Title	Cationic Iridium/Chiral Bidentate Phosphoramidite Catalyzed Asymmetric Hydroarylation
Author(s)	Shirai, Tomohiko; Yamamoto, Yasunori
Citation	Synthesis-stuttgart, 54(21), 4764-4772 https://doi.org/10.1055/a-1683-9455
Issue Date	2021-11-01
Doc URL	http://hdl.handle.net/2115/87608
Rights	This is an Accepted Manuscript of an article published by Thieme Publishing Group in Synthesis on 14 December 2021, available online at https://www.thieme-connect.de/products/ejournals/abstract/10.1055/a-1683-9455
Type	article (author version)
File Information	PDF43915209-882510333.pdf

Cationic Iridium/Chiral Bidentate Phosphoramidite Catalyzed Asymmetric Hydroarylation

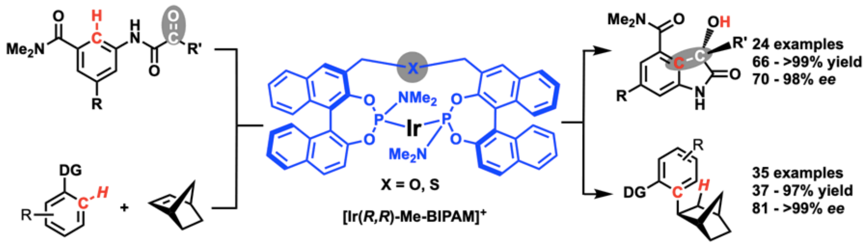
Tomohiko Shirai[a]
Yasunori Yamamoto*[b]

[a] Department of Materials Science and Engineering, National Institute of Technology, Kochi College Otsu, Monobe, Nangoku, Kochi 783-8508, Japan

[b] Division of Chemical Process Engineering and Frontier Chemistry Center (FCC), Faculty of Engineering, Hokkaido University, Kita 13, Nishi 8, Kita-ku, Sapporo, Hokkaido 060-8628, Japan

yasuyama@eng.hokudai.ac.jp

Click here to insert a dedication.



Received:
Accepted:
Published online:
DOI:

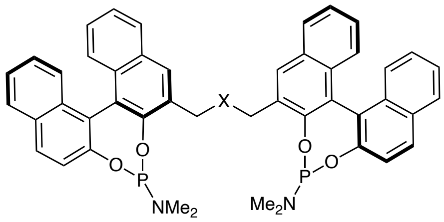
Abstract In this personal account, we summarize our investigations on the asymmetric direct addition of C(sp^2)-H bond to unsaturated compounds such as C=O, C=C using cationic Iridium-chiral *O*-linked bidentate phosphoramidite (Me-BIPAM) and *S*-linked bidentate phosphoramidite (S-Me-BIPAM) catalyst system.

1. Introduction
2. Highly enantioselective intramolecular hydroarylation of α-ketoamides
3. Highly enantioselective intermolecular hydroarylation of bicycloalkenes
4. Conclusions

Key words Asymmetric synthesis, C–H functionalization, hydroarylation, iridium catalyst, chiral bidentate phosphoramidite

1 Introduction

Transition-metal-catalyzed C–C bond-forming reactions via C–H bond activation are the ultimate atom-economical processes. In particular, direct additions of arenes to double bonds such as C=O, C=N and C=C, called hydroarylation reactions, are complete atom-economy.[1,2] Furthermore, the enantioselective transformations by C-H activation constitute an ideal tool for the synthesis of chiral building blocks.[2] Our group has already demonstrated that cationic iridium (I)/chiral bidentate phosphoramidite (Me-BIPAM) complexes can catalyze the asymmetric direct addition of C(sp^2)–H bond to unsaturated compounds such as C=O, C=C.[3] On the other hand, we have developed moderate π-acidic chiral bidentate phosphoramidite ligands[4] for the transition-metal-catalyzed asymmetric nucleophilic addition reactions of organoboronic acid derivatives for 15 years (Figure 1).[5] We previously showed that a chiral bidentate phosphoramidite ligand achieved high enantioselectivities for arylation reactions of C=C,[6] C=N,[7] and C=O[8] bond. These chiral bidentate phosphoramidite ligands can be easily prepared from the corresponding linked-binol.[3c,6a,7a,8] In this account paper, we summarize our recently developed cationic iridium/Me-BIPAM-catalyzed asymmetric hydroarylation of unsaturated bonds with activation of sp^2 carbon-hydrogen bond. As a result of various investigations, we found that the newly developed cationic iridium/Me-BIPAM complex has excellent catalytic activity for the asymmetric intramolecular hydroarylation of ketones with the activation of sp^2 carbon-hydrogen bond (Scheme 1).[3a] At the same time, mechanistic studies revealed the rate-limiting step in the estimated catalytic cycle.[3b] Furthermore, in the process of tuning the catalyst, we found that the newly developed catalytic system consisting of a novel sulfur-bridged bidentate phosphoramidite ligand (S-Me-BIPAM) and cationic iridium is effective for the asymmetric intermolecular hydroarylation of bicycloalkenes via activation of the sp^2 carbon-hydrogen bond (Scheme 4 and 8).[3c,d]



(*R*,*R*)-Me-BIPAM (X = O)
(*R*,*R*)-N-Me-BIPAM (X = NMe)
(*R*,*R*)-S-Me-BIPAM (X = S)
(*R*,*R*)-SO$_2$-Me-BIPAM (X = SO$_2$)
(*R*,*R*)-CH$_2$-Me-BIPAM (X = CH$_2$)

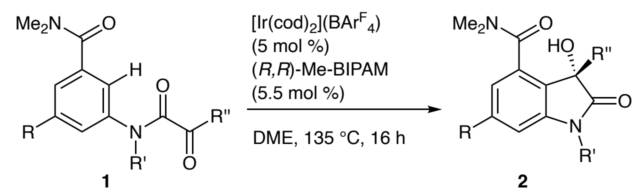
Figure 1 Chiral bidentate phosphoramidite ligands.

2 The highly enantioselective intramolecular hydroarylation of α-ketoamides[3a,b]

Intramolecular cyclizations by C–H bond activation have been reported for the efficient synthesis of oxindole derivatives.[10] In 2009, Shibata and co-workers reported cationic Ir/(*S*)-H$_8$-BINAP-catalyzed enantioselective synthesis of a chiral 4-acetyl-3-hydroxy-3-methyl-2-oxindole with 72% *ee* using the methodology of direct C–H bond functionalization.[11] During study on Me-BIPAM for enantioselective bond-forming reactions, we achieved direct synthesis of chiral 3-substituted 3-hydroxy-2-oxindoles from α-keto amides using a cationic iridium and (*R*,*R*)-Me-BIPAM (Scheme 1).[3a]

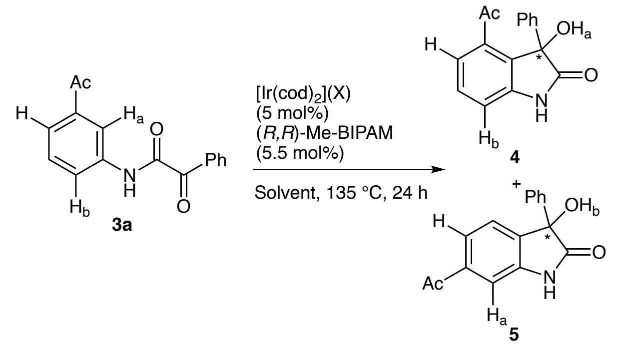
We examined the enantioselective hydroarylation using an α-keto amide (**3**) in the presence of a cationic iridium/(*R*,*R*)-Me-BIPAM catalyst (Table 1). All reactions selectively gave 4-acetyl-3-hydroxy-3-

phenyl-2-oxindole (**4**) with complete regioselectivity.[12] BAr^F_4 anion was more suitable than other counter anions, and the yield and enantioselectivity were moderate (62%, 71% ee) (entries 1-6). In the further optimization of solvent, 1,2-dimethoxyethane (DME) was the best one (90%, 88% ee) (entry 8).



Scheme 1 Iridium catalyzed intramolecular hydroarylation.

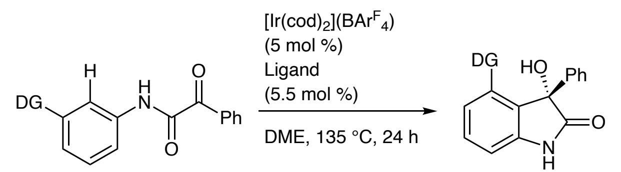
Table 1 Optimization of reaction conditions for intramolecular hydroarylation.



Entry	Catalyst (mol%)	Solvent	Yield of 4/5 (%)	*ee* of 4/5 (%)
1	$[Ir(cod)_2](BAr^F_4)$ (5)	PhCl	62 / trace	71 / -
2	$[Ir(cod)_2](BF_4)$ (5)	PhCl	37 / trace	53 / -
3	$[Ir(cod)_2](SbF_6)$ (5)	PhCl	12 / trace	38 / -
4	[Ir(cod)2](OTf) (5)	PhCl	15 / trace	29 / -
5	$[Ir(cod)_2](ClO_4)$ (5)	PhCl	3 / trace	29 / -
6	$[Ir(cod)_2]Cl$ (5)	PhCl	n.r.	n.r.
7	$[Ir(cod)_2](BAr^F_4)$ (5)	THF	94 / trace	66 / -
8	$[Ir(cod)_2](BAr^F_4)$ (5)	DME	90 / trace	88 / -
9	$[Ir(cod)_2](BAr^F_4)$ (5)	Dioxane	28 / trace	77 / -

[a] Reaction conditions: a-ketoamide (0.25 mmol), iridium catalyst (5 mol%), and (*R,R*)-Me-BIPAM (1.1 equiv. to Ir) in solvent (1 mL), stirred for 24 h at 135 °C

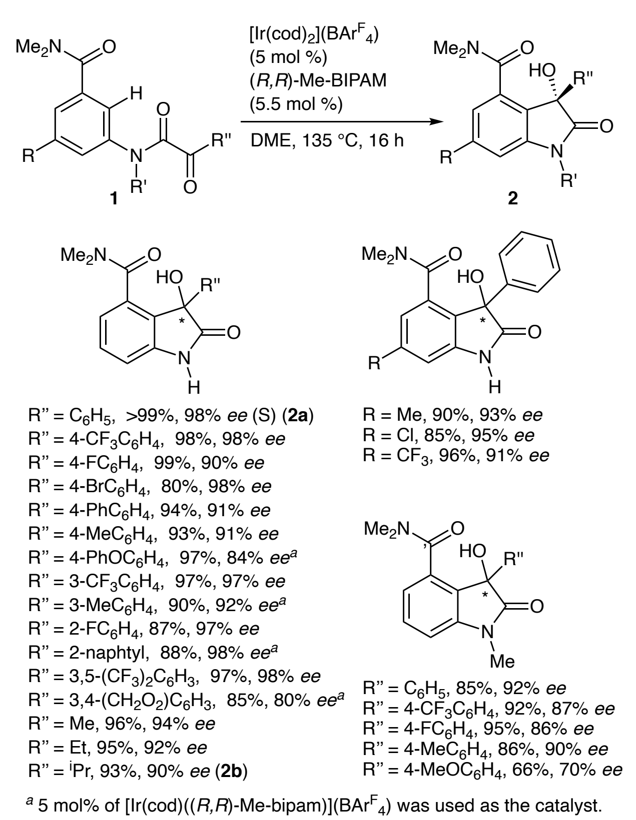
Table 2 Optimization of directing groups for intramolecular hydroarylation.



Entry	DG	Ligand	Yield (%)	*ee* (%)
1	Ac	(*R,R*)-Me-BIPAM	90	88
2	Bz	(*R,R*)-Me-BIPAM	90	88
3	CO_2Me	(*R,R*)-Me-BIPAM	37	95
4	$CONMe_2$	(*R,R*)-Me-BIPAM	>99	98 (S)
5[c]	$CONMe_2$	(*R,R*)-Me-BIPAM	>99	98 (S)
6[d]	$CONMe_2$	(*R,R*)-Me-BIPAM	96	97 (S)
7	NHAc	(*R,R*)-Me-BIPAM	63	82
8	H	(*R,R*)-Me-BIPAM	n.r.	-

[a] Reaction conditions: a-ketoamide (0.25 mmol), iridium catalyst (5 mol%), and (*R,R*)-Me-BIPAM (1.1 equiv to Ir) in DME (1 mL), stirred for 24 h at 135 °C. [b] The absolute configuration of the chiral center within the product is given in parentheses. [c] Reaction mixture was stirred at 135 °C, 16 h. [d] Iridium catalyst (3 mol%) was used.

We also examined another directing group (Table 2). The dimethyl amino carbonyl group was most effective and the enantioselectivity improved to 98% *ee* (entry 4). The enantioselectivity was not impaired even when the reaction time was 16 hours or when the catalyst amount was 3 mol%. (entries 5 and 6). The directing group was essential in this reaction (entry 8). The absolute configuration of the product was assigned as S enantiomer from X-ray crystallographic analysis of the compound of **2a**.[13] The cationic Ir/Me-BIPAM catalyst achieved highly enantioselective hydroarylation of various α-keto amides (Scheme 2). In some cases, the enantioselectivity was raised by using the preformed $[Ir(cod)((R,R)\text{-Me-BIPAM})](BAr^F_4)$ complex. A variety of aliphatic α-keto amides also gave 3-alkyl-3-hydroxy-2-oxindoles in excellent selectivities (90-94% ee). A methyl group on the nitrogen atom also achieved good yields and enantioselectivities (70-92% ee).



Scheme 2 Enantioselective intramolecular hydroarylation of α-ketoamides.

In NMR study, some signals for iridium hydride species were observed over 100 °C (Figure 2). Although, iridium hydride was detected at 100 °C, the yield was low under catalytic reaction (Equation 1). These results showed that the addition to carbonyl group proceeded at 135 °C. As result of the reaction of substrate **1b** in the presence of D_2O (6 equiv.), the unreacted substrate **1b-D** (30%) and product **2b-D** (68%) were observed (Equation 2). Deuterium was observed at the *ortho* position of the keto amide group (11%-D at H_b and 44%-D at H_d), the *ortho* position of the *N,N*-dimethyl carbamoyl group (10%-D at H_a) in the substrate, and the 5- and 7-positions of the product (11%-D at H_a and H_d). These results showed that the C–H bond cleavage occurred in a fast and reversible manner prior to the carbonyl insertion.[10,13] Deuterium was also observed at the *N,N*-dimethyl carbamoyl group in both the substrate (**1b-D**) and product (**2b-D**). The intermolecular kinetic isotope effect (KIE) of the reaction employing substrates **1a** and **1a-D** was found to be 1.85 at the early stage of the reaction (Equation 3).[14] These experimental observations for the C–H bond cleavage step

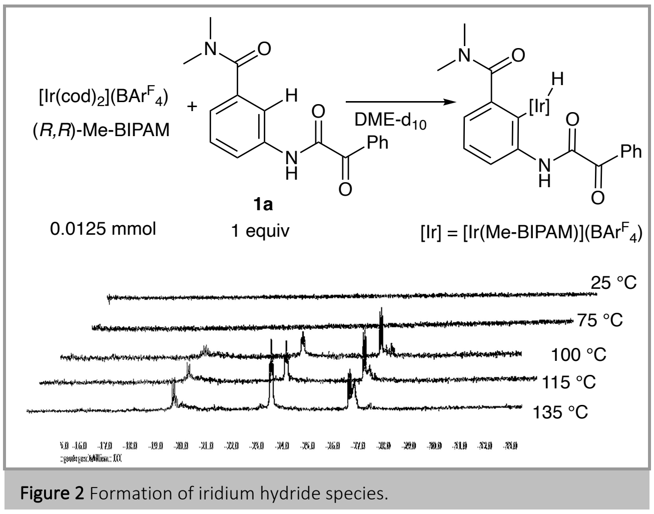
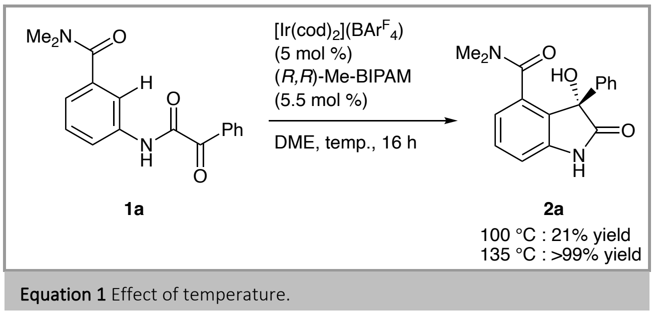
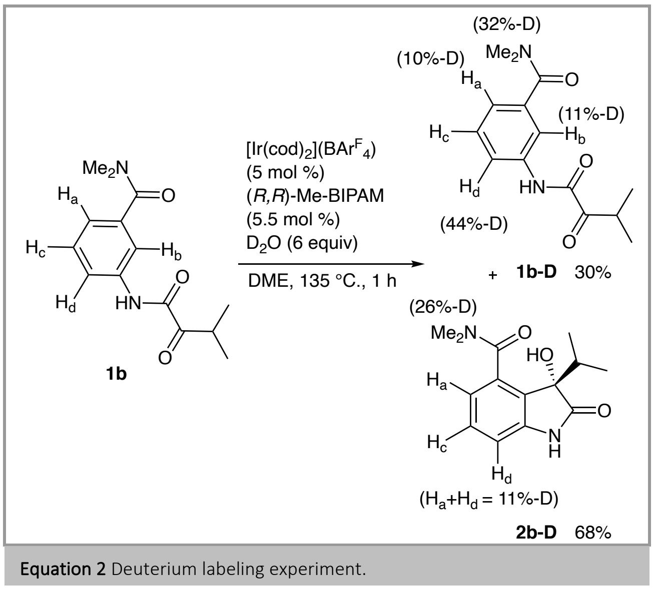


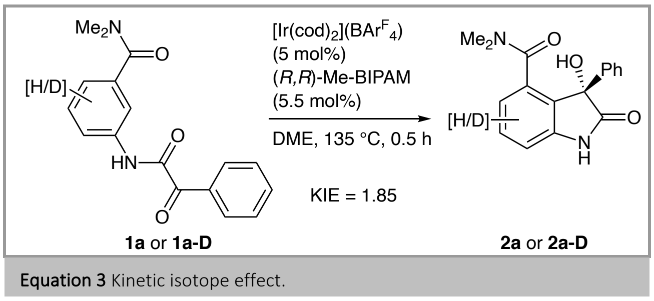
Figure 2 Formation of iridium hydride species.



Equation 1 Effect of temperature.



Equation 2 Deuterium labeling experiment.



Equation 3 Kinetic isotope effect.

showed that C–H bond cleavage occurred before the turnover-limiting step in the catalytic cycle, and secondary isotope effect was observed.[15]

To determine the turnover-limiting step of this reaction, Hammett plot analysis for substituent (X) at the para position to the reactive C–H bond indicated a linear correlation (ρ = -0.99) (Figure 3). This result showed that the nucleophilicity of aryl-iridium accelerated the addition to carbonyl group. Next, the Hammett plot for substituents (Y) at the para position to the ketone group was also attempted to confirm the hypothesis as mentioned above (Figure 4). The results showed a small linear relationship (ρ = -0.099 and -0.34).

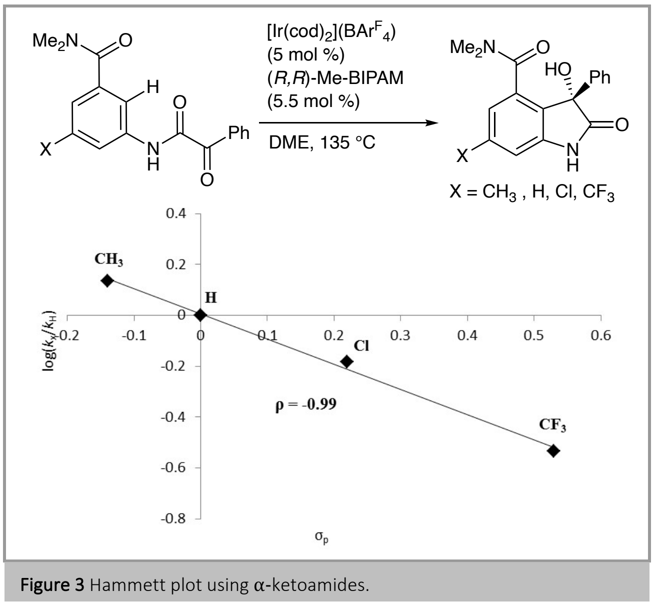


Figure 3 Hammett plot using α-ketoamides.

These experimental and kinetic data suggested that the turnover-limiting step in this reaction was the insertion of a carbonyl group into the aryl-iridium intermediate than to the C–H bond cleavage step.[13b] The catalytic cycle begins with the reaction of Ir/Me-BIPAM with substrate **1** to give the aryl iridium intermediate **b**. The hydroarylation of the carbonyl group gives the iridium alkoxide species **d** through intermediate **c**. Finally, reductive elimination occurs, yielding product **2** and regenerating the catalyst.

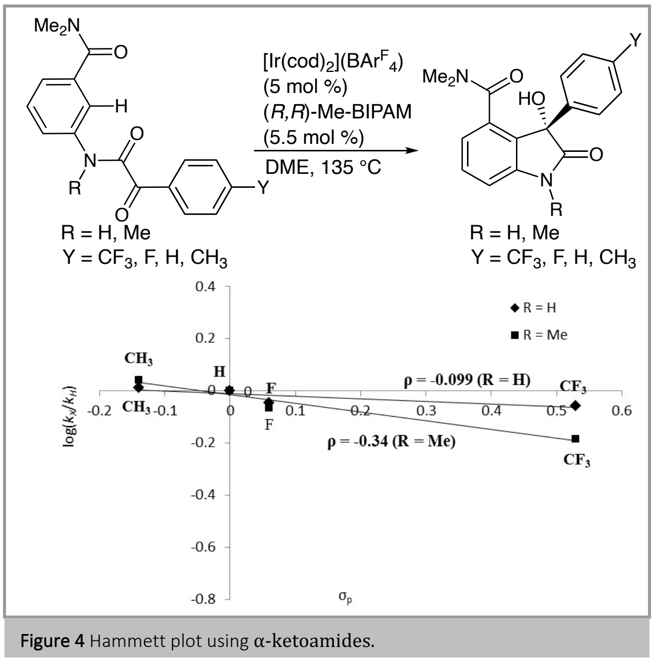
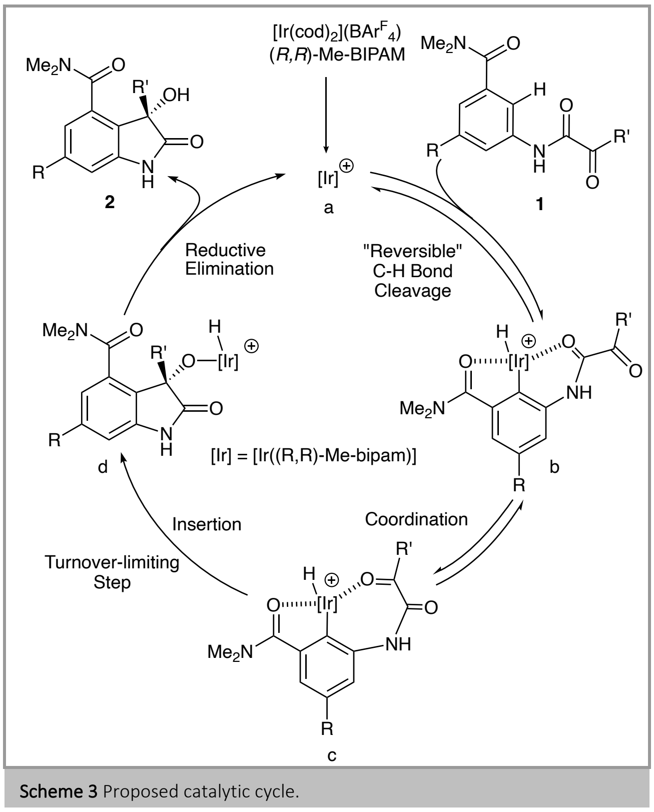


Figure 4 Hammett plot using α-ketoamides.



Scheme 3 Proposed catalytic cycle.

To further investigate the carbonyl insertion process (intermediate **c** in Scheme 3), DFT calculations were performed with B3LYP/LANL2DZ level of theory (Figure 5). At first, the two minimum energy modes of Ar-[Ir((*R,R*)-Me-BIPAM)]-H (**b1** and **b2**) were calculated ($\Delta E_{b1\text{-}b2}$ = 2.64 kcal/mol). Next, the turnover-limiting and stereo-determining step, which is coordinated with the two carbonyl groups (the aryl-iridium intermediate **c** in Scheme 3) were calculated. The conformation **c2** giving the experimentally observed *S* product has a low energy for reaction from the intermediate in which the carbonyl oxygen is coordinated to the iridium center at the *Si*-face after the C–H bond cleavage process. Conversely, coordination at the *Re*-face of the carbonyl group (**c1**) has a high energy than *Si*-face coordination (**c2**) ($\Delta E_{c1\text{-}c2}$ = 3.10 kcal/mol). Thus, the enantioselective insertion to Si-face of the carbonyl group was showed through less steric congestion intermediate **c2**.

3 The highly enantioselective intermolecular hydroarylation of bicycloalkene (Scheme 4)[3c,d]

Although some effort has been made to develop efficient catalytic systems for direct asymmetric intermolecular additions of arenes to alkenes, there have been no reports showing high levels of enantioselectivity, catalytic activity, and generality.[16-19] In 2000, Togni et al. reported [CpIr((*R*)-MeO-BIPHEP)] catalyzed asymmetric hydroarylation of 2-norbornene with benzamide.[20] For asymmetric hydroarylation of 2-norbornene (**7a**) using 2'-methoxyacetophenone (**6a**) giving an ortho-alkylated product (**8a**), we considered the reaction conditions including the iridium precursor, chiral ligand, and solvent (Table 3). Because our previous developed asymmetric hydroarylation of ketones was effectively catalyzed by an [Ir(cod)$_2$](BAr^F$_4$)/bidentate bis(phosphoramidite) (Me-BIPAM) complex, we examined several chiral BIPAM ligands (entries 1-3). The use of (*R,R*)-Me-BIPAM as the ligand gave **8a** in 93% yield with 52% *ee*, and higher *ee* was achieved by changing the linker atom of the linked-BINOL unit from oxygen to nitrogen ((*R,R*)-N-Me-BIPAM, 35% yield, 73% *ee*, entry 2). The use of a sulfur-linked bis(phosphoramidite) ligand ((*R,R*)-S-Me-BIPAM) achieved highest enantioselectivity (82% yield, 88% *ee*, entry 3).

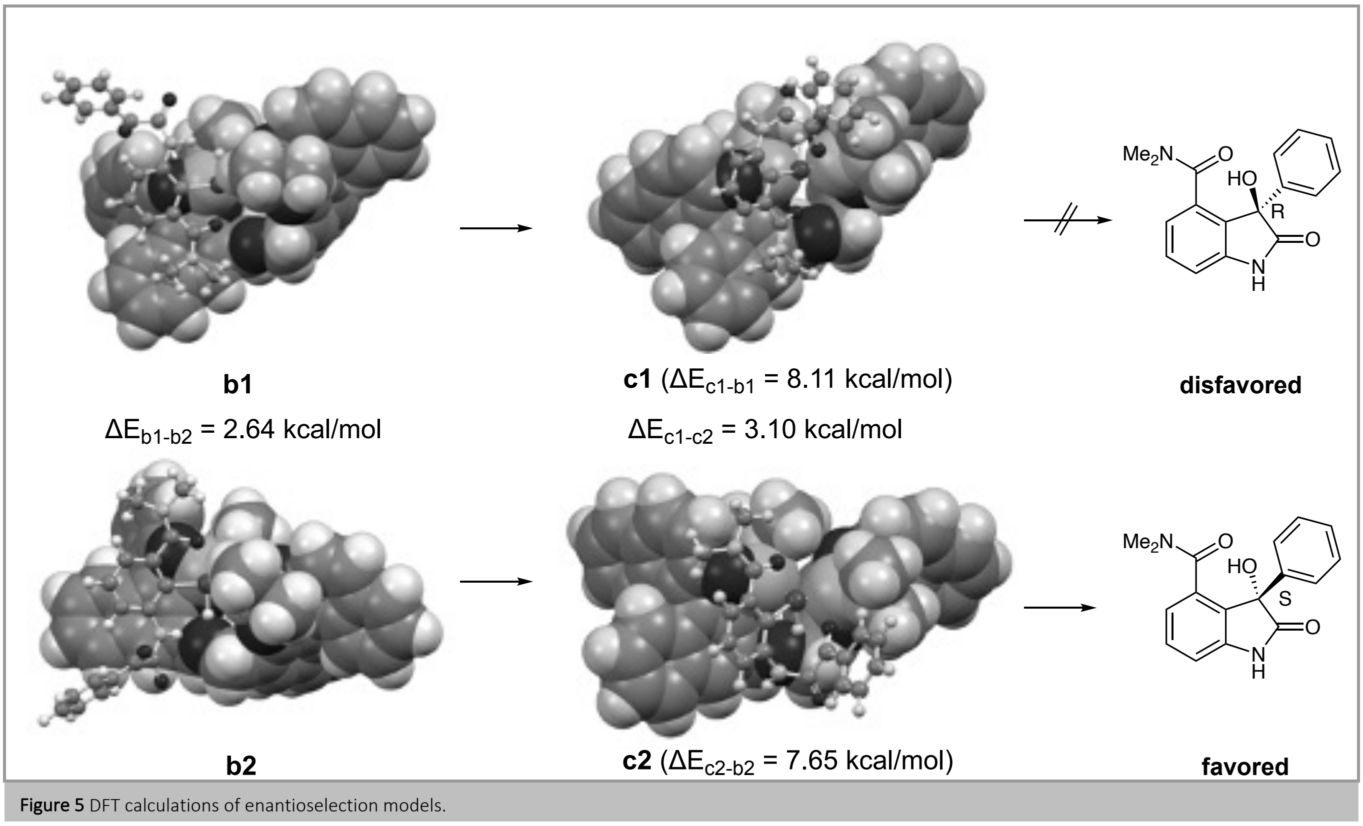
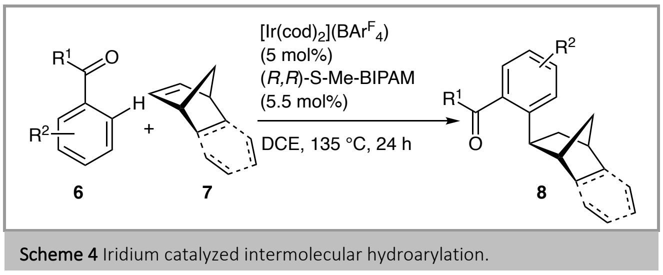
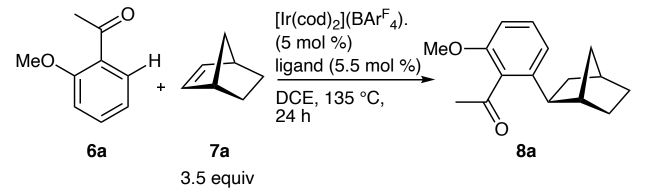


Figure 5 DFT calculations of enantioselection models.



Scheme 4 Iridium catalyzed intermolecular hydroarylation.

Table 3 Optimization of precursors and ligands.

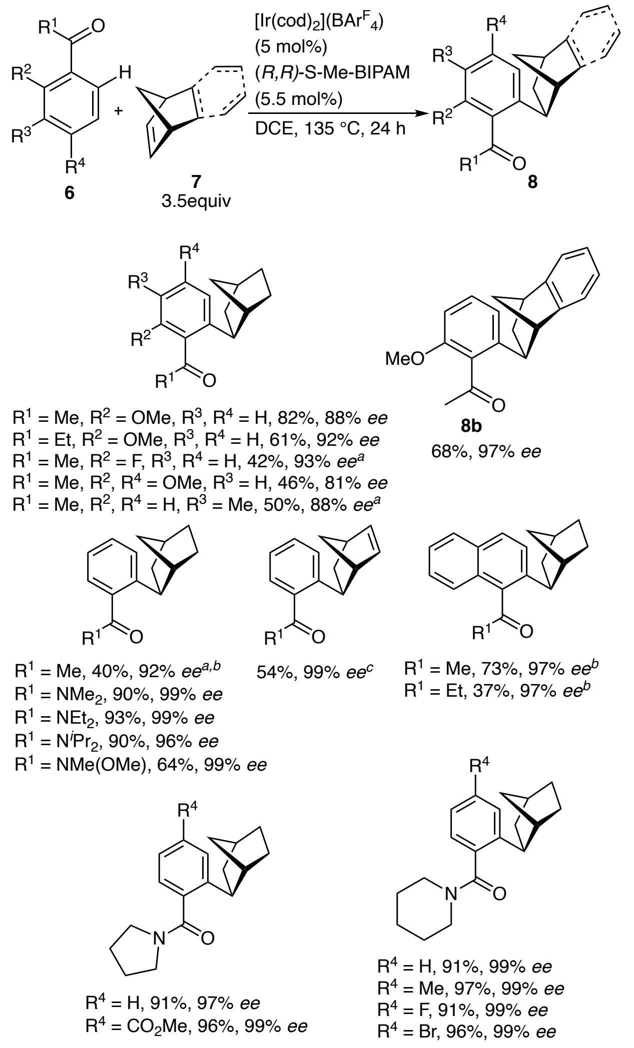


Entry	Ligand	Yield (%)	*ee* (%)
1	(*R,R*)-Me-BIPAM	93	52
2	(*R,R*)-N-Me-BIPAM	35	73
3	(*R,R*)-S-Me-BIPAM	82	88

[a] Reaction conditions: arene (0.25 mmol), iridium catalyst (5 mol%), and ligand(1.1 equiv to Ir) in solvent (1 mL) were stirred for 24 h at 135 °C.

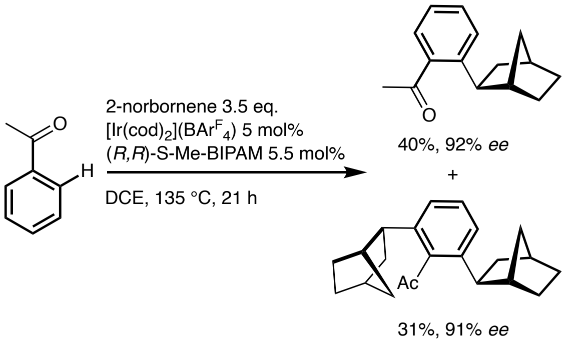
Under the optimized catalytic conditions, we examined the substrate scope for enantioselective hydroarylation of 2-norbornene (Scheme 5). For the hydroarylation using ketone-directing group, various substituents such as OMe, F, Me showed high enantioselectivities. The hydroarylation reactions of 2-norbornene with various benzamides were examined. A range of amide-based directing groups, such as diethyl-, diisopropyl-, and Weinreb-amide was also tolerated and gave the hydroarylated product. In the hydroarylation of acetophenone as a substrate, a mixture of mono- and di-ortho-alkylated products was formed (Equation 4). Pyrrolidine- and piperidine-derived amides also gave desired products, respectively. Para-substituents were tolerated and potentially reactive functional groups such as aryl ester and bromide showed good results. The amide-directed hydroarylation only gave mono-ortho-alkylated product. X-ray diffraction analysis of a single crystal of **8b** showed that the absolute configuration of **8b** is R at C1 and S at C8 and C9.[21] The acetyl group of **8b** was also orthogonal to the phenyl ring for steric hindrance. Amide directing group showed the limited bond rotation by a congested environment. So, the hydroarylation with benzamides could give only mono-ortho-alkylated products (Equation 5).[22]

For the reaction mechanism, we carried out an asymmetric hydroarylation of substrate **9** in the presence of D_2O (10 equiv.) under optimized conditions ((A) in Scheme 6). The reaction gave 35% of the unreacted substrate **9-D** and 64% of product **10-D**. Deuterium incorporation was not showed at the ortho position of the amide group in the substrate. This result showed that C–H bond cleavage occurred in a non-reversible manner before the insertion of alkene. In addition, comparison of the initial rate constants for the addition of normal and deuterated *N,N*-piperidyl benzamide (**11** and **11-D**) to 2-norbornene in separate vessels revealed KIE of 2.08 ((B) in Scheme 6). These results showed that the turnover-limiting step in our developed asymmetric hydroarylation includes the C–H bond cleavage step.[14,15] A catalytic cycle was shown in Scheme 7. We proposed a catalytic cycle involving chelation-assisted C–H bond cleavage, migratory insertion of a bicycloalkene into the Ir–C bond, and C–H bond-forming reductive elimination of the resulting organoiridium species.[15]

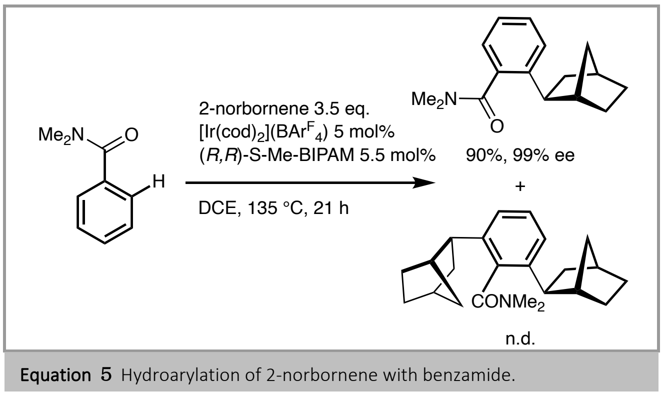


[a] Reaction conditions: 14 (2 equiv), 15 (0.25 mmol), iridium catalyst (5 mol%), and (*R,R*)-S-Me-BIPAM (1.1 equiv to Ir) in DCE (1 mL) was stirred for 24 h at 135 °C. [b] 0.5 mL of DCE were used as solvent. [c] 10 mol% of catalyst was used.

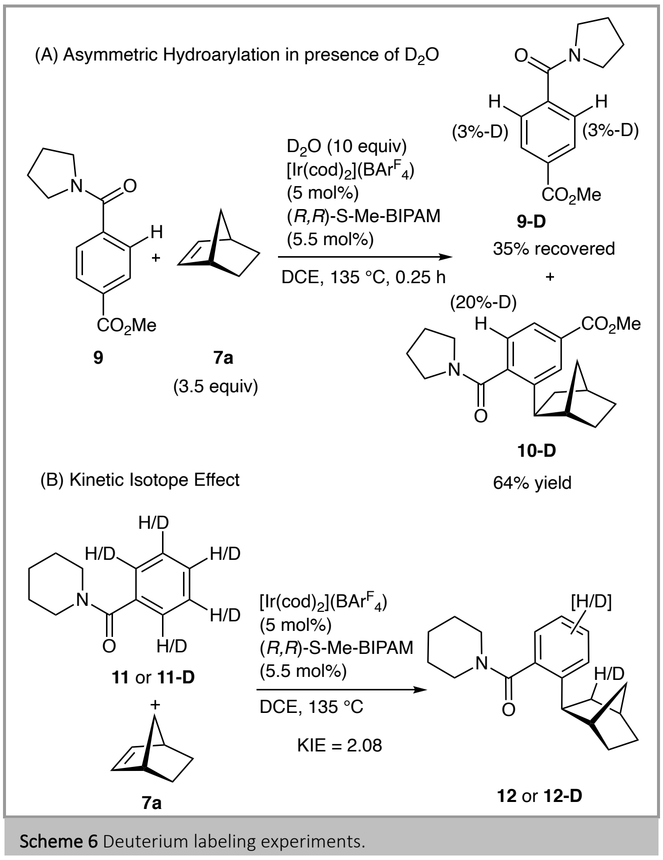
Scheme 5 Substrate scope of asymmetric hydroarylation.



Equation 4 Hydroarylation with unfunctionalized acetophenone.



Equation 5 Hydroarylation of 2-norbornene with benzamide.

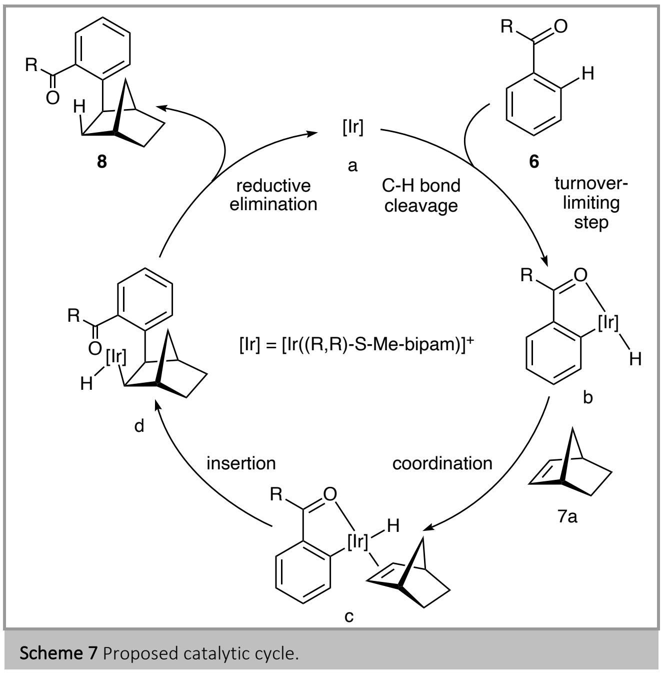


Scheme 6 Deuterium labeling experiments.

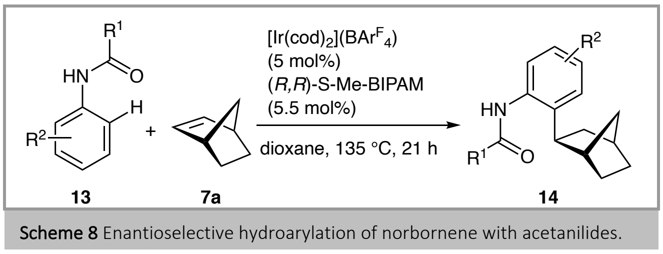
The amide-based DG showed the best performance in our developed reaction compared with the ketone. But, in general, it is difficult to convert tertiary amides to other functional groups.[23] Because aniline derivatives such as acetanilides can be easily transformed to other functional groups compared with amides, we examined an iridium/(*R,R*)-S-Me-BIPAM-catalyzed direct asymmetric alkylation of acetanilides with 2-norbornene (Scheme 8). In 2017, Shibata and co-workers reported cationic iridium/chiral bis(phosphine) catalyzed enantioselective C–H addition of acetanilide to α,β-unsaturated carbonyl compounds in moderate yield with good enantioselectivity.[24]

We examined reaction conditions in the arylation of 2-methylacetanilide **13a** to 2-norbornene (Table 4). When [Ir(cod)$_2$](BAr^F$_4$) is used in dichloroethane (DCE), reaction proceeds in high yield and excellent enantioselectivity (entry 1, 89%, 97% ee). The use of 1,4-dioxane gave the best result (entry 5). (*R,R*)-SO$_2$-Me-BIPAM also showed in good yield with high enantioselectivity. The use of (*R,R*)-Me-BIPAM or (*R,R*)-CH$_2$-Me-BIPAM showed unsatisfactory results.

The scope of aniline derivatives gave the desired products in good yield with high enantioselectivity (Scheme 9). Alkyl substituents such as ethyl, isopropyl and tertiary butyl group on the amide group showed the good results. Furthermore, a broad range of substituents on benzene ring were tolerated. The reaction of 2,3- or 2,4-disubstituted acetanilides with 2-norbornene also gave the products in good yields with high enantioselectivities. In contrast to the reaction of benzamide derivatives, the use of acetanilide only gave the dialkylation product (Equation 6) Thus, the selectivity of mono- or di-alkylation was found to depend on the ease of bond rotation of the directing group. To gain the reaction mechanism, we examined the reaction with D$_2$O in the presence of 2-norbornene. Then 67% deuterium incorporation in C6 position of recovered substrate as shown in Equation 7. This H/D scrambling showed that the C–H activation was reversible. We proposed the similar catalytic cycle for the arylation of acetanilide derivatives as for the benzamide derivatives (Scheme 10).

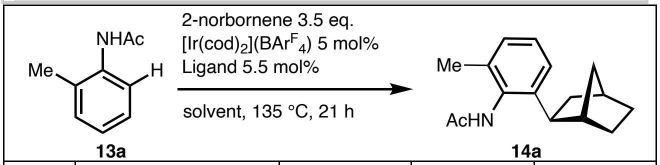


Scheme 7 Proposed catalytic cycle.



Scheme 8 Enantioselective hydroarylation of norbornene with acetanilides.

Table 4 Optimization of reaction conditions.

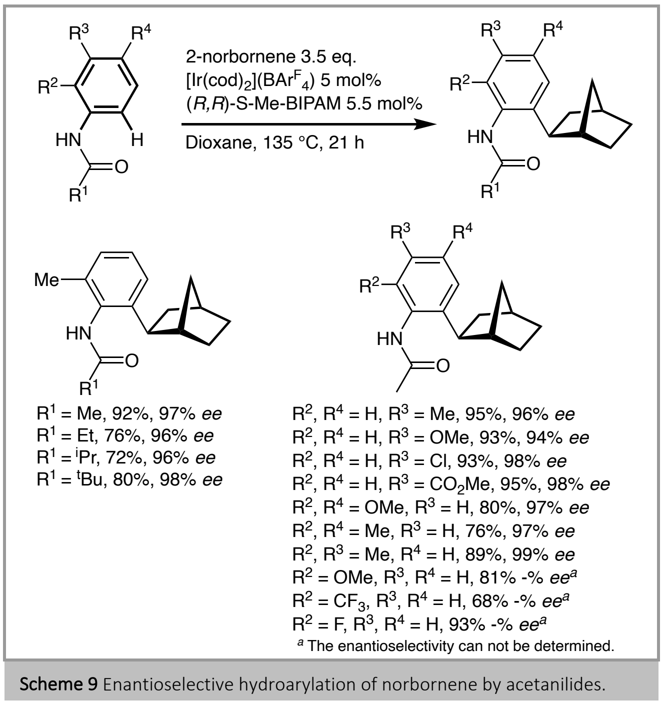


Entry	Ligand	Solvent	Yield (%)	*ee* (%)
1	(*R,R*)-S-Me-BIPAM	DCE	89	97
2	(*R,R*)-S-Me-BIPAM	Toluene	90	93
3	(*R,R*)-S-Me-BIPAM	DME	69	97
4	(*R,R*)-S-Me-BIPAM	THF	71	99
5	(*R,R*)-S-Me-BIPAM	Dioxane	92	97
8	(*R,R*)-Me-BIPAM	DCE	52	73
9	(*R,R*)-SO$_2$-Me-BIPAM	DCE	85	96
10	(*R,R*)-CH$_2$-Me-BIPAM	DCE	75	16

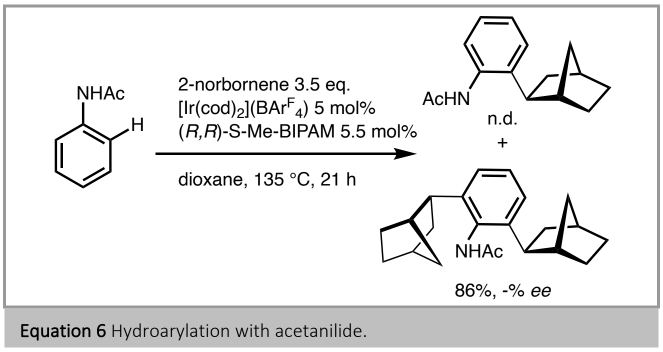
^{a} Reaction conditions: 13a (0.25 mmol), 2-norbornene (3.5 equiv.) iridium catalyst (5 mol%), and (*R,R*)-S-Me-BIPAM (1.1 equiv. to Ir) in solvent, stirred for 21 h at 135 °C.

4 Conclusion

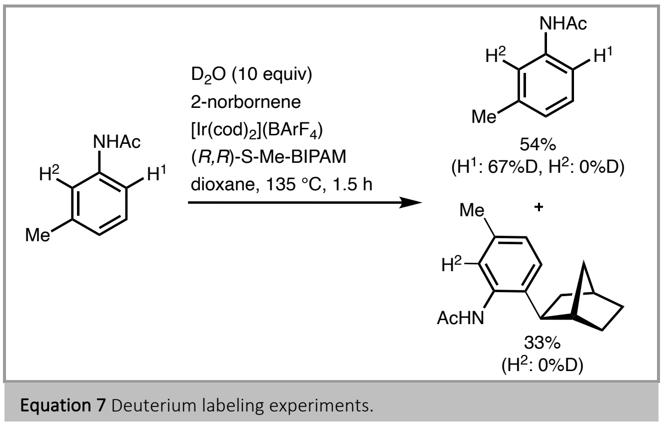
In this account, we summarized our recent efforts to use chiral bidentate phosphoramidites for enantioselective hydroarylation. Using the cationic iridium complex [Ir(cod)$_2$](BAr$^{F}_4$) and the chiral O-linked bidentate phosphoramidite (*R,R*)-Me-BIPAM, enantioselective intramolecular hydroarylation of α–ketoamides gave various types of optically active 3-substituted 3-hydroxy-2-oxindoles in high yields with complete regioselectivity and high enantioselectivities. In the mechanistic studies, all the data showed that carbonyl insertion into aryl-iridium was included in the turnover-limiting step of the catalytic cycle. On the other hand, highly enantioselective cationic iridium-catalyzed hydroarylation of bicycloalkenes was achieved using a newly synthesized sulfur-linked bis(phosphoramidite) ligand (S-Me-BIPAM). The hydroarylation reactions of 2-norbornene with *N,N*-dialkyl benzamide gave the mono-ortho-alkylation products with excellent enantioselectivities. We also developed the highly enantioselective direct arylation of 2-norbornene using aniline derivatives by cationic Ir/(*R,R*)-S-Me-BIPAM complex.



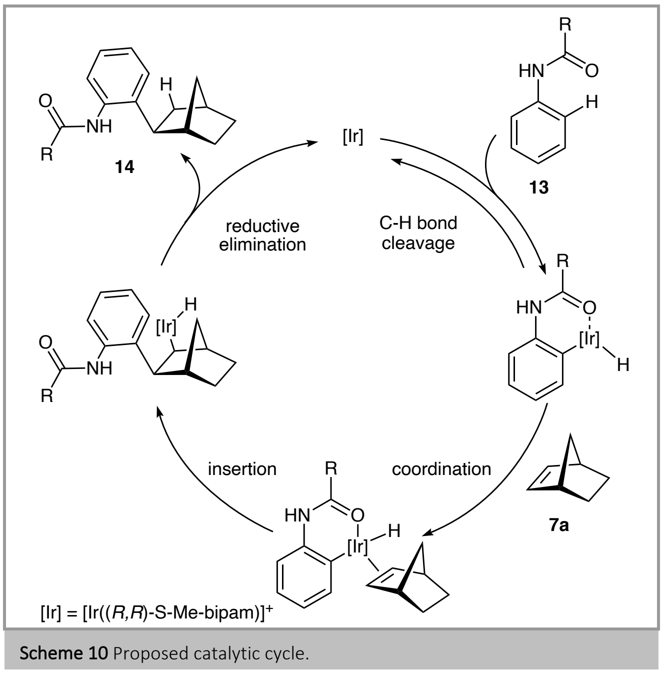
Scheme 9 Enantioselective hydroarylation of norbornene by acetanilides.



Equation 6 Hydroarylation with acetanilide.



Equation 7 Deuterium labeling experiments.



Scheme 10 Proposed catalytic cycle.

References

(1) (a) Kakiuchi, F.; Kochi, T.; *Synthesis,* **2008**, 3013. (b) Satoh, T.; Miura, M. *Chem. Eur. J.* **2010**, *16*, 11212. (c) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.,* **2010**, *110*, 624. (d) Colby, D. A.; Tsai, A. S.; Bergman, R. G.; Ellman, J. A. *Acc. Chem. Res.* **2012**, *45*, 814. (e) Patureau F. W.; Wencel-Delord, J.;. Glorius, F. *Aldrichimica Acta* **2012**, *45*, 31. (f) Song, G.; Wang, F.; Li, X. *Chem. Soc. Rev.* **2012**, *41*, 3651. (g) Arockiam, P. B.; Bruneau, C.; Dixneuf, P. H. *Chem. Rev.* **2012**, *112*, 5879. (h) Yan, G.; Wu, X.; Yang, M. *Org. Biomol. Chem.* **2013**, *11*, 5558. (i) Yang, L.; Huang, H. *Chem. Rev.* **2015**, *115*, 3468.

(2) (a) Giri, R.; Shi, B.-F.; Engle, K. M.; Maugel, N.; Yu, J.-Q. *Chem. Soc. Rev.* **2009**, *38*, 3242. b) Yang, L.; Huang, H. *Catal. Sci. Technol.* **2012**, *2*, 1099. (c) Cramer, N. *Chimia,* **2012**, *66*, 869. (d) Wencel-Delord, J.; Colobert, F. *Chem. Eur. J.* **2013**, *19*, 14010. (e) Pan, S. Shibata, T. *ACS Catal.* **2013**, *3*, 704. (f) Motevalli, S.; Sokeirik, Y.; Ghanem. A. *Eur. J. Org. Chem.* **2016**, 1459. (g) Newton, C. G.; Wang, S.-G.; Oliveira, C. C.; Cramer, N. *Chem. Rev.* **2017**, *117*, 8908. (h) Dong, Z.; Ren, Z.; Thompson, S. J.; Xu, Y. Dong, G. *Chem. Rev.* **2017**, *117*, 9333. (i) Hummel, J. R.; Boerth, J. A.; Ellman, J. A. *Chem. Rev.* **2017**, *117*, 9163. (j) Woźniak, Ł.; Tan, J.-F.; Nguyen, Q.-H.; Madron du Vigné, A.; Smal, V.; Cao, Y.-X.; Cramer, N. *Chem Rev.* **2020**, *120*, 10516. (k) Achar, T. K.; Maiti, S.; Jana, S.; Maiti, D. *ACS Catal.* **2020**, *10*, 13748. (l) Aldhous, T. P.; Chung, R. W. M.; Dalling, A. G.; Bower, J. F. *Synthesis* **2021**, *53*, 2961.

(3) (a) Shirai, T.; Ito, H.; Yamamoto, Y. *Angew. Chem. Int. Ed.* **2014**, *53*, 2658. (b) Shirai, T.; Yamamoto, Y. *Organometallics* **2015**, *34*, 3459. (c) Shirai, T.; Yamamoto, Y. *Angew. Chem. Int. Ed.* **2015**, *54*, 9894. (d) Shirai, T.; Yamamoto, Y. *Asian J. Org. Chem.* **2018**, *7*, 1054. (e) Shirai, T.; Yamamoto, Y. *J. Synth. Org. Chem. Jpn.* **2018**, *76*, 601.

(4) For transition-metal/BIPAM-catalyzed asymmetric hydroarylation of C=O, C=N with arylboronic acids, see (a) Yamamoto, Y.; Miyaura, N. *Wako Organic Square* **2007**, *20*, 2. (b) Hydrogenation: Kurihara, K.; Yamamoto, Y.; Miyaura, N. *Tetrahedron Lett.,* **2009**, *50*, 3158. (c) Yamamoto, Y. *J. Org. Synth. Soc. Jpn.* **2013**, *71*, 716.

(5) (a) Berthon-Gelloz, G.; Hayashi. T. In *Boronic Acids: Preparation and Applications in Organic Synthesis, Medicine and Materials, Second Edition*; Hall, D. G. (Ed.); Wiley-VHC Verlag GmbH, Weinheim, **2011**, 263. (b) Tian, P.; Dong, H.-Q. Lin, G.-Q. *ACS Catal*. 2012, **2**, 95. (c) Edwards, H. J.; Hargrave, J. D.; Penrose, S. D.; Frost, C. G.; *Chem. Soc. Rev.* **2010**, *39*, 2093. (d) Hargrave, J. D.; Allen, J. C.; Frost, C. G. *Chem. Asian J.* **2010**, *5*, 386.

(6) (a) Yamamoto, Y.; Kurihara, K.; Sugishita, N.; Oshita, K.; Piao, D.; Miyaura, N. *Chem. Lett.* **2005**, *34*, 1224. (b) Kurihara, K.; Sugishita, N.; Oshita, K.; Piao, D.-G.; Yamamoto, Y.; Miyaura, N. *J. Organomet. Chem.* **2007**, *692*, 428. (c) Yamamoto, Y.; Kurihara, K.; Takahashi, Y.; Miyaura, N. *Molecules* **2013**, *18*, 14.

(7) (a) Kurihara, K.; Yamamoto, Y.; Miyaura, N. *Adv. Synth. Catal.* **2009**, *351*, 260. (b) Yamamoto, Y.; Takahashi, Y.; Kurihara, K.; Miyaura, N. *Aust. J. Chem.* **2011**, *64*, 1477. (c) Kato, N.; Shirai, T.; Yamamoto, Y. *Chem. Eur. J.* **2016**, *22*, 7739.

(8) (a) Yamamoto, Y. Kurihara, K. Miyaura, N. *Angew. Chem. Int. Ed.* **2009**, *48*, 4414. (b) Yamamoto, Y.; Shirai, T.; Watanabe, M.; Kurihara, K.; Miyaura, N. *Molecules* **2011**, *16*, 5020. (c) Yamamoto, Y.; Shirai, T.; Miyaura, N. *Chem. Commun.* **2012**, *48*, 2803 (2012); (d) Yamamoto, Y.; Yohda, M.; Shirai, T.; Ito, H.; Miyaura, N. *Chem. Asian J.* **2012**, *7*, 2446. (e) Yohda, M.; Yamamoto, Y. *Org. Biomol. Chem.* **2015**, *13*, 10874. (f) Yohda, M.; Yamamoto, Y. *Tetrahedron: Asymmetry* **2015**, *26*, 1430.

(9) For synthesis of linked BINOL, see (a) Matsunaga, S.; Das, J.; Roels, J.; Vogl, E. M.; Yamamoto, N.; Iida, T.; Yamaguchi, K.; Shibasaki, M. *J. Am. Chem. Soc.* **2000**, *122*, 2252. (b) Kumagai, N.; Matsunaga, S.; Kinoshita, T.; Harada, S.; Okada, S.; Sakamoto, S.; Yamaguchi, K.; Shibasaki, M. *J. Am. Chem. Soc.* **2003**, *125*, 2169. (c) He, L.; Chen, X.-H.; Wang, D.-N.; Luo, S.-W.; Zhang, W.-Q.; Yu, J.; Ren, Lei.; Gong, L.-Z. *J. Am. Chem. Soc*. **2011**, *133*, 13504.

(10) (a) Jia, Y.-X.; Kündig, E. P. *Angew. Chem. Int. Ed.* **2009**, *48*, 1636. (b) Perry, A.; Taylor, R. J. K. *Chem. Commun.* **2009**, 3249. (c) Ueda, S.; Okada, T.; Nagasawa, H. *Chem. Commun.* **2010**, *46*, 2462. (d) Klein, J. E. M. N.; Perry, A.; Pugh, D. S.; Taylor, R. J. K. *Org. Lett.* **2010**, *12*, 3446. (e) Wu, T.; Mu, X.; Liu, G. *Angew. Chem. Int. Ed.* **2011**, *50*, 12578. (f) Mu, X.; Wu, T.; Wang, H.-Y.; Guo, Y.-l.; Liu, G. *J. Am. Chem. Soc.* **2012**, *134*, 878. (g) Moody, C. L.; Franckevičius, V.; Drouhin, P.; Klein, J. E. M. N.; Taylor, R. J. K. *Tetrahedron Lett.* **2012**, *53*, 1897. (h) Zhang, H.; Chen, P.; Liu, G. *Synlett* **2012**, *23*, 2749.

(11) Tsuchikama, K.; Hashimoto, Y.-K.; Endo, K.; Shibata, T. *Adv. Synth. Catal.* **2009**, *351*, 2850.

(12) (a) Shiota, H.; Ano, Y.; Aihara, Y.; Fukumoto, Y.; Chatani, N. *J. Am. Chem. Soc.* **2011**, *133*, 14952. (b) Ye, B.; Donets, P. A.; Cramer, N. *Angew. Chem. Int. Ed.* **2014**, *53*, 507.

(13) CCDC 980114 The data can be obtained free charge from The Cambridge Crystallographic Data Center www.ccdc.cam.ac.uk/data_request/cif.

(14) (a) Li, Y.; Zhang, X.-S.; Chen, K.; He, K.-H.; Pan, F.; Li, B.-J.; Shi, Z.-J.*Org. Lett.* **2012**, *14*, 636. (b) Sharma, S.; Park, E.; Park, J.; Kim, I. S. *Org. Lett.* **2012**, *14*, 906. (c) Wang, G.-W.; Zhou, A.-X.; Wang, J.-J.; Hu, R.-B.; Yang, S.-D. *Org. Lett.* **2013**, *15*, 5270.

(15) Simmons, E. M;. Hartwig, J. F. *Angew. Chem. Int. Ed.* **2012**, *51*, 3066.

(16) (a) Nishimura, T.; Ebe, Y.; Hayashi, T. *J. Am. Chem. Soc.* **2015**, *137*, 5899 (2015); (b) Nagamoto, M.; Ebe, Y.; Nishimura, T. *J. Org. Synth. Soc. Jpn.* **2017**, *75*, 421.

(17) For asymmetric hydroheteroarylation of alkenes, see (a) Wilson, R. M.; Thalji, R. K.; Bergman, R. G.; Ellman, J. A. *Org. Lett.* **2006**, *8*, 1745. (b) Rech, J. C.; Yato, M.; Duckett, D.; Ember, B.; LoGrasso, P. V.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2007**, *129*, 490. (c) Tsai, A. S.; Wilson, R. M.; Harada, H.; Bergman, R. G.; Ellman, J. A. *Chem. Commun.* **2009**, 3910. (d) Wentzel, M.; T. Reddy, V. J.; Hyster, C. J.; Douglas, T. K. *Angew. Chem. Int. Ed.* **2009**, *48*, 6121. (e) Pan, S.; Ryu, N.; Shibata, T. *J. Am. Chem. Soc.* **2012**, *134*, 17474. (f) Sevov, C. S.; Hartwig, J. F. *J. Am. Chem. Soc.* **2013**, *135*, 2116. (g) Song, G.; O, W. W. N.; Hou, Z. *J. Am. Chem. Soc.* **2014**, *136*, 12209. (h) Lee, P.-S.; Yoshikai, N. *Org. Lett.* **2015**, *17*, 22. (i) Filloux, C. M.; Rovis, T. *J. Am. Chem. Soc.* **2015**, *137*, 508.

(18) For asymmetric intermolecular hydroarylations, see (a) Kakiuchi, F.; Gendre, P. L.; Yamada, A.; Ohtaki, H.; Murai, S. *Tetrahedron: Asymmetry* **2000**, *11*, 2647. (c) Shibata, T.; Shizuno, T. *Angew. Chem. Int. Ed.* **2014**, *53*, 5410.

(19) For asymmetric intramolecular hydroarylations, see (a) Thalji, R. K.; Ellman, J. A.; Bergman, R. G. *J. Am. Chem. Soc.* **2004**, *126*, 7192. (b) Harada, H.; Thalji, R. K.; Bergman, R. G.; Ellman, J. A. *J. Org. Chem.* **2008**, *73*, 6772.

(20) Aufdenblatten, R.; Diezi, S.; Togni, A. *Monatsh. Chem.* **2000**, *131*, 1345. For asymmetric intermolecular hydroarylations of 2-norbornene, see (a) Dorta, R.; Togni, A. *Chem. Commun*. **2003**, 760. (b) Tsuchikama, K.; Kasagawa, M.; Hashimoto, Y.; Endo, K.; Shibata, T. *J. Organomet. Chem.* **2008**, *693*, 3939.

(21) CCDC 1400933 The data can be obtained free charge from The Cambridge Crystallographic Data Center www.ccdc.cam.ac.uk/data_request/cif.

(22) Crisenza, G. E. M.; McCreanor, N. G.; Bower, J. F. *J. Am. Chem. Soc.* **2014**, *136*, 10258.

(23) Conversion of Amide: (a) Hie, L.; Nathel, N. F. F.; Shah, T. K.; Baker, E. L.; Hong, X.; Yang, Y.-F.; Liu, P.; Houk, K. N.; Garg, N. K. *Nature*, **2015**, *524*, 79. (b) Volkov, A.; Tinnis, F.; Stagbrand, T.; Trillo, P.; Adolfsson, H. *Chem. Soc. Rev.* **2016**, *45*, 6685.

(24) Acetanilide: Shibata, T.; Michino, M.; Kurita, H.; Tahara, Y.-K.; Kanyiva, K. S. *Chem. Eur. J.* **2017**, *23*, 88.