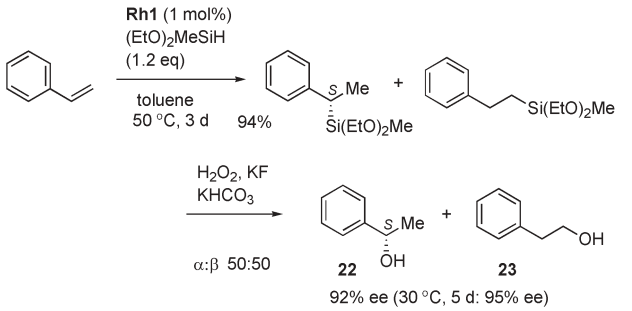
The nickel-Phebox complex **Ni1** (X = OTf) (5 mol%), which was generated *in-situ* with silver triflate, also catalyzed Michael addition of ethyl cyanoacetate and methyl vinyl ketone at 4 °C to give the corresponding adduct in 55% yield.[15]

4.4 Asymmetric hydrosilylation of alkenes

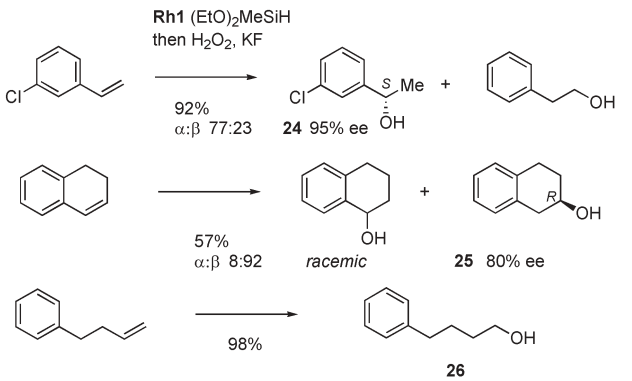
As is well known, not only Rh(I) species but also Rh(III) species are good catalysts for hydrosilylation of ketones and alkenes with certain hydrosilanes.[21] Chiral rhodium-catalyzed reactions were also reported in some intramolecular cases. Rh(Phebox) catalysts were applied to this asymmetric hydrosilylation of alkenes in the presence of several alkoxyhydrosilanes (Scheme 16).[22] The catalysis proceeded at 50 °C for 3 days with 1 mol% of Rh(*ip*-Phebox)$Cl_2(H_2O)$ **Rh1** and $(EtO)_2MeSiH$. Styrene could be converted to the



Scheme 15



Scheme 16



Scheme 17

corresponding hydrosilane-adduct followed by oxidation to produce a *ca*. 50 : 50 mixture of 1-phenylethanol **22** and 2-phenylethanol **23** in *ca*. 90% yield. However, the ee of 1-phenylethanol reached to as high as 95%. Use of $AgBF_4$ and $AgPF_6$ accelerated the reaction to completion within 12 h giving a similar stereoselectivity.

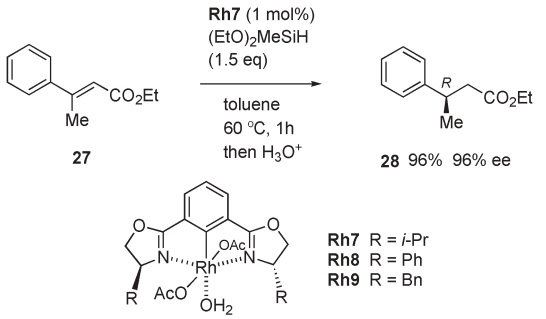
m-Chlorostyrene gave the highest ratio of 1-phenylethanol derivative **24** in a high regioselectivity of 77% with 95% ee (Scheme 17). Very interestingly, dihydronaphthalene was converted mainly to the β-hydroxy compound with high 80% ee for **25**. In addition, the aliphatic terminal alkene 4-phenyl-1-butene was exclusively converted to the terminal primary alcohol **26**. The regioselectivity for the hydrosilylation of mono-substituted alkenes with Rh(Phebox) catalyst remained unmeasured.

4.5 Asymmetric conjugate reductions

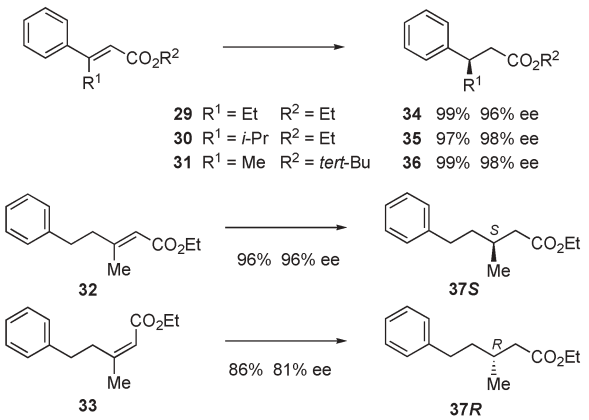
Reduction of α,β-unsaturated compounds was examined with the Rh(Phebox) catalysed system. (*E*)-Ethyl 3-phenylbut-2-enoate **27** was subjected to the reaction at 60 °C for 1 h with Rh(*ip*-Phebox) acetate catalyst **Rh7** (1 mol%) and diethoxymethylsilane, followed by hydrolysis, to give (*R*)-3-phenylbutanoate **28** in 96% yield and 96% ee (Scheme 18).[23,24] Further investigation of this reaction revealed the acetate complexes to be more active than the chloride complexes. The structure of **Rh7** was analyzed by X-ray diffraction.

Several (*E*)-unsaturated esters **29–32** were reduced enantioselectivity with over 90% ee, while (*Z*)-isomer **33** was reduced with reverse absolute configuration (Scheme 19).

The reduction of α,β-unsaturated ketones commonly suffers from 1,2-reduction. In this context, Ojima reported



Scheme 18

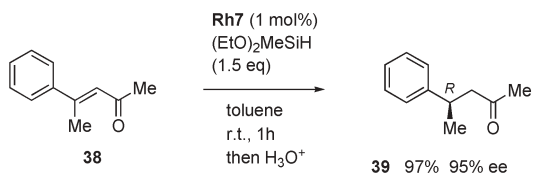


Scheme 19

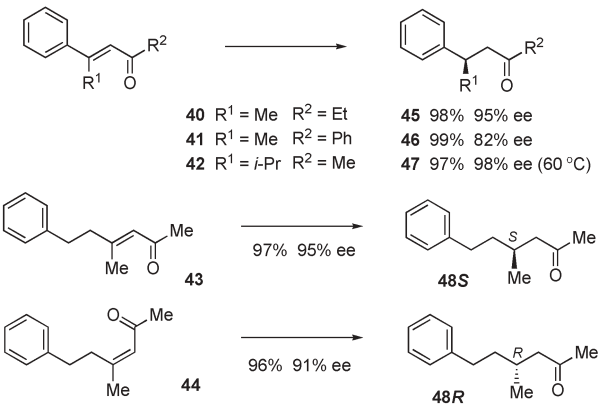
the regio-controlled reduction of α,β-unsaturated ketones with Wilkinson's catalyst in combination with Et_3SiH or Et_2MeSiH for 1,4-reduction (conjugate reduction) or Ph_2SiH_2 for 1,2-reduction.[21] It was found with Rh(*ip*-Phebox) acetate catalyst **Rh7** exclusively leads to conjugate reduction with $(EtO)_2MeSiH$. (*E*)-4-Phenyl-3-penten-2-one **38** was readily converted at room temperature for 1 h to (*R*)-4-phenylpentan-2-one **39** in 97% yield and 95% ee (Scheme 20).[24] The catalysts **Rh8** (*ph*) and **Rh9** (*bn*) resulted in lower enantioselectivity, 81% ee and 73% ee, respectively.

Bulky substituents R^2 decreased the enantioselectivity, while (*E*) and (*Z*) isomers **43** and **44** gave the reverse absolute configuration upon reduction (Scheme 21).

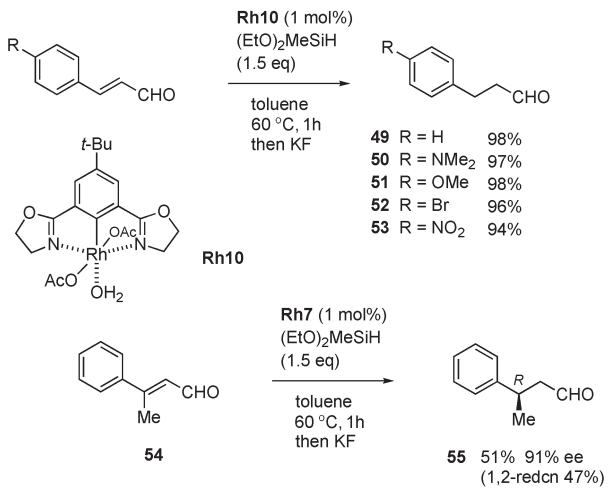
Reduction of cinnamaldehydes were examined with non-chiral catalyst **Rh10** to show highly selective conjugate reduction (Scheme 22).[25] On the other hand, the chiral catalyst **Rh7** decreased the selectivity, to form 1,2-reduction products, cinnamyl alcohols in *ca*. 15–30%. Also, asymmetric reduction of **54** with chiral catalyst **Rh7** resulted in decrease of selectivity



Scheme 20



Scheme 21



Scheme 22

for the conjugate reduction, but the ee was as high as 91% for **55**.

The stereochemical course of the asymmetric conjugate reduction of the esters and the ketones was considered by reference to Fig. 5. The starting Rh(III) catalysts are reduced by the hydrosilanes to the Rh(I) species, which react with the hydrosilane to give the hypothetical rhodium–hydride complex, (Phebox)RhH[Si(OEt)$_2$Me]. Upon interaction of the unsaturated substrate with the active hydride complex the hydride attacks the β-carbon atom to give the *R*-absolute configuration. The *Re*-face coordination in **B** may be disfavored by steric repulsion between the carbonyl function and isopropyl group of the oxazoline rings.

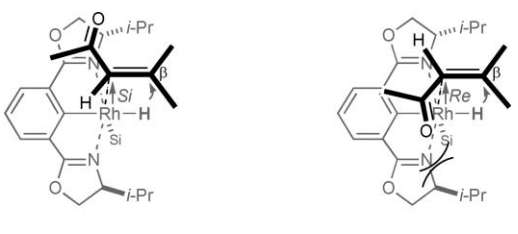


Fig. 5

4.6 Asymmetric reductive aldol reaction

Thus, Rh(Phebox) catalyst can demonstrate its catalytic activity for asymmetric conjugate addition, which can provide optically active esters and ketones with chiral carbon at the β-position. Alternatively, chiral copper and cobalt complexes have been shown to exhibit high efficiency and enantioselectivity for conjugate reduction of nitroalkenes and α,β-unsaturated nitriles as well as α,β-unsaturated carbonyl groups.[26]

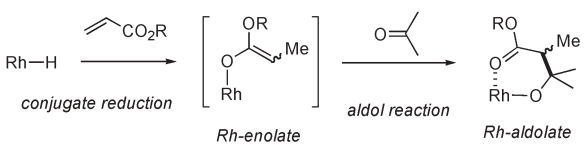
The conjugate reduction of α,β-unsaturated esters, acrylates, by an intermediate rhodium–hydride leads to Rh-enolate species, so that the presence of carbonyl compounds in the reaction mixture may be able to cause aldol-condensation giving Rh-aldolates (Scheme 23). The possibility of this reductive aldol reaction means that no strong base such as *tert*-BuLi to generate ester enolate anions are necessary. The intermediate enolate can be generated from acrylates by use of metal catalysts and a hydride source such as hydrosilanes or hydroboranes.[27]

Under similar conditions mentioned above for asymmetric conjugate reduction, benzaldehyde and *tert*-butyl acrylate could be coupled with $(EtO)Me_2SiH$ in the presence of 1 mol% Rh(*ip*-Phebox) acetate complex **Rh7**, followed by hydrolysis to give the corresponding Mukaiyama-aldol type product **56** in 93% yield, 94 : 6 *anti* : *syn* ratio, and 94% ee for *anti*.[27] The benzyl catalyst **Rh9** exhibited a higher *anti* : *syn* ratio, up to 98 : 2, with $(EtO)_2MeSiH$, and Me_2PhSiH or $MePh_2SiH$ attained the highest enantioselectivity of 96% ee (Scheme 24). A variety of aromatic or aliphatic aldehydes were subjected to the reductive aldol reaction to give extremely high *anti*-selectivity with high enantioselectivity, whereas most *syn*-products were in lower ee.

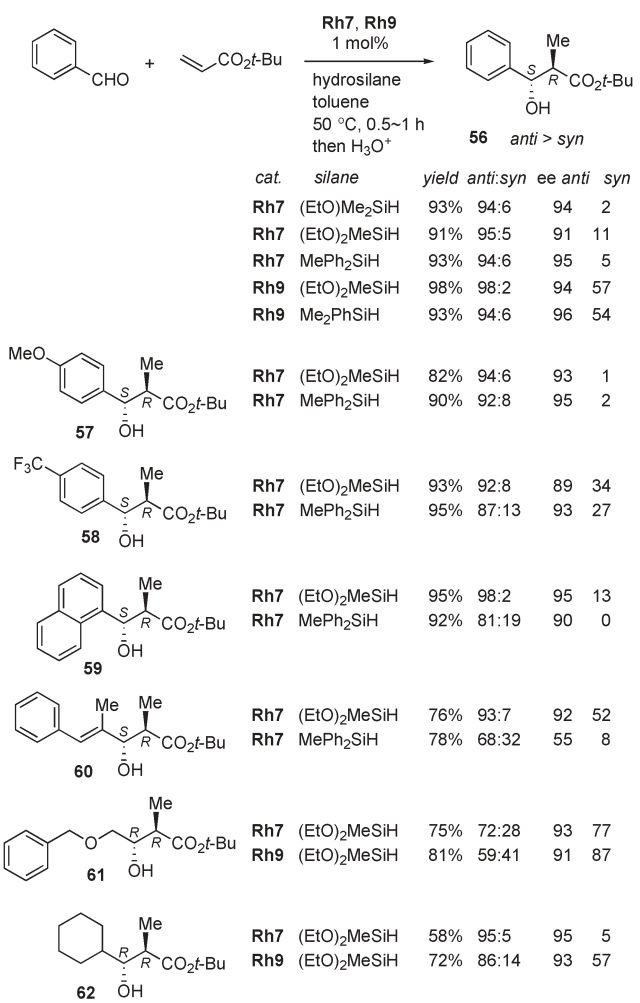
On the basis of absolute configuration of the *anti*-aldol compounds, a chair like cyclic transition state consisting of rhodium–(*E*)-enolate and a coordinating aldehyde moiety was hypothesized, where the rhodium atom having one vacant site can act a Lewis acid to capture the carbonyl group at the equatorial position, as described previously in the allylation reaction (Scheme 25). The *Si*-face of the coordinating benzaldehyde was attacked to give the 3*S* absolute configuration of the aldol product. The free silylketene acetal generated *in situ* might attack the activated aldehyde, but the observed background reaction gave *syn*-selectivity with only low enantioselectivity.

When trimethylsilyl acrylate **63** was adopted as an enolate source, the corresponding carboxylic acid **64** was directly obtained after hydrolysis with high enantioselectivity (Scheme 26). Simple crystallization afforded optically pure *anti*-carboxylic acid.[28]

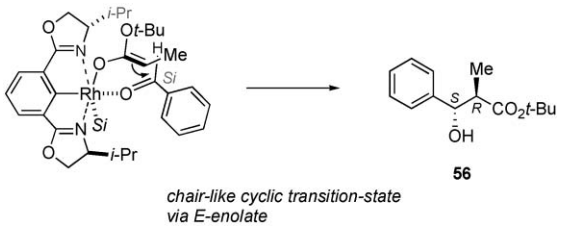
In terms of substituent diversity of the Phebox-ligand, some derivatives have been designed and synthesized. 4-NO_2- and 4-MeO-Phebox complexes **Rh11** and **Rh12** were readily



Scheme 23

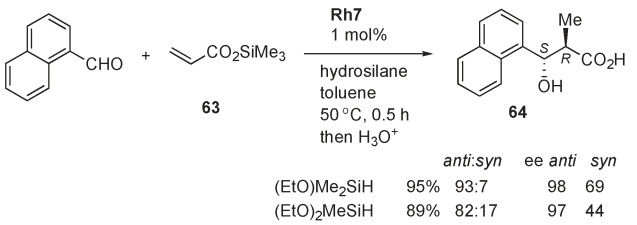


Scheme 24

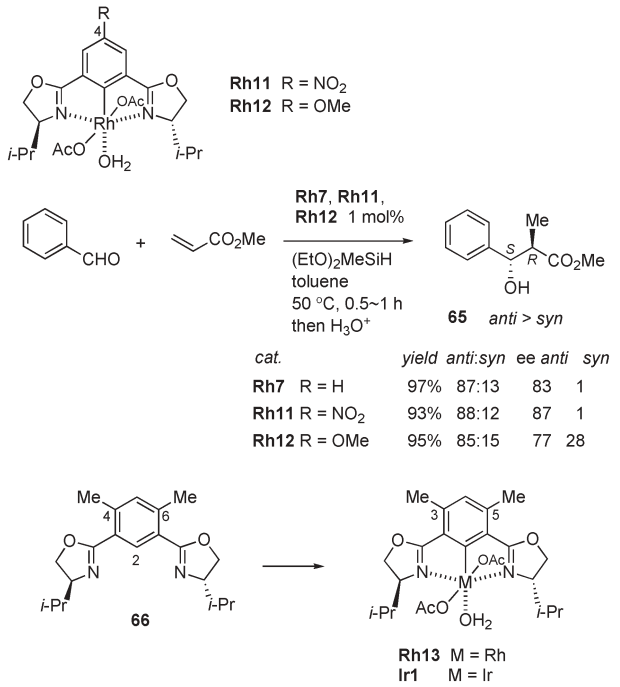


Scheme 25

prepared from commercially available 5-substituted isophthalic acids. We observed a weak electronic effect on stereoselectivity for asymmetric reductive aldol reaction with methyl



Scheme 26



Scheme 27

acrylate giving **65**.[28] 4-NO_2 complex **Rh11** exhibited slightly higher enantioselectivity. Use of 4-MeO complex **Rh12** decreased the enantioselectivity to 77% from 87% for the 4-NO_2 complex (Scheme 27). By contrast, 4,6-dimethyl Phebox-H ligand precursor **66** improved the yield of the C–H bond activation step, probably because of prevention of undesirable C–H bond activation at 4,6-positions.[29] The corresponding 3,5-dimethyl-Phebox-Rh complex **Rh13** was obtained in 81% yield, and it showed similar catalytic efficiency to that of **Rh7** for the asymmetric conjugate reduction and reductive aldol reaction. Under the same conditions, iridium–Phebox complex **Ir1** could be obtained.[29] However, the iridium complex exhibited lower catalytic activity than that the rhodium complex.

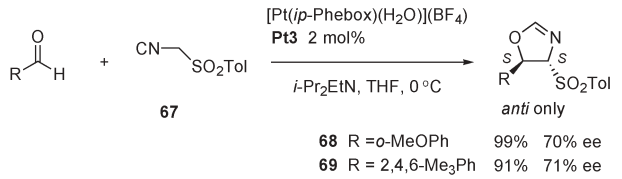
As for the asymmetric reductive aldol reactions, Fuller and Morken reported Rh-BINAP and iridium-Pybox catalysts to show high *syn*-selectivity with high enantioselectivity.[30] Recently, Riant and co-workers demonstrated that several aromatic ketones were used as acceptor substrates to attain high *erythro* selectivity and high enantioselectivity with chiral-phosphine/copper catalysts.[31]

4.7 Asymmetric aldol reaction with isocyanide

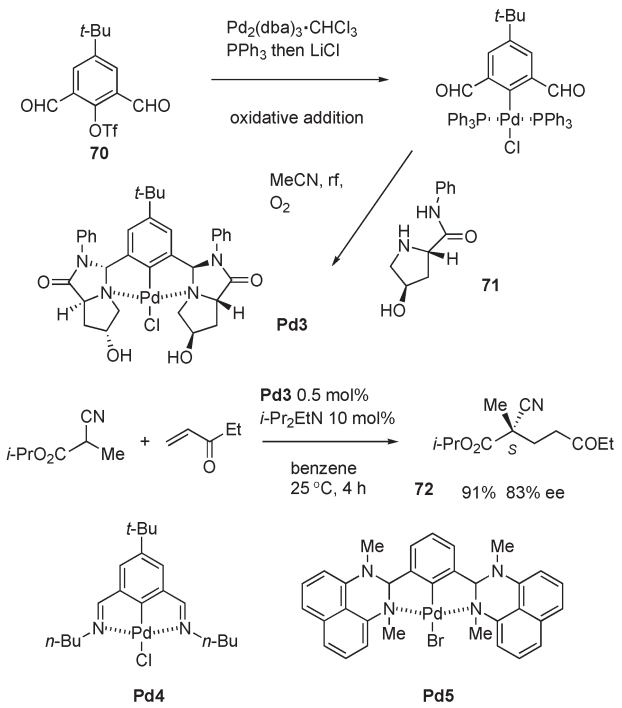
Although isocyanides **67** formed stable complexes with Rh(Phebox) species as described above, they reacted with benzaldehyde derivatives at 0 °C in THF in the presence of [Pt(*ip*-Phebox)(H_2O)](BF_4) **Pt3** (2 mol%) and diisopropylethylamine (10 mol%) to give the corresponding aldol adducts in high yields with *ca.* 70% ee and complete *trans*-selectivity (Scheme 28).[32]

5 Related tridentate pincers: synthesis and catalysis

Uozumi and co-workers reported that N,C,N-pincer palladium complexes were prepared by an unique ligand



Scheme 28



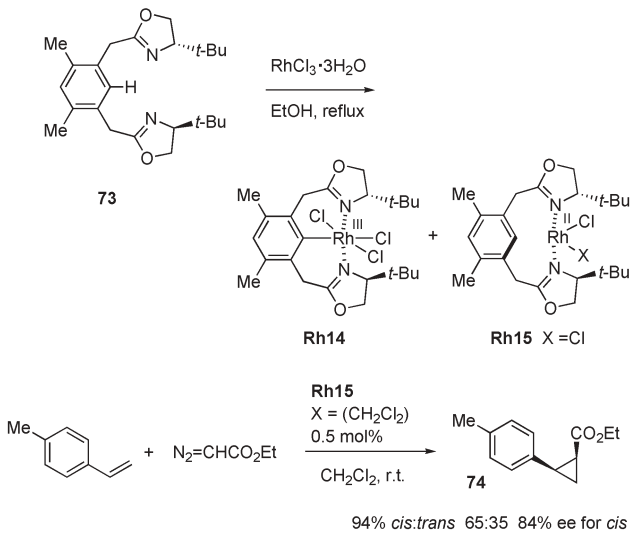
Scheme 29

introduction method, in which oxidative addition of 2,6-diformylphenyl triflate **70** to a Pd(0) complex produced the corresponding phenyl complex followed by dehydrative imine formation on the complex with chiral amine **71** to give N,C,N pincer complex **Pd3** (Scheme 29).[33] The chiral Pd-complex exhibited high efficiency for asymmetric Michael addition of α-cyanoesters and vinyl ketones giving **72**. For the Heck reaction, N,C,N-pincer palladium complexes **Pd4** and **Pd5** exhibited high turnover number 10^6–10^8.[34]

Bis-methylene tethered bisoxazolinyl benzene **73** reacted with $RhCl_3 \cdot 3H_2O$ in refluxing ethanol to give a C–H bond activation product of Rh(III) **Rh14** and the reduction product Rh(II) **Rh15**. The latter complex exhibited high efficiency for asymmetric cyclopropanation and aziridination (Scheme 30).[35]

6 Concluding remarks

Intelligent design of ligands for transition-metal complexes will become increasingly important to optimise efficiency in homogenous catalysis and asymmetric catalysis, not only for academic curiosity, but also for industrial production. The chemistry of N,C,N bisoxazolinyl-pincer ligands developed in this decade has been demonstrated here to show that they can make complexes which are highly stable owing to the presence of a covalent bond and their tridentate structure. Moreover



Scheme 30

they can efficiently activate the catalytic activity of the metal atoms. I strongly believe that efficient catalysts derived from this pincer design will appear in the future and will be of benefit to catalysis and organic synthesis.

Acknowledgements

I thank Dr Y. Motoyama for his initial set up of Phebox chemistry at Toyohashi University of Technology. I also thank Daiko Foundation and The Mitsubishi Foundation for financial support.

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