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Rollover Cyclometalation Pathway in Rhodium Catalysis: Dramatic NHC Effects in the C−H Bond Functionalization

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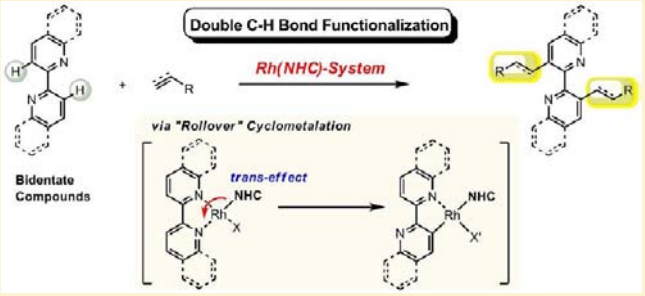
Supporting Information

ABSTRACT: Organometallic chelates are readily obtained upon coordination of metal species to multidentate ligands. Because of the robust structural nature, chelation frequently serves as a driving force in the molecular assembly and chemical architecture, and they are used also as an efficient catalyst in numerous reactions. Described herein is the development of a Rh(NHC) catalytic system for the hydroarylation of alkenes and alkynes with 2,2′-bipyridines (bipy) and 2,2′-biquinolines; the most representative chelating molecules. Initially generated (bipy)Rh(NHC) chelates become labile because of the strong *trans*-effect of *N*-heterocyclic carbenes, thus weakening a rhodium−pyridyl bond, which is *trans* to the bound NHC. Subsequent rollover cyclometalation leads to the C−H bond activation, eventually giving rise to double functionalization of chelate molecules. Density functional calculations are in good agreement with our mechanistic proposal based on the experimental data. The present study elucidated for the first time the dramatic NHC effects on the rollover cyclometalation pathway enabling highly efficient and selective bisfunctionalization of 2,2′-bipyridines and 2,2′-biquinolines.



INTRODUCTION

A recent research emphasis on the transition metal-catalyzed direct functionalization of stable C−H bonds has opened a new era of synthetic chemistry due to its great simplicity in designing a synthetic route to complex molecules when compared to the conventional methods, in which prefunctionalized substrates are required. As a result, synthetic chemists can now be benefited from utilizing the C−H bond activation strategy to develop straightforward and environmentally benign chemical processes.[1] Significant advances have been made in recent years to demonstrate that well designed catalytic systems (ML_n) can activate poorly reactive C−H bonds to generate their L_mM−C organometallic intermediates.[2] In order to obtain such reactive C−M bonds more efficiently and selectively, a range of strategies have been practiced with the judicious choice of metal species. Among those approaches, the most effective way to activate the desired C−H bond is the introduction of directing groups at the proximity such as amides, esters, or various heterocycles (Figure 1a).[3] This strategy can reliably designate the position of reacting C−H bonds driven by the favorable formation of 5- or 6-membered metalacyclic intermediates.[4] This route to generate metalacycles in situ has been extensively utilized for the subsequent C−C, C−N, C−O and C−X (X: halides) bond formation.[5]

On the other hand, when organic compounds contain more than one coordinating heteroatom, formation of stable multidentate metal chelates is highly favored upon the coordination of metal center to the multiple heteroatoms. Representatively, 2,2′-bipyridine (bipy) or 1,10-phenanthroline (phen) readily forms stable chelates (bipy)ML_n or (phen)ML_n (Figure 1b). As a result, catalytic functionalization on the molecular backbone of those ligating compounds has been considered to be extremely difficult due to the robust nature of

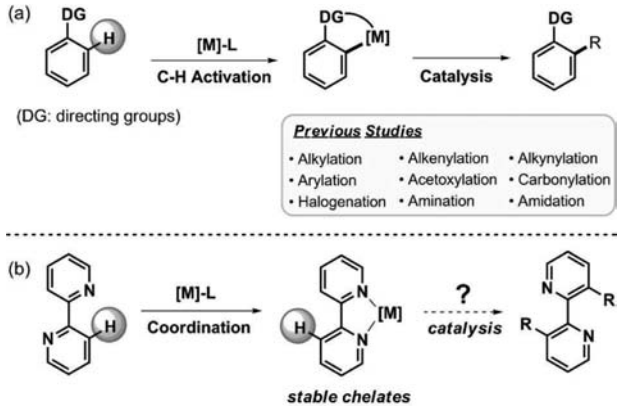


Figure 1. (a) Classical cyclometalation strategy for the *ortho*-C−H bond functionalization. (b) Formation of stable chelates inhibiting a cyclometalation pathway.

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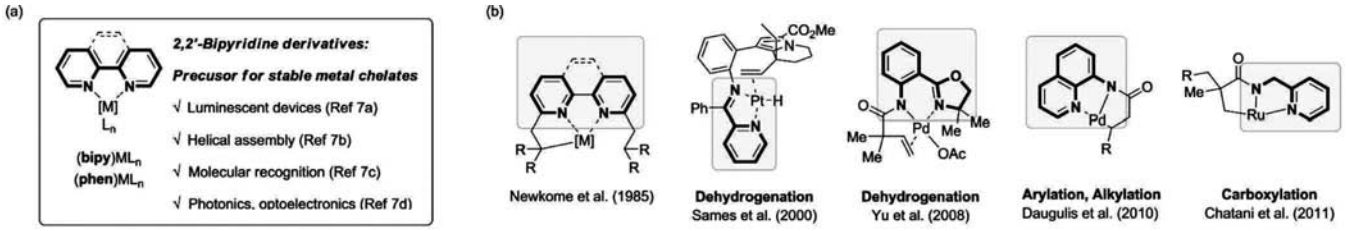
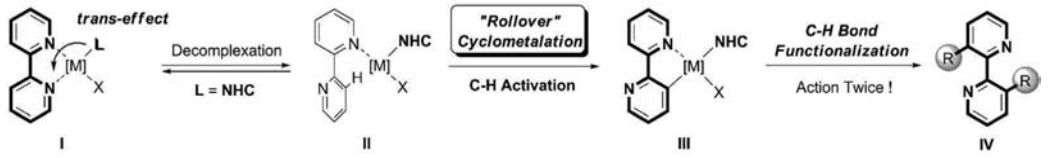


Figure 2. Bidentate metal chelates: (a) chelates of 2,2′-bipyridine and phenanthroline derivatives utilized in various areas of chemistry; (b) bidentate chelates used as a directing group in organic transformations.

Scheme 1. Present Study of the Catalytic Utilization of Rollover Cyclometalation Pathway Initiated by *trans*-Effect



the chelation bonds. Indeed, it was found that a wide range of compounds bearing bipyridyl, 2-aminomethylpyridyl, or 8-aminoquinolinyl unit reacts with metal species to furnish metal chelates, which guide site-selective activation of most accessible C−H bonds (Figure 2).[6] The facile formation of metal chelates often serves as a driving force in molecular assembly and chemical architecture.[7] In addition, an excellent redox ability of these metal chelates has been well harnessed in the development of efficient catalytic reactions.[8]

The fact that cyclometalation of 2,2′-bipyridine and analogues is extremely difficult to achieve especially in a catalytic manner can be ascribed to the difficulty of the initial decomplexation of stable metal chelates, which step is essential for the subsequent rotation and C−H bond activation to maintain the cyclometalation cycle. In this context, we hypothesized that when a strong σ-donating ligand (L) such as *N*-heterocyclic carbene (NHC) is bound to a metal center of (bipy)MLX (**I**), it may exert a high *trans*-effect to weaken a metal−pyridyl bond *trans* to L (Scheme 1).[9,10] It was anticipated that this strong *trans*-effect of L allows for the facile decomplexation of **I** leading to **II**, thus enabling subsequent rotation around the bipyridyl axis and then C−H bond activation eventually to afford a metalacycle species **III**. This "rollover" cyclometalation pathway was previously investigated *mainly in a stoichiometric manner*, wherein scope of the studies was rather limited to the isolation of the rollover cyclometalated complexes,[11] but following functionalizations have been rare.[12] Although the Rh-catalyzed double functionalization of 2,2′-bipyridine was briefly reported by Miura et al., only limited substrate scope was presented under harsh reaction conditions.[12a] Therefore, the successful development of a *catalytic rollover cyclometalation* approach would be highly inspiring to open a new avenue in transition metal catalysis giving rise to doubly functionalized compounds such as **IV**, which can still maintain the chelating ability. Upon securing such an efficient and selective catalytic system, a significant progress will be anticipated to follow in the areas of catalysis, molecular assembly and materials architecture.

In order to develop a process based on the catalytic rollover cyclometalation pathway of 2,2′-bipyridine derivatives, the following aspects were initially envisaged to consider: (i) search for suitable ligands displaying an optimal *trans*-effect to make a *trans* metal−pyridyl bond highly labile, (ii) optimization of a metal catalyst system to facilitate the C−H bond activation, (iii) facile insertion of functional groups into the metalacycles, and (iv) no inhibitory effects of the first introduced functional group toward the second rollover cyclometalation process of monofunctionalized 2,2′-bipyridine intermediates. Recently, we have developed the highly efficient rhodium(NHC)-catalyzed C−C, C−N, C−O bond formation reaction,[13] and it was found that NHCs were especially effective for the facile generation of key rhodacycle intermediates[13a,c] presumably due to the strong σ-donating ability and unique steric environment of NHCs.[14] Along with these studies, we hypothesized that the nature of NHCs might be beneficial to trigger a rollover cyclometalation of metal-ligated 2,2′-bipyridines *most desirably in a catalytic manner*, thus enabling eventual double functionalizations.[15] Herein, we report the realization of this novel concept of rollover cyclometalation of 2,2′-bipyridine and its analogues by developing Rh(NHC)-catalyzed bishydroarylation of alkenes and alkynes.[16] Mechanistic studies and computational calculations support our proposal of the dramatic NHC effects exerting *trans*-influence. A synthetic application of utilizing chiral organocatalysts, accessible through this study, is also presented.

RESULTS AND DISCUSSION

Optimization of Reaction Conditions. At the outset of our studies, we screened optimal conditions of a Rh-catalyzed hydroarylation of 2,2′-bipyridine (**1a**) with 3,3-dimethyl-1-butene (**2**, Table 1). When a NHC precursor **L1** (SIMes·HCl) was used in combination with Rh(acac)$_3$ catalyst and *t*-BuONa base, a monohydroarylated adduct **3a** was obtained as a major product along with a doubly hydroarylated compound **4a** after 2 h at 130 °C albeit in a low combined yield (entry 1). A full conversion was observed with prolonged reaction time leading to a bishydroarylated adduct **4a** in major (entry 2). Both rhodium catalyst and base were essential to the reaction progress (entries 3, 4). To our delight, when IMes·HCl (**L2**), an unsaturated analogue of **L1**, was employed, reaction efficiency and selectivity were significantly increased even with lower loading of catalyst and base in shorter reaction time (entries 5, 6). It needs to be mentioned that *catalytic amounts of t-BuONa base were sufficient*, still giving rise to an excellent degree of the reaction efficiency (entry 6), thus greatly improving functional group tolerance. Bases other than *t*-

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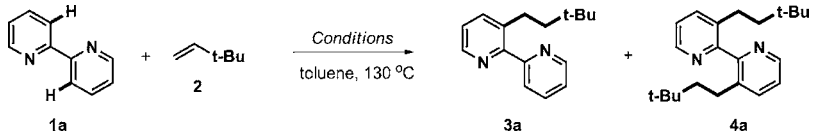
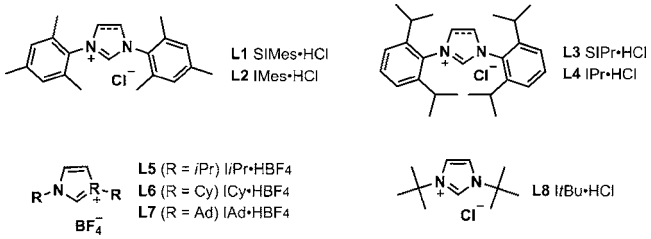
Table 1. Optimization of Reaction Conditions[a]



1a 2 3a 4a

entry	catalyst (mol %)	ligand (mol %)	base (equiv)	time (h)	3a (%)[b]	4a (%)[b]
1	$Rh(acac)_3$ (10)	**L1** (10)	*t*-BuONa (2.1)	2	26	9
2	$Rh(acac)_3$ (10)	**L1** (10)	*t*-BuONa (2.1)	12	24	57
3	–	**L1** (10)	*t*-BuONa (2.1)	12	–	–
4	$Rh(acac)_3$ (10)	**L1** (10)[c]	–	12	–	–
5	$Rh(acac)_3$ (3)	**L2** (3)	*t*-BuONa (2.1)	2	–	94
6	$Rh(acac)_3$ (3)	**L2** (3)	*t*-BuONa (0.3)	2	–	97
7	$Rh(acac)_3$ (3)	**L2** (3)	Cs_2CO_3 (0.3)	2	– (16)[d]	– (5)[d]
8	$Rh(acac)_3$ (3)	PPh_3 (3)	*t*-BuONa (2.1)	2	8	1
9	$Rh(acac)_3$ (3)	PCy_3 (3)	*t*-BuONa (2.1)	2	5	<1
10	$Rh(acac)_3$ (3)	**L3** (3)	*t*-BuONa (2.1)	2	3	<1
11	$Rh(acac)_3$ (3)	**L4** (3)	*t*-BuONa (2.1)	2	4	<1
12	$Rh(acac)_3$ (3)	**L5** (3)	*t*-BuONa (2.1)	2	<1	–
13	$Rh(acac)_3$ (3)	**L6** (3)	*t*-BuONa (2.1)	2	<1	–
14	$Rh(acac)_3$ (3)	**L7** (3)	*t*-BuONa (2.1)	2	<1	–
15	$Rh(acac)_3$ (3)	**L8** (3)	*t*-BuONa (2.1)	2	10	3
16	$[Rh(cod)Cl]_2$ (1.5)	**L2** (3)	*t*-BuONa (0.3)	2	–	91
17	Rh(cod)(IMes)Cl (3)	–	*t*-BuONa (0.3)	2	<1	93
18	$Pd(OAc)_2$ (3)	**L2** (3)	*t*-BuONa (2.1)	2	–	–
19	$Ni(acac)_2$ (3)	**L2** (3)	*t*-BuONa (2.1)	2	–	–
20	$PtCl_2$ (3)	**L2** (3)	*t*-BuONa (2.1)	2	–	–

[a]Reaction conditions: 2,2′-bipyridine (**1a**, 0.3 mmol), **2** (1.5 mmol) in toluene (0.4 mL) at 130 °C. [b]NMR yield (internal standard: 1,1,2,2-tetrachloroethane). [c]Isolated carbene (SIMes) was used. [d]Rh(cod)(IMes)Cl (3 mol %) was used instead of $Rh(acac)_3$/**L2**.



BuONa were not effective to the reaction (e.g., entry 7), and the use of phosphine ligands instead of NHC gave poor conversion and selectivity (entries 8, 9). As predicted, structure of NHC ligands critically influenced the reaction efficiency, and NHCs (**L3**–**L8**) bearing modified electronic and/or steric environment displayed only negligible reactivity (entries 10–15). Interestingly, a Rh(I)-IMes species, prepared either in situ or separately, displayed similar reactivity and selectivity when compared to the corresponding Rh(III) catalyst (entries 16, 17), implying that a catalytically active Rh(I) species is generated even in case of employing Rh(III) precursors.[17] Despite this result, we decided to use $Rh(acac)_3$ as a catalyst precursor in subsequent studies because of the ease of handling and stability of the complex to the air and moisture. On the other hand, the use of transition metals other than rhodium species was completely ineffective under the employed reactions (entries 18–20).

Reaction Scope. Under the above optimized conditions (0.03 equiv of $Rh(acac)_3$/**L2** ligand and 0.3 equiv of *t*-BuONa base at 130 °C for 2 h), substrate scope of the bishydroarylation reaction was next investigated (Table 2). A wide range of aliphatic terminal alkenes were doubly reacted at the 3,3′-position of 2,2′-bipyridine in excellent yields (**4a**–**4c**). The hydroarylation was highly selective at the terminal olefins in the presence of an internal double bond (**4d**). It was interesting to note that the internal olefin was slightly isomerized under the employed conditions to imply that a rhodium hydride species might be generated in situ during the course of the catalytic pathway (vide infra). Terminal olefins substituted with benzyl or cyclohexyl groups underwent the desired reaction in high yields (**4e** and **4f**, respectively). Alkenes bearing easily removable hydroxy-protecting groups such as benzyl or silyl moieties were readily reacted without causing a problem to give the desired bishydroarylated products (**4g** and **4h**). While both vinyl- and allylsilanes were facile reactants, the latter one required 1 equiv of *t*-BuONa base to obtain a satisfactory product yield (**4i** and **4j**, respectively). As predicted, 4-vinyl-1-cyclohexene was reacted exclusively at the terminal double bond (**4k**). On the other hand, alkenes containing strained internal double bonds such as norbornene were smoothly reacted (**4l**).

Substituted bipyridine derivatives were also reacted with alkenes in excellent efficiency and selectivity. For instance, 5,5′-dimethyl- and 6,6′-dimethyl-2,2′-bipyridine underwent the desired reaction with 3,3-dimethyl-1-butene to furnish the corresponding doubly hydroarylated products in high yields (**4m** and **4n**, respectively).

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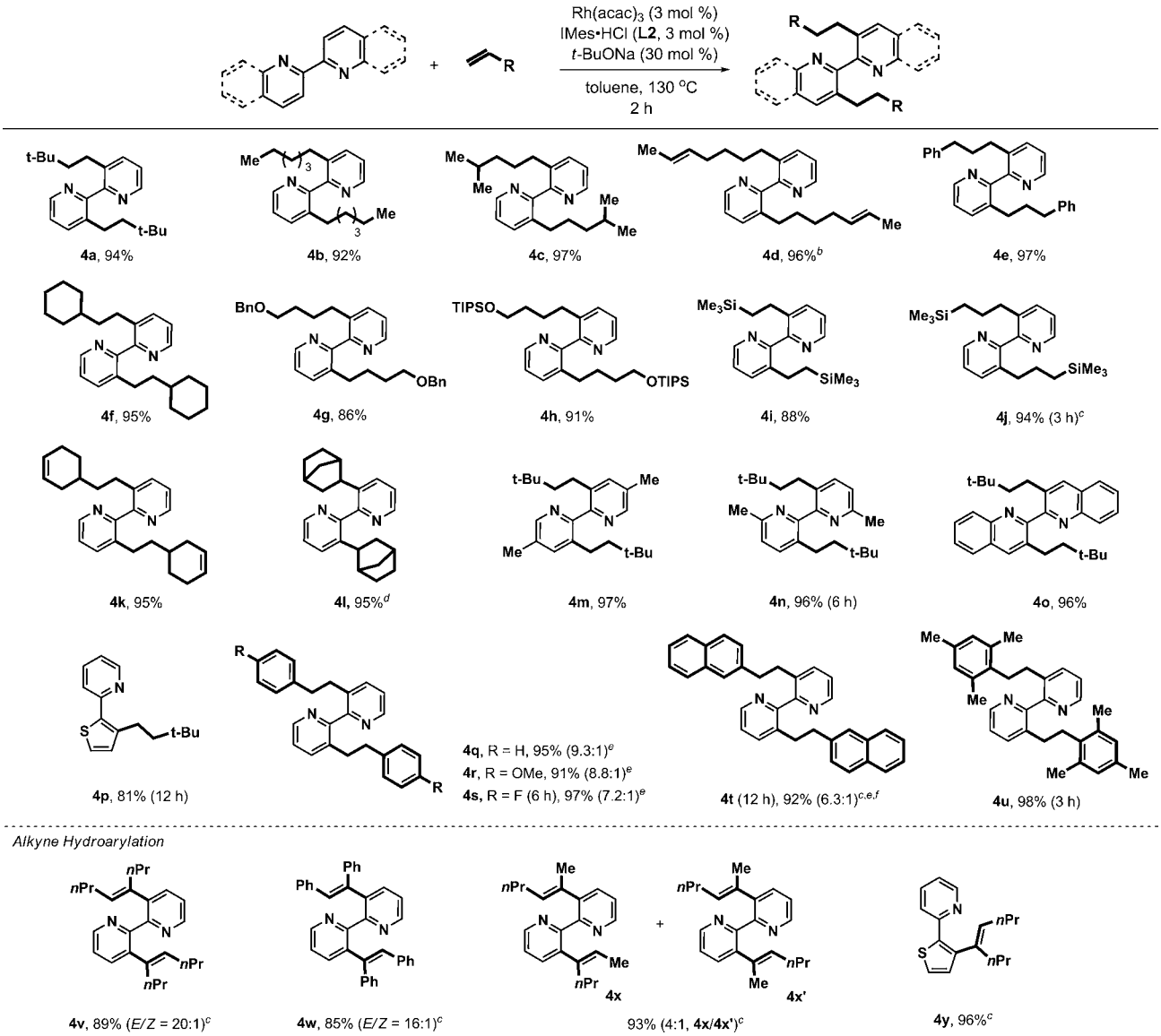
Table 2. Scope of the Rh(NHC)-Catalyzed Bishydroarylation of 2,2′-Bipyridine Derivatives[a]



[a]Reaction conditions: substrates (0.3 mmol), olefins (5 equiv), $Rh(acac)_3$ (3 mol %), IMes·HCl (3 mol %), *t*-BuONa (30 mol %) in toluene (0.4 mL) at 130 °C for 2 h. Isolated yields are indicated. [b]Yield was determined after hydrogenation. [c]1 equiv of base was used. [d]Mixture of *endo*- and *exo*-products. [e]Ratio of linear and branched product in parentheses, and only major products are shown. [f]3 equiv of olefin was used.

In addition to 2,2′-bipyridines, 2,2′-biquinoline also underwent the olefin bishydroarylation in excellent yield (**4o**), thus significantly expanding the synthetic utility of the present protocol (vide infra). It needs to be addressed that the hydroarylation took place exclusively at the 3,3′-position of this substrate without forming any isomeric side products (e.g., reaction at the 8,8′-position). This result is in complete accord with the initially postulated "rollover" cyclometalation pathway. Interestingly, hydroarylation of 2-(thiophen-2-yl)pyridine occurred exclusively at the thiophenyl ring under the present catalytic conditions (**4p**). Such regioselectivity is exactly the same as in a stoichiometric, *not catalytic*, study of rollover cyclometalation of 2-(thiophen-2-yl)pyridine, which was previously reported by Nonoyama et al.[18]

In contrast to hydroarylation of aliphatic alkenes, which proceed exclusively in an *anti*-Markovnikov manner leading to only linear products, reactions with aryl olefins took place to furnish a mixture of linear and branched hydroarylation products, but favoring the former isomers. For example, a reaction of 2,2′-bipyridine with styrene under the present conditions afforded an excellent yield of bishydroarylated isomeric products in favor of a linear over branched one with 9.3:1 ratio (**4q**, herein only major product is shown). This trend was similarly observed with other vinylarenes regardless of electronic variation (**4r**, **4s** and **4t**). In stark contrast, a complete control of regioselectivity was attained when 2-vinylmestylene was subjected to the conditions, in which a linear bishydroarylated compound was obtained as a single product in excellent yield (**4u**) to suggest that a steric factor is highly important for the control of selectivity.

Next, we envisioned that the Rh(NHC)-catalyzed rollover cyclometalation process could also be applied to hydroarylation of alkynes.[12a,20g,h] Indeed, we were pleased to find that 4-octyne was readily reacted with 2,2′-bipyridine to afford a doubly alkenylated product **4v** in high yield with the use of 1 equiv of *t*-BuONa base. It is noteworthy that the reaction was highly

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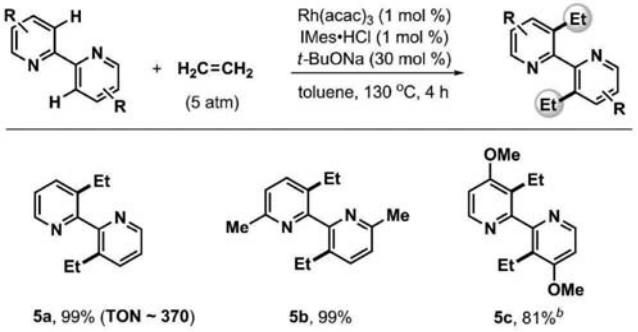
Table 3. Bishydroarylation with Gaseous Ethylene[a]



[a]Conditions: substrates (2 mmol), ethylene (5 atm), $Rh(acac)_3$ (1 mol %), IMes·HCl (1 mol %) and *t*-BuONa (30 mol %) in toluene (4 mL). [b]Substrate (1 mmol), $Rh(acac)_3$ (3 mol %), IMes·HCl (3 mol %) and *t*-BuONa (1 equiv) in toluene (4 mL) at 130 °C for 36 h.

stereoselective in that a *syn*-addition pathway was mainly operative leading to an *E*-isomer as a major product. A similar result was also observed in the reaction of diphenylacetylene (**4w**). On the other hand, hydroarylation of unsymmetric alkynes such as 2-hexyne resulted in a mixture of regioisomers (**4x**). As in the alkene hydroarylation of 2-(thiophen-2-yl)pyridine (**4p**), an alkyne was similarly monohydroarylated at the thienyl side leading to **4y** in high yield.

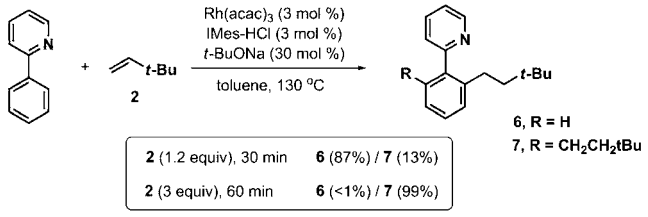
It needs to be indicated that Miura et al. briefly reported the Rh-catalyzed *ortho*-alkenylation of aromatic *N*-heterocycles including 2,2′-bipyridine as mentioned in the Introduction.[12a] In their procedure, terminal silylacetylenes were employed as the only type of alkynes using a catalyst system consisting of $[RhCl(cod)]_2$ and PPh_3 at 160 °C. Although this previous report offered an inspiring possibility to introduce an olefinic functional group into heterocycles, it also revealed some critical aspects such as limited substrate scope and harsh reaction conditions. Notably, as can be seen below in the mechanistic description, we believe that the introduction of NHC ligand dramatically improves the activity and selectivity of the resultant Rh-NHC catalyst system, thus solving most of the problems associated with the use of the Rh-PR_3 system.

We were pleased to observe that the developed bishydroarylation procedure could readily be applied to gaseous alkenes, still maintaining excellent reaction efficiency (Table 3). For instance, when 2,2′-bipyridines were allowed to react with gaseous ethylene (5 atm), the corresponding doubly ethylated bipyridine products were obtained in quantitative yields even with a reduced catalyst loading (1 mol %). Turnover number of the rhodium catalyst was measured to reach up to 370 on the basis of one hydroarylation conversion (**5a**). This excellent performance was proved to be general with respect to other substrate variants. For instance, 6,6′-dimethyl-2,2′-bipyridine was diethylated in a quantitative yield (**5b**). Notably, sterically congested 4,4′-dimethoxy-2,2′-bipyridine was also diethylated at the 3,3′-position in acceptable yield (**5c**).

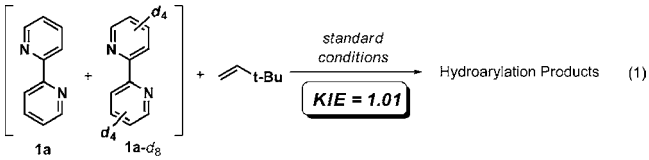
As anticipated, the present hydroarylation procedure was applied to 2-phenylpyridine in a similar manner (Scheme 2).[19−21] A notable aspect in this case was that the degree of reaction progress, obtainable products accordingly, could be controlled upon choosing the stoichiometry of employed alkenes. Indeed, whereas a monohydroarylation adduct (**6**) was obtained in major by using 1.2 equiv of olefin, a bishydroarylated product **7** was isolated quantitatively by using 3 equiv of olefin.

Mechanistic Studies on the Present Reaction. To investigate the key aspect of the C−H bond cleavage process in

Scheme 2. Hydroarylation of 2-Phenylpyridine

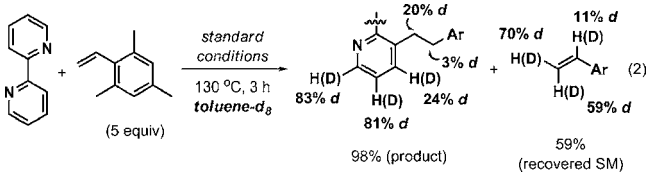


the present Rh(NHC)-catalyzed hydroarylation reaction, we first performed a kinetic isotope effect (KIE) study. An intermolecular competition reaction between **1a** and **1a**-d_8 revealed no detectable isotopic effect (eq 1), suggesting that



the C−H bond cleavage is not involved in the rate-determining stage. This result is in sharp contrast to a precedent *stoichiometric* process,[22] in which KIE was observed to be 2.8 in a Pt-mediated "rollover" cyclometalation of *N*-(2′-pyridyl)-7-azaindole. However, it needs to be mentioned that a negligible KIE value was also observed in a range of transition metal catalyzed hydroarylation reactions, wherein reductive elimination was claimed to be the rate-determining step.[19e,20b,21a,b]

As discussed above, while the present hydroarylation was highly selective for terminal alkenes, internal acyclic double bonds were observed to be partially isomerized to attest the intermediacy of a rhodium hydride species (Table 2, **4d**). Moreover, when a hydroarylation reaction was carried out in a deuterated toluene solvent, a significant extent of deuterium incorporation took place at both the bipyridyl backbone and alkyl part of the product (eq 2). This scrambling result can be



explained by assuming that a rhodium hydride, which will be generated by the reversible oxidative addition of the rhodium

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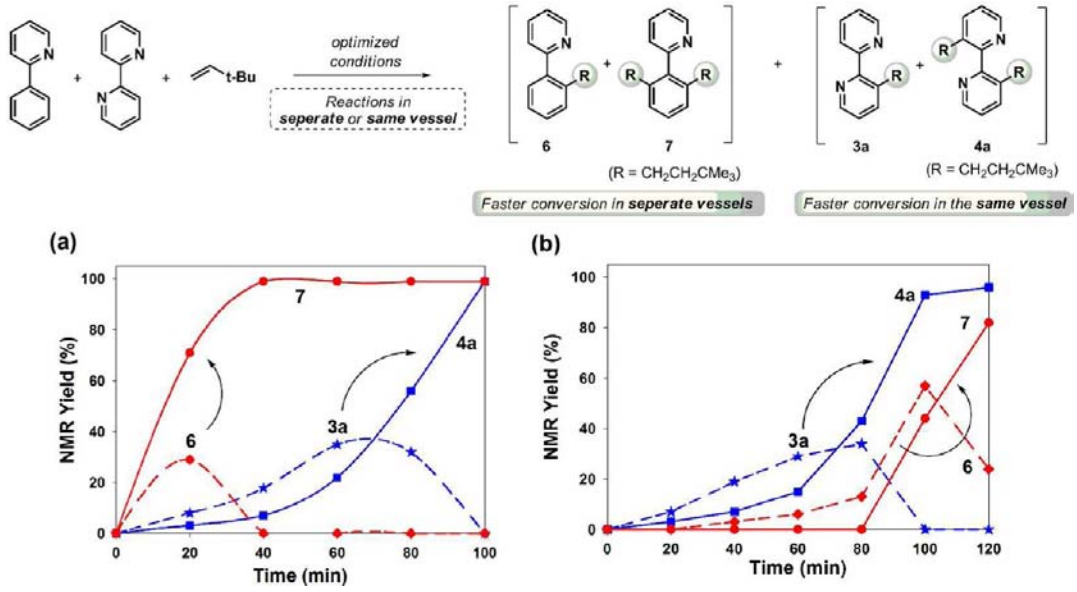


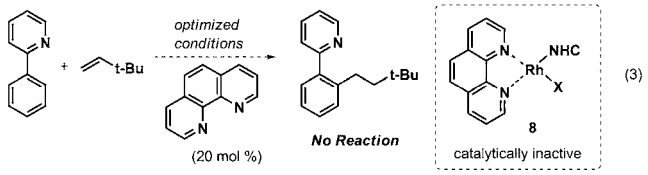
Figure 3. Reaction profiles between 2,2′-bipyridine and 2-phenylpyridine. (a) Reaction in separate vessels. (b) Reaction in the same vessel.

center to 2,2′-bipyridine, is exchanged reversibly with toluene-d_8 solvent to provide a rhodium deuteride species as seen in the precedent literature.[23] Accordingly, it is assumed that an olefin insertion of the rhodium-hydride(deuteride) species and subsequent β-hydride elimination should be reversible on the basis of the fact that deuterium scrambling occurred significantly at the double bond of recovered alkenes (eq 2).[24]

It was interesting to note that the hydroarylation rate was significantly different between 2-phenylpyridine and 2,2′-bipyridine depending the employed conditions. When each substrate was reacted *in a separate vessel*, 2-phenylpyridine was rapidly consumed to reach a full conversion within 30 min giving rise to a doubly alkylated product **7** in quantitative yield (Figure 3a). It was evident from the reaction profile that the bishydroarylation product **7** was formed sequentially via a monohydroarylated adduct **6**. On the other hand, 2,2′-bipyridine reacted noticeably slowly when compared to 2-phenylpyridine, taking more than 100 min to get a full conversion giving a doubly alkylated product **4a** also via a monohydroarylated species **3a**.

However, quite intriguingly, this reactivity pattern was completely reversed when two substrates were allowed to react competitively *in the same vessel*. Under these conditions, 2,2′-bipyridine started the reaction first while hydroarylation of 2-phenylpyridine did not occur until when 2,2′-bipyridine was consumed by about 50% (Figure 3b). This observation indicates that the reaction of 2-phenylpyridine was significantly retarded by the presence of bidentate compounds, herein 2,2′-bipyridine and its hydroarylated products being **3a** and **4a**.[25] A similar inhibitory effect was observed when hydroarylation of 2-phenylpyridine was tried in the presence of substoichiometric 1,10-phenanthroline (eq 3). No conversion was observed in this case, strongly implying that, as reported previously,[26] a highly stable chelate like **8** was generated first being catalytically inactive.

DFT Calculations. In order to obtain additional insights into the mechanistic details, we performed the density functional calculations using a model reaction of ethylene hydroarylation with 2,2′-bipyridine. Geometry optimization was performed using B3LYP functional,[27] and a single point energy



calculation was performed using B3LYP-D3.[28] We used the Stuttgart relativistic small-core effective core-potential (SRSC-ECP) basis[29] for Rh atom and 6-31G* all electron basis for all other main group elements. To test the effect of adding f-polarization function for Rh, we also used the Def2-TZVP basis[30] for Rh and 6-311G** for other elements. Both basis sets yielded similar results for the bipyridine case,[31] justifying the use of smaller SRSC and 6-31G* basis. Gibbs free energy was corrected by the frequency calculation. All calculations were performed using the Q-CHEM quantum chemistry package.[32]

In accordance with our experimental results, a rhodium complex Rh(O-*t*-Bu)(IMes)(bipy) was selected as a catalytically active species entering into the catalytic cycle. Prior to studying a full catalytic cycle, an equilibrium structure of that species was first investigated. At the outset of our studies, we postulated that the key rollover cyclometalation pathway will be triggered by a strong *trans*-effect of a NHC ligand, which weakens a metal−pyridyl bond positioned *trans* to NHC. Indeed, our calculations for the bond length, bond energy, and bond activation energy for the rollover decomplexation step all support this postulate (Figure 4): (i) the bond distance l_1 of the *trans* Rh−N bond relative to NHC (IMes in this case) is longer than l_2 of the corresponding *cis* bond by 0.037 Å, (ii) the *trans* Rh−N bond energy is smaller (weaker) than the *cis* counterpart by 7.6 kcal/mol, and (iii) the activation energy to rupture this *trans* Rh−N bond is smaller (easier) than that for the *cis* Rh−N bond by 9.0 kcal/mol.[11e] The calculated *trans*/*cis* bond length difference for the present system is within the range of previously reported values (0.03−0.09 Å) obtained from other types of metal complexes involving the similar *trans*-influence.[9c]

For comparison, we also considered a PPh_3 ligand (Figure 4b) and analyzed the same equilibrium properties of the Rh−N bonds in Rh(O-*t*-Bu)(PPh_3)(bipy). We found that substituting

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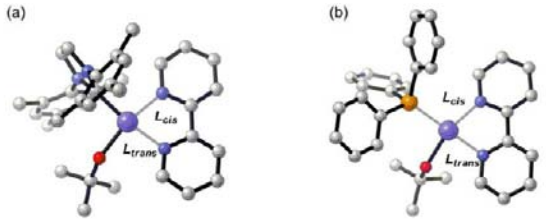


Ligand	L_{trans} (Å)	L_{cis} (Å)	ΔL (Å)	BE_{trans}	BE_{cis}	$\Delta G^{\ddagger}_{trans}$ [a]	$\Delta G^{\ddagger}_{cis}$ [a]
IMes	2.088	2.051	0.037	14.6	22.2	16.8	25.8
PPh_3	2.085	2.072	0.013	20.6	19.7	23.8	30.8

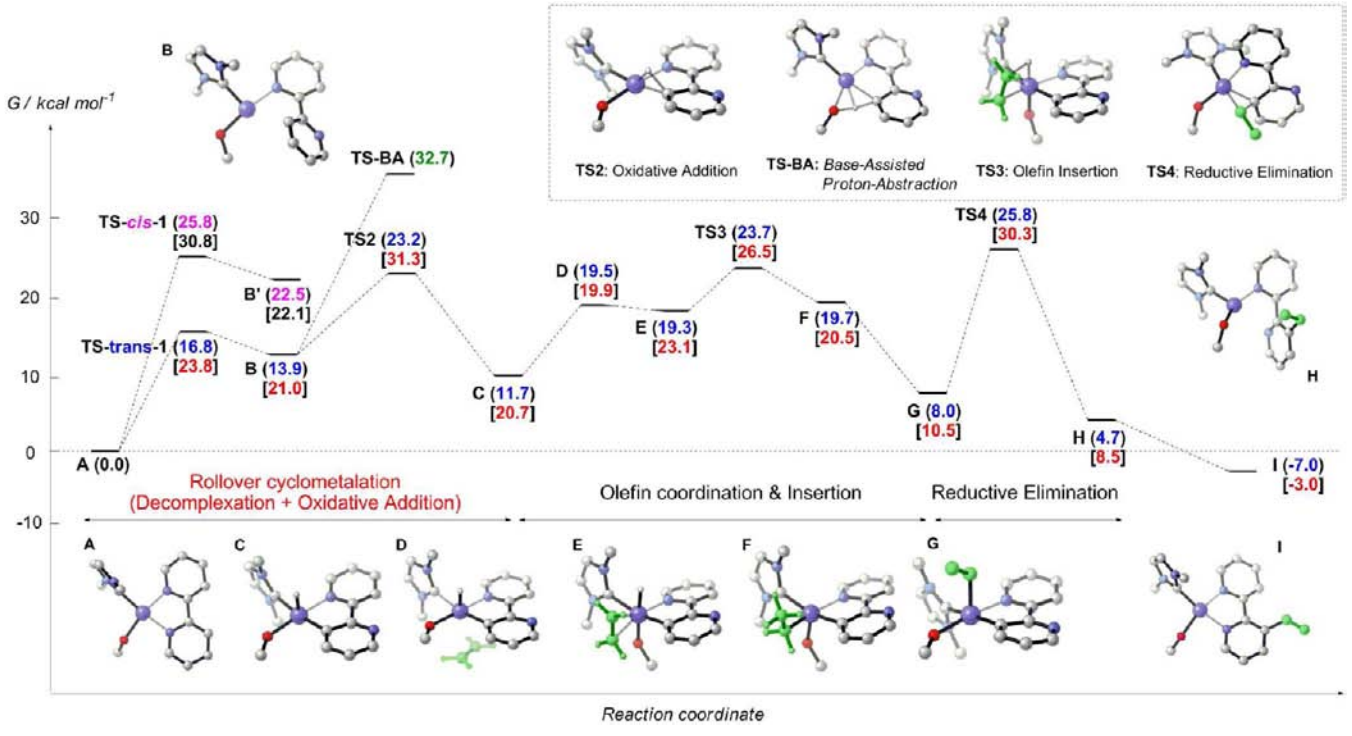
Figure 4. Equilibrium structure of Rh-bipyridine complexes: (a) Rh(O-*t*-Bu)(IMes)(bipy); (b) Rh(O-*t*-Bu)(PPh_3)(bipy). The ΔG values are in kcal/mol. [a]The activation energy of the initial decomplexation step.

IMes with the phosphine ligand leads to smaller *trans*/*cis* bond length difference (PPh_3: 0.013 Å vs IMes: 0.037 Å), a much higher bond energy for the *trans* Rh−N bond (PPh_3: 20.6 vs IMes: 14.6 kcal/mol), and a higher activation barrier for breaking the *trans* Rh−N bond (PPh_3: 23.8 vs IMes: 16.8 kcal/mol). These calculations clearly show that a much lesser *trans*-effect and a more difficult rollover decomplexation process are displayed with PPh_3 relative to IMes. This ligand change from IMes to PPh_3, however, does not significantly alter the properties of the corresponding *cis* Rh−N bond (Figure 4).

Scheme 3 depicts the calculated lowest energy path for the postulated catalytic cycle. As described above, the first step required for the formation of a monodentate rhodium complex **B** involves an endothermic bond rupture of the stable chelate Rh-bipyridyl bond where the strong σ-donating NHC ligand (IMes herein) is believed to help weakening the *trans* Rh−N bond relative to NHC. The C−H bond is then cleaved via the oxidative addition to generate a Rh-hydride species **C**. In this C−H bond activation step, a base-assisted proton abstraction route[33] was also studied, but it yielded a much higher activation barrier, 32.7 kcal/mol as compared to 23.2 kcal/mol of the direct oxidative addition path, hence not considered further.[34] The observation that an internal double bond in substrates was partially isomerized during the course of hydroarylation reaction can be attributed to the in situ formation of a rhodium hydride, and this experimental result also supports the oxidative addition pathway in the C−H bond activation in accord with the calculations. This oxidative addition step is assumed to be reversible on the basis of the deuterium scrambling data (eq 2) and the partial olefin isomerization. Complexation with ethylene (**D**) and subsequent structural reorganization (**E**) will be followed to give a *syn*-geometry being suitable for the olefin insertion process. Ethylene insertion occurs relatively easily via a transition state **TS3** to form **F**, which subsequently rearranges to a stable rhodium-ethyl species **G**. For reasons similar to the reversible formation of **C**, this ethylene insertion into the rhodium hydride species (**D**−**F**) is postulated to proceed reversibly.[23,24] The final reductive elimination of Rh(III)(IMes)(O-*t*-Bu)(ethyl)(bipy) complex **G** then has the highest barrier of 25.8 kcal/mol, marginally higher than the initial rollover cyclometalation step (23.2 kcal/mol), followed by recomplexation to deliver the Rh-(monoethylated)-bipyridine species **I**. Obviously, species **I** will continue the same reaction sequence: decomplexation, rollover cyclometalation, olefin insertion, and then reductive elimination to complete the second alkylation.

As shown in the calculated reaction profile (Scheme 3), changing a ligand from NHC (IMes, energy values in blue) to

Scheme 3. Energy Profile of the Rh-Catalyzed Hydroarylation Reaction of 2,2′-Bipyridine with Ethylene Using IMes (Round Bracket in Blue) and PPh_3 (Square Bracket in Red) Ligand at the B3LYP-D3/6-31G(d) Level (IMes and *t*-BuO^- Are Shown a Simpler Way for Clarity)



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phosphine (PPh_3, energy values in red) significantly increases the rollover cyclometalation barrier. This overall barrier of rollover cyclometalation can be further decomposed to the following terms: decomplexation, complexation (backward of decomplexation), and oxidative addition. When we compared each term, the major contribution of ligand effect was lowering the initial decomplexation, while energetics of other steps are largely unchanged. This comparison indicates that *one of the key roles of NHC ligand is to facilitate the critical rollover process* (Figure 5).[35] These DFT results are consistent with the low

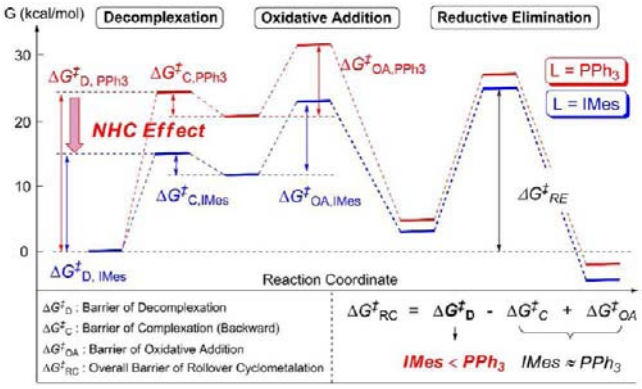
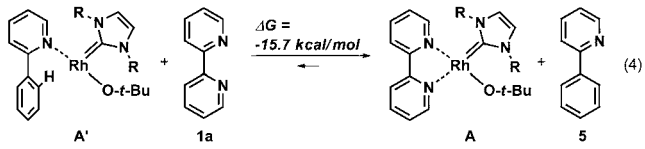


Figure 5. Schematic diagram for the NHC effect on the catalytic hydroarylation.

reactivity and selectivity experimentally observed with the Rh-phosphine catalyst system (Table 1, compare entries 5 and 8). Although a full examination of all employed ligands for our theoretical calculations is beyond the scope of the present study, a comparison between IMes and PPh_3 suggests that the initial rollover cyclometalation process may be a key factor being responsible for the observed dramatic variations of reactivity and selectivity depending on the ligands tested (Table 1).

The observation that the hydroarylation rate of 2,2′-bipyridine was much slower than that of 2-phenylpyridine in a separate vessel as shown in Figure 3a was explained also by the DFT calculations. While hydroarylation of 2,2′-bipyridine requires a decomplexation step of an initially formed ligated complex leading to C−H bond cleavage with a significant activation barrier (16.8 kcal/mol, Scheme 3), the reaction of 2-phenylpyridine does not include such a rollover step. This difference is reflected into to a net barrier of 25.8 kcal/mol to reach **TS4** (turnover frequency determining transition state, TDTS)[36] for 2,2′-bipyridine, but the TDTS for 2-phenylpyridine is only 19.6 kcal/mol (Figure S3 in the Supporting Information) and hence much faster. Results of the competition experiments (Figure 3) can be reasoned if we compare the relative binding affinity of 2-phenylpyridine and 2,2′-bipyridine toward the rhodium metal center (eq 4). The calculations show

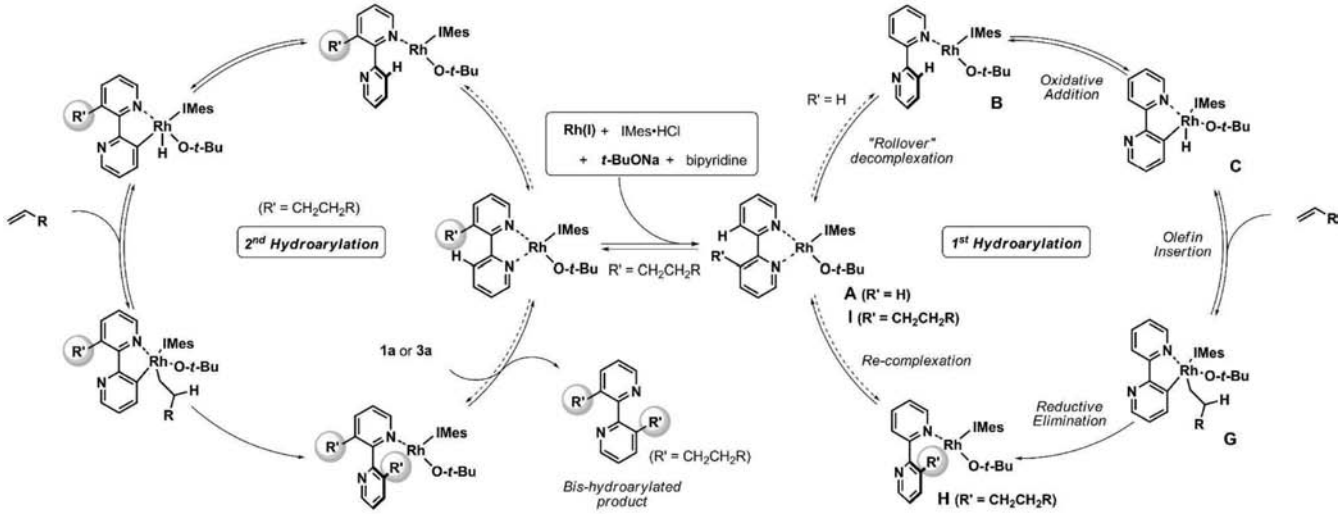


that, as predicted, a bidentate chelate **A** is considerably more stable than a monodentate complex **A**′ by 15.7 kcal/mol, implying that the effective concentration of the Rh-(2-phenylpyridine) species (**A**′) would be *initially negligible* due to the almost exclusive shift of equilibrium toward the Rh-bipyridine complex (**A**) even in the presence of 2-phenylpyridine.

The above computational calculations as well as the experimental data led us to propose a mechanistic pathway of the present bishydroarylation (Scheme 4). Irrespective of the oxidation state of the employed rhodium precursors, it is postulated that a Rh(I) complex ligated to *tert*-butoxide and NHC (IMes herein) is the catalytically active species based on the experimental data. After passing through all sequences from Rh(I)(IMes)(O-*t*-Bu)(bipy) **A** (R′= H) to a monoalkylated bipyridine **H** (R′ = CH_2CH_2R), it re-enters into the second catalytic cycle by starting with a bidentate complex **I** (R′ = CH_2CH_2R) to follow the same pathway as in the first catalytic cycle, eventually providing the bishydroarylated product.

Synthetic Application. Our present study offers a straightforward access to 3,3′-disubstituted bipyridine, biquinoline and their derivatives with excellent regio- and seterose-lectivity. As a synthetic application of the developed procedure, a preparative route was quickly established for the formation of

Scheme 4. Proposed Mechanistic Pathway of the Rh(NHC)-Catalyzed Bishydroarylation Reaction



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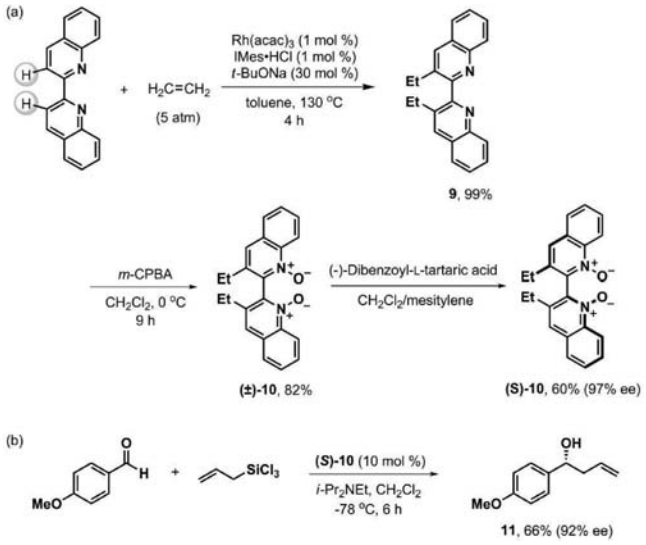
optically active 3,3′-dialkyl-2,2′-biquinoline *N*,*N*′-dioxides, derivatives of which display a high promise as an efficient chiral organocatalyst.[37,38] Hydroarylation of gaseous ethylene (5 atm) with 2,2′-biquinoline was readily performed to afford 3,3′-diethyl-2,2′-biquinoline (**9**) in quantitative yield using 1 mol % of a rhodium/IMes catalyst (Scheme 5a). Subsequent

Scheme 5. Synthesis of Optically Active 3,3′-Diethyl-2,2′-biquinoline *N*,*N*′-dioxide and Its Catalytic Usage in the Asymmetric Allylation



double *N*-oxidation of **9** proceeded easily with *meta*-chloroperbenzoic acid (*m*-CPBA) to give racemic *N*,*N*′-dioxide **10**. Optical resolution of (±)-**10** was successfully carried out with (−)-dibenzoyl-L-tartaric acid to provide (*S*)-3,3′-diethyl-2,2′-biquinoline *N*,*N*′-dioxide (***S*-10**) in good chemical yield (60%) and with high optical purity (97% ee). To our delight, the obtained compound ***S*-10** (10 mol %) was observed to catalyze an allylation reaction of aldehydes with trichloroallylsilane with high enantiomeric excess (92% ee, Scheme 5b).[38b] For reference, no conversion of this allylation was observed in the absence of **10**. Considering the fact that the previous synthetic routes to the biquinoline *N*,*N*′-dioxide and its derivatives suffer from lack of substrate scope even requiring multiple synthetic steps,[37] our present approach offers notable advantages overcoming most known synthetic difficulties.

CONCLUSION

In summary, we have demonstrated that a NHC ligand displays dramatic effects on the resultant Rh(NHC) catalyst system to trigger a rollover cyclometalation pathway of chelating molecules such as 2,2′-bipyridines and 2,2′-biquinolines. Our hypothesis that a strong *trans*-effect of NHCs would be a crucial factor to weaken a Rh-pyridyl bond *trans* to the ligated NHC with significant reduction of the activation barrier of the subsequent rollover cyclometalation step was proved experimentally and theoretically. Therefore, the Rh(NHC) catalyst system allowed highly efficient and selective hydroarylation of alkenes and alkynes. Our result is significant in that for the first time the "rollover" cyclometalation process was *catalytically* applied to the double C−H bond functionalization of chelating molecules using a Rh(NHC) catalyst system. The rhodium-catalyzed bishydroarylation of alkenes and alkynes delivered alkyl- and alkenyl bipyridine and biquinoline products in excellent yields, respectively. Synthetic utility of those obtained compounds was also demonstrated in an asymmetric organocatalytic reaction. Equipped with the new tool, a straightforward and practical access to a broad range of derivatives of chelating compounds is now accessible, while it was not easy by the precedent synthetic methods, and, therefore, the result of this study is anticipated to stimulate a significant advance in various areas such as catalysis, molecular assembly, or materials architecture.

ASSOCIATED CONTENT

Supporting Information

Detailed experimental procedures and characterization of new compounds, including ^{1}H and ^{13}C NMR spectra. Computational details including Cartesian coordinates of reported intermediates. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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