ORGANOMETALLICS

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Rhodium(III)-Catalyzed Nonaromatic sp^2 C−H Activation/Annulation Using NHC as a Directing and Functionalizable Group

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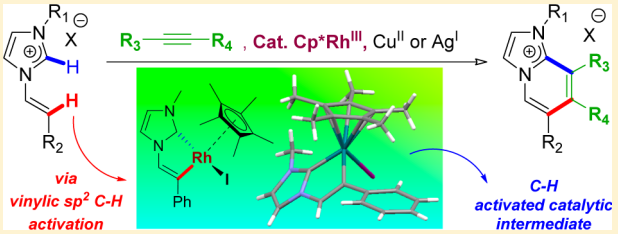
Supporting Information

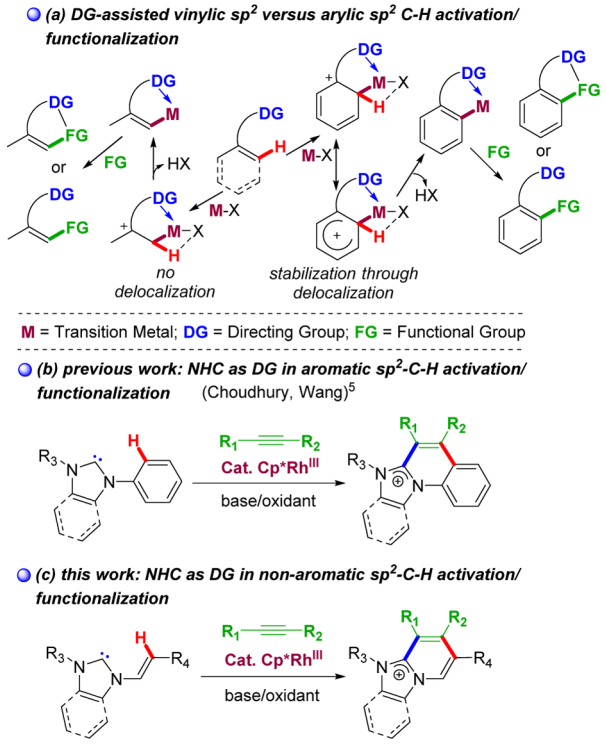
ABSTRACT: In parallel to the directing-group-assisted sp^2 C−H bond activation−functionalization of aromatic backbones, a similar exercise with nonaromatic sp^2 C−H bonds is also in high demand in synthetic chemistry despite several challenges pertinent to the latter process. In the presented protocol, N-heterocyclic carbene (NHC) motifs, appended to nonaromatic sp^2 C−H bond-containing organic molecules, have been used for developing a rhodium(III)-catalyzed annulation reaction with internal alkynes to synthesize a class of imidazo[1,2-*a*]pyridinium architectures. Mechanistic studies highlight the directing role of the NHC ligand during the C−H activation process and intermediacy of the C−H-activated Rh-NHC metallacycle in the catalysis.



INTRODUCTION

C−H bonds are undoubtedly the most prominent and ubiquitous in organic molecules, and they are relatively inert toward easy derivatization. The direct functionalization of C−H to C−E (E = C, O, N) bonds represents one of the most straightforward methods for the synthesis of functional molecules.[1] Activation and functionalization of a selected C−H bond by using a suitable directing group on the organic substrate that facilitates the temporary coordination of a transition metal catalyst to interact with the targeted C−H bond is well established in organic synthesis[2] (Scheme 1a). Particularly, Rh(III)-catalyzed aromatic sp^2 C−H functionalization with various nitrogen and oxygen donors as directing groups has been serving as a powerful protocol for synthesizing heterocyclic compounds for quite a long time. Alongside this step-economical, highly productive synthetic strategy, another intriguing research topic has been developed to encompass nonaromatic sp^2 (e.g., vinylic) C−H activation−functionalization leading to the construction of useful heterocyclic backbones.[3] However, few technical challenges remain in the case of nonaromatic sp^2 C−H bond activation processes. For example, a directing group such as carbonyl appended in the olefinic moiety could activate it toward some other parallel transformations such as conjugate addition, which are not possible in aromatic systems. Moreover, the generated positive charge after electrophilic attack by a metal center on the aromatic system can be stabilized by delocalization within the aromatic ring, whereas for a nonaromatic system it may be absent. Additionally, the substituents on the double bond can hinder the activation of nonaromatic sp^2 C−H due to steric reasons. Nevertheless, the development of newer strategies involving utilization of a variety of nonaromatic sp^2 C−H-containing organic substrates is still in high demand.

Scheme 1. DG-Assisted sp^2 C−H Activation



Motivated by our recent discovery of a unique reactivity of N-heterocyclic carbenes (NHCs)[4] as directing group for arene/

Received: June 30, 2016

DOI: 10.1021/acs.organomet.6b00530
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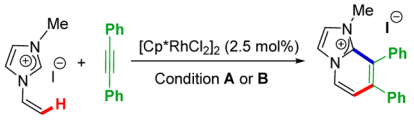
heteroarene C−H activation and also as a functionalizable unit in the oxidative annulation of arene and pyridine backbones with alkynes to construct positively charged π-conjugated organic materials (Scheme 1b),[5] we envisioned extending this strategy to nonaromatic sp^2 C−H bonds as well. Thus, by using an appended NHC ligand, *N*-vinyl imidazolium salts and related substrates were explored in rhodium(III)-catalyzed C−H activation−annulation with internal alkynes to synthesize imidazo[1,2-*a*]pyridinium motifs (Scheme 1c). Notably, imidazo[1,2-*a*]pyridines, like other aza-fused scaffolds, are key motifs in some drug candidates[6] and are traditionally synthesized via formation of an imidazole ring.[7]

RESULTS AND DISCUSSION

Encouraged by our previous methodology for aromatic C−H annulation, we tested the catalytic C−H activation/annulation reaction of a nonaromatic sp^2 C−H bond, by reacting the substrate **1a** with alkyne **2a** in the presence of AgOTf (3 equiv), NaOAc (4 equiv), and $[Cp^*RhCl_2]_2$ (2.5 mol %) in 1,2-dichloroethane (DCE) at 100 °C for 24 h, which furnished the desired annulated product **3a** in good yield (70%) (Scheme 2).

Scheme 2. Rh^{III}-Catalyzed Nonaromatic sp^2 C−H Activation−Annulation

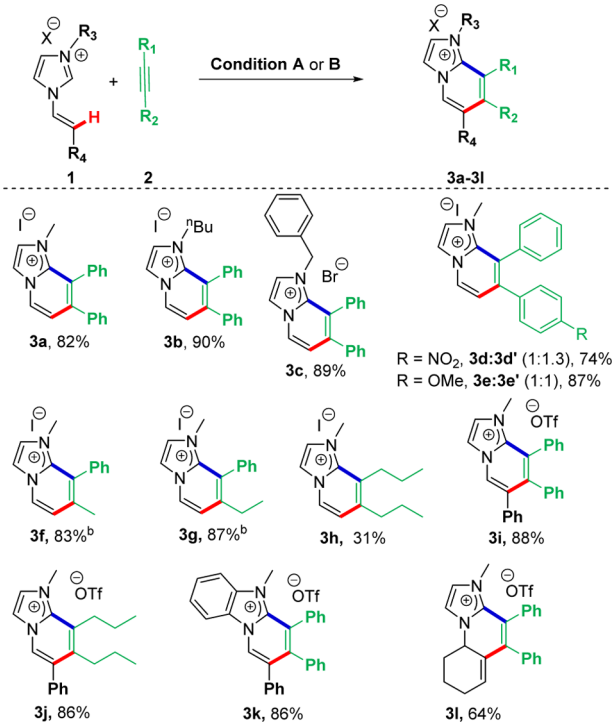


Condition **A**:
NaOAc (4 equiv), AgOTf (3 equiv), DCE, 100 ^{0}C, 24 h; Yield = 70%
Condition **B**:
$Cu(OAc)_2.H_2O$ (2.5 equiv), MeOH, 80 ^{0}C, 12 h; Yield = 82%

However, this methodology suffers from the use of a large amount of additives (3 equiv of AgOTf and 4 equiv of NaOAc). Interestingly the same reaction by using $Cu(OAc)_2{\cdot}H_2O$ (2.5 equiv) in MeOH instead of AgOTf and NaOAc also provided **3a** in good yield (82%) after 12 h at 80 °C (Scheme 2). Further efforts to reduce the use of additives by using O_2 as oxidizing agent decreased the yield drastically. Similarly the use of solvent such as dimehtylformamide also resulted in a decrease in yield of **3a**. Control experiments proved that the Rh-precatalyst and the copper/silver salts were crucial for this transformation (see Supporting Information for details).

Motivated by these results, we have checked the substrate scope with various imidazolium salts having different N-substituents and also with several internal alkynes. The results are shown in Table 1. The annulation reaction was well tolerated with different N-substituents such as methyl, butyl, and benzyl in the imidazolium substrates, and it provided good yields (82−90%) of the corresponding products (**3a**, **3b**, and **3c**) with diphenylacetylene. Diarylacetylenes bearing either an electron-withdrawing (NO_2) or -donating (OMe) group on one of the phenyl rings produced both regioisomeric products (**3d**/**3d′** and **3e**/**3e′**) in 74% and 87% overall yields, respectively. In contrast, aryl-alkyl unsymmetrical alkynes were found to be successfully employed in the reaction to provide the imidazo[1,2-*a*]pyridinium products with high regioselectivity. Thus, 1-phenyl-1-propyne and 1-phenyl-1-butyne reacted with the imidazolium substrate **1a** to yield single regioisomeric products **3f** and **3g**, respectively, in high

Table 1. Susbtrate Scope of the Rh^{III}-Catalyzed NHC-Directed Annulation of a Nonaromatic sp^2 C−H Bond[a]



[a]Condition A: $[Cp^*RhCl_2]_2$ (2.5 mol %), NaOAc (4 equiv), AgOTf (3 equiv), DCE, 100 °C, 24 h. Condition B: $[Cp^*RhCl_2]_2$ (2.5 mol %), $Cu(OAc)_2{\cdot}H_2O$ (2.5 equiv), MeOH, 80 °C, 12 h. For **3i**, **3j**, **3k**, and **3l**, condition A was used. Under condition B, the isolated yields of **3i**−**l** were 25%, trace, 15%, and <5%, respectively. [b]The other regioisomer was found to be in trace amount as analyzed by ^{1}H NMR spectroscopy.

yields. Notably, an electron-deficient alkyne, dimethyl acetylene dicarboxylate (DMAD), when reacted under similar conditions, did not furnish the desired product in appreciable amount. Interestingly the modification of *N*-vinyl to *N*-styryl within the starting imidazolium substrate was also successful in furnishing the annulated products **3i** (88%) and **3j** (86%) but by using AgOTf as oxidant. A benzimidazolium substrate was also well tolerated in providing the annulated product **3k** in excellent yield. Furthermore, the nonaromatic sp^2 C−H bond of a cyclohexenyl ring attached as the N-substituent also underwent the annulative transformation successfully and provided the corresponding product **3l** in good yield (64%). With $Cu(OAc)_2$, the isolated yields of **3i**−**l** were found to be less (5−25%).

This particular protocol provided us an opportunity to compare the reactivity of a nonaromatic versus aromatic sp^2 C−H bond toward annulative functionalization within a single molecular platform. For this investigation, we have modified the imidazolium substrate by introducing a competitive situation of vinyl sp^2 versus phenyl sp^2 C−H activation in the same molecule and tested for the annulation reaction under standard catalytic conditions. It resulted in a mixture of products with a ratio of products **3m**:**3n** = 1:2.6, indicating the higher reactivity of the aryl sp^2 C−H than the vinylic sp^2 C−H bond (Scheme 3a). Similar results were reported in the case of an intermolecular competition experiment also.[8] Further we have replaced the phenyl substituent with pyridyl and subjected it to the standard reaction conditions. We observed the complete

DOI: 10.1021/acs.organomet.6b00530
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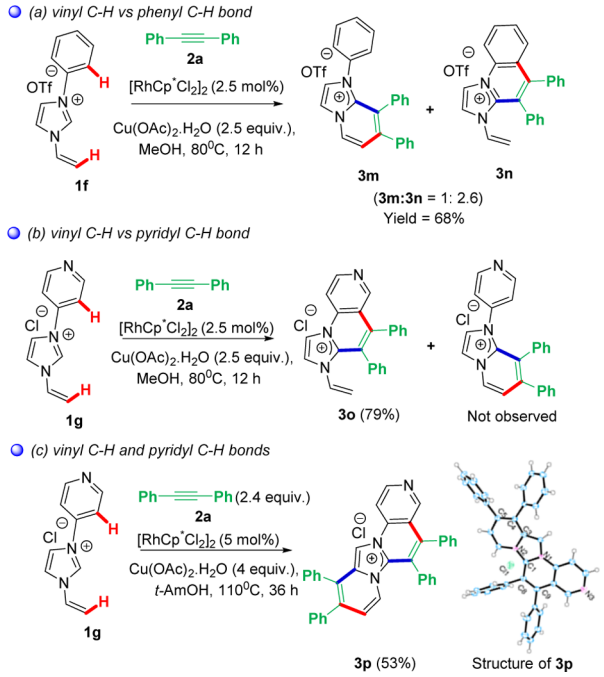
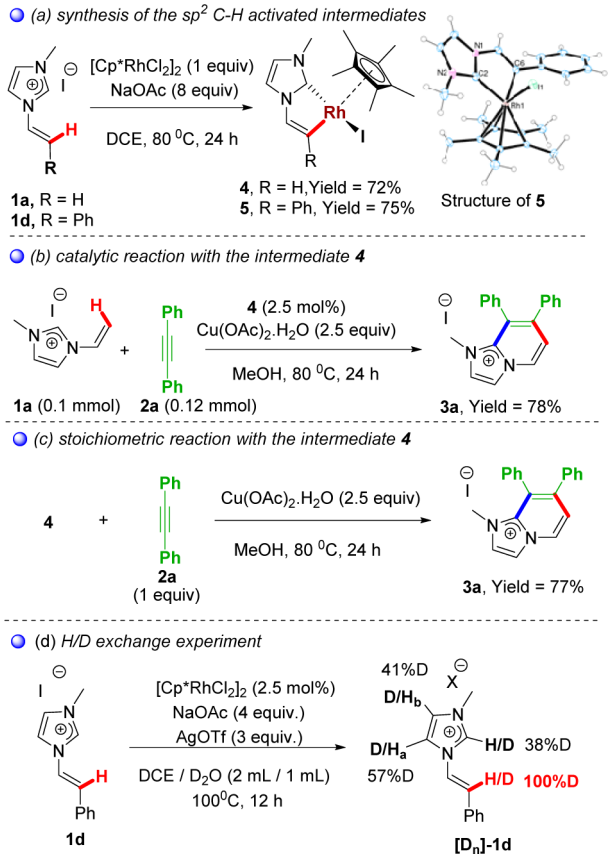
Scheme 3. Competitive Annulation Reactions



Scheme 4. Control Mechanistic Experiments

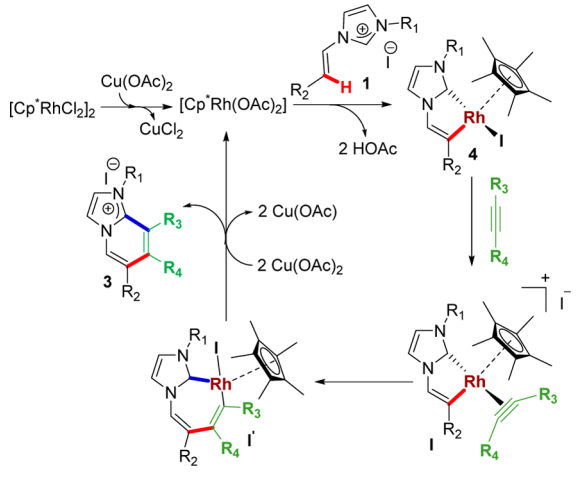


switching of reactivity toward pyridyl sp^2 C−H over the vinylic sp^2 C−H under the competitive situation and produced **3o** in good yield (Scheme 3b). These results suggested that the regioselectivity in the present sp^2 C−H activation was guided by the electronic nature of the N-substituents within the NHC motif.[5b,9] Interestingly charging the reaction with excess alkyne at higher temperature provided a double sp^2 C−H (aromatic as well as nonaromatic) activated product **3p**, wherein the second annulation was directed by an abnormal carbene generated from C(5)$_{im}$−H deprotonative metalation (Scheme 3c).

To understand the reaction mechanism, we first isolated the plausible NHC-vinylic sp^2 C−H activated rhodium(III) intermediates **4** and **5** by using NaOAc as a base in the reaction of imidazolium substrate and $[Cp^*Rh^{III}Cl_2]_2$ in DCE at 80 °C (Scheme 4a). Full spectroscopic characterization of the complexes was accomplished by ^{1}H and $^{13}C\{^1H\}$ NMR spectroscopic and mass spectrometric (ESI-MS) methods. Single-crystal X-ray diffraction analysis of complex **5** unambiguously confirmed the structure. The intermediacy of the complex **4** was further tested by carrying out both catalytic and stoichiometric reactions (Scheme 4b,c), and successful performance thereof supported the proposal. For understanding the reversibility of the C−H activation reaction we performed an H/D exchange experiment with the styryl substrate **1d** under Rh/AgOTf conditions and monitored it by ^{1}H NMR spectroscopy (Scheme 4d). We could not use Cu(II) here because of paramagnetic interference in the ^{1}H NMR spectroscopy. Unlike in our previous reports with phenyl and pyridyl sp^2 C−H activation,[5a,b] the high incorporation of D into the styryl sp^2 C−H suggested a very high degree of reversibility for the activation of this bond with rhodium under catalytic conditions. This might be due to the greater reactivity of the Rh−C$_{(styryl\ sp^2)}$ bond with the proton. Along with this, the D incorporation at different imidazolium C−H bonds was also observed (C(2)−H (38%), C(4)−H (57%), and C(5)−H (41%)), suggesting a moderate to good reversibility for the metalation at these positions. A kinetic isotope effect (KIE) value of ∼0.85 for the styryl C−H bond was obtained from a preliminary parallel experiment, suggesting that the involvement of the cleavage of this C−H bond in the rate-limiting step was unlikely (see Supporting Information for details).

On the basis of these mechanistic studies and our previous results[5] along with the reported directing-group-assisted C−H activation−annulation reactions,[2,3] a plausible catalytic cycle is proposed as shown in Scheme 5. The first step is likely to be the formation of a five-membered cyclometalated complex **4** from **1a** via vinylic C−H activation directed by the in-built NHC ligand coordination. Then the alkyne coordinates and generates intermediate **I**. Insertion of the coordinated alkyne

Scheme 5. Mechanistic Proposal



DOI: 10.1021/acs.organomet.6b00530
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into the Rh−C bond produces seven-membered rhodacycle intermediate **I′**. Reductive elimination from **I′** generates the annulated product **3** and the Cp*Rh(I) species. Then the reduced rhodium(I) species is reoxidized by Cu(II) to continue the catalytic cycle via further NHC-directed C−H activation and functionalization.

CONCLUSION

In conclusion, we successfully utilized NHC as a directing group in Rh(III)-catalyzed nonaromatic sp^2 C−H activation−functionalization reactions with a variety of internal alkynes, leading to important imidazo[1,2-*a*]pyridinium salts in good yields. The reactions were well tolerated with various types of imidazolium salts and internal alkynes. The mechanistic investigation was accomplished through isolation of NHC-bound sp^2 C−H activated rhodacycle intermediates. The intermediacy of such metallacycles for the follow-up alkyne insertion and reductive elimination steps, relevant to the catalytic cycle, was further confirmed by performing control catalytic and stoichiometric reactions with the isolated complexes. We were also able to compare the competitive reactivity of aromatic versus nonaromatic sp^2 C−H bonds toward annulative transformation in a single molecular platform by this methodology.

EXPERIMENTAL SECTION

A. General Methods and Materials. ^{1}H, ^{13}C{^{1}H}, and ^{19}F NMR spectra were recorded on Bruker AVANCE III 400, 500, and 700 MHz NMR spectrometers at room temperature unless mentioned otherwise. Chemical shifts (δ) are expressed in ppm using the residual proton resonance of the solvent as an internal standard ($CHCl_3$: δ = 7.26 ppm for ^{1}H spectra, 77.2 ppm for ^{13}C{^{1}H} spectra; CH_3CN: δ = 1.94 ppm for ^{1}H spectra, 1.3 ppm for ^{13}C{^{1}H} spectra, DMSO δ = 2.5 ppm for ^{1}H spectra, 39.52 ppm for ^{13}C{^{1}H} spectra). All coupling constants (J) are expressed in hertz (Hz) and are given only for ^{1}H−^{1}H couplings unless mentioned otherwise. The following abbreviations were used to indicate multiplicity: s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), dt (doublet of triplets), m (multiplet). ESI mass spectroscopy was performed on a Bruker microTOF QII spectrometer. Single-crystal X-ray diffraction data were collected using a Bruker SMART APEX II CCD diffractometer with graphite-monochromated Mo Kα (λ = 0.710 73 Å) radiation at different temperatures for each crystal. Dry solvents and reagents were obtained from commercial suppliers and used without further purification. Deuterated solvents and $RhCl_3{\cdot}xH_2O$ were purchased from Aldrich. $[Cp^*RhCl_2]_2$,[10] 1-nitro-4-(phenylethynyl)benzene,[11] and 1-methoxy-4-(phenylethynyl)-benzene[11] were synthesized according to reported procedures.

B. General Procedure for the Annulation Reactions. Procedure A: To a Schlenk tube were added **1** (0.1 mmol), $Cu(OAc)_2{\cdot}H_2O$ (0.25 mmol), $[Cp^*RhCl_2]_2$ (0.0025 mmol), and **2** (0.12 mmol). Then the tube was kept under vacuum for 10 min. After that, the tube was filled with argon. To this mixture was added degassed MeOH (3.0 mL), and the reaction mixture was refluxed at 80 °C for 12 h. After cooling to room temperature the mixture was filtered through a short Celite pad, which was further washed with acetonitrile. The filtrate was concentrated under reduced pressure, and the residue was absorbed onto a small amount of alumina. The pure product was isolated by column chromatography (neutral alumina) using a MeOH/$CHCl_3$ (5% MeOH in $CHCl_3$) solvent system. Procedure B: To a Schlenk tube were added **1** (0.1 mmol), NaOAc (0.4 mmol), AgOTf (0.3 mmol), $[Cp^*RhCl_2]_2$ (0.0025 mmol), and **2** (0.12 mmol). Then the tube was kept under vacuum for 10 min. After that, the tube was filled with argon. To this mixture was added degassed $ClCH_2CH_2Cl$ (3.0 mL), and the reaction mixture was refluxed at 100 °C for 24 h. After the reaction, a similar workup described in procedure A was followed to isolate the products.

C. Experimental Characterization Data for the Annulated Products (3a−p). *1-Methyl-7,8 diphenylimidazo[1,2-a]pyridin-1-ium Iodide (**3a**).* Yield = 79%. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 9.48 (d, J = 6.9 Hz, 1H), 9.02 (d, J = 0.8 Hz, 1H), 8.22 (d, J = 0.6 Hz, 1H), 7.46−7.32 (m, 6H), 7.22 (d, J = 6.7 Hz, 3H), 7.10 (d, J = 6.0 Hz, 2H), 3.46 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 147.1, 137.7, 136.6, 131.4, 131.2, 129.7, 129.3, 129.2, 128.9, 128.7, 128.6, 128.4, 124.4, 119.8, 115.3, 38.5. HRMS (ESI, positive ion): M^+ = 285.1397 (calculated 285.1386 for $[C_{20}H_{17}N_2]^+$).

*1-Butyl-7,8-diphenylimidazo[1,2-a]pyridin-1-ium Iodide (**3b**).* Yield = 90%. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 9.60 (d, J = 6.9 Hz, 1H), 9.11 (d, J = 2.1 Hz, 1H), 8.23 (d, J = 2.1 Hz, 1H), 7.41−7.33 (m, 4H), 7.28 (dd, J = 7.8,1.3 Hz, 2H), 7.22−7.15 (m, 3H), 7.04 (dd, J = 7.6, 1.7 Hz, 2H), 3.80−3.73 (m, 2H), 1.44 (dt, J = 15.6, 7.8 Hz, 2H), 0.90−0.85 (m, 2H), 0.65 (t, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 147.6, 137.1, 136.7, 131.5, 130.9, 129.8, 129.7, 129.3, 128.9, 128.6, 128.4, 127.3, 124.0, 119.8, 116.1, 49.8, 33.1, 19.5, 13.4. HRMS (ESI, positive ion): M^+ = 327.1866 (calculated 327.1856 for $[C_{23}H_{23}N_2]^+$).

*1-Benzyl-7,8-diphenylimidazo[1,2-a]pyridin-1-ium Bromide (**3c**).* Yield = 89%. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 9.94 (d, J = 6.9 Hz, 1H), 9.56 (d, J = 1.9 Hz, 1H), 7.98 (d, J = 1.9 Hz, 1H), 7.43 (d, J = 6.9 Hz, 1H), 7.32 (t, J = 7.5 Hz, 1H), 7.23−7.18 (m, 8H), 7.07 (d, J = 7.3 Hz, 2H), 7.02 (d, J = 6.5 Hz, 2H), 6.65 (d, J = 6.9 Hz, 2H), 5.07 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 148.1, 137.4, 136.6, 134.1, 131.1, 130.5, 129.7, 129.3, 129.1, 128.8, 128.7, 128.4, 127.4, 126.6, 124.1, 120.1, 116.9, 53.2. HRMS (ESI, positive ion): M^+ = 361.1716 (calculated 361.1699 for $[C_{26}H_{21}N_2]^+$).

*1-Methyl-8-(4-nitrophenyl)-7-phenylimidazo[1,2-a]pyridin-1-ium Iodide and 1-Methyl-7-(4-nitrophenyl)-8-phenylimidazo[1,2-a]-pyridin-1-ium Iodide (**3d** + **3d′** (1:1.3)).* Yield = 74%. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 9.50 (d, J = 6.9 Hz, 1H), 9.41 (d, J = 6.9 Hz, 0.8H), 9.02 (d, J = 2.1 Hz, 1H), 8.93 (d, J = 1.9 Hz, 0.8H), 8.21 (d, J = 8.6 Hz, 1.5H), 8.17 (s, 1H), 8.10 (s, 0.8H), 8.08 (d, J = 8.7 Hz, 2H), 7.81 (d, J = 8.6 Hz, 1.6H), 7.49−7.32 (m, 9.2H), 7.25−7.21 (m, 2.8H), 7.10 (dd, J = 7.8, 1.4 Hz, 1.7H), 3.51 (s, 2.3H), 3.47 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) = 148.5, 147.7, 147.6, 144.7, 143.1, 138.4, 137.7, 137.5, 136.0, 133.2, 131.3, 130.6, 130.3, 129.5, 129.5, 129.2, 129.1, 129.0, 128.9, 128.7, 125.3, 123.6, 122.7, 120.0, 119.2, 115.6, 115.4, 39.0, 38.6. HRMS (ESI, positive ion): M^+ = 330.1235 (calculated 330.1237 for $[C_{20}H_{16}N_3O_2]^+$).

*8-(4-Methoxyphenyl)-1-methyl-7-phenylimidazo[1,2-a]pyridin-1-ium Iodide and 7-(4-Methoxyphenyl)-1-methyl-8-phenylimidazo-[1,2-a]pyridin-1-ium Iodide (**3e** + **3e′** (1:1)).* Yield = 87%. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 9.41 (d, J = 6.5 Hz, 2H), 8.91 (s (broad), 2H), 8.20 (s, 2H), 7.45−7.30 (m, 7H), 7.21 (s (broad), 5H), 7.09 (s, 2H), 7.02 (d, J = 8.0 Hz, 2H), 6.85 (d, J = 7.7 Hz, 2H), 6.70 (d, J = 7.8 Hz, 2H), 3.78 (s, 3H), 3.72 (s, 3H), 3.50 (s, 3H), 3.43 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 160.4, 159.8, 147.3, 146.7, 138.0, 137.8, 136.7, 132.5, 131.4, 131.4, 130.8, 129.7, 129.3, 128.9, 128.8, 128.8, 128.7, 128.6, 128.5, 128.4, 124.3, 123.6, 122.9, 120.0, 119.8, 115.1, 115.0, 114.1, 113.9, 55.4, 55.3, 38.7, 38.6. HRMS (ESI, positive ion): M^+ = 315.1499 (calculated 315.1492 for $[C_{21}H_{19}N_2O]^+$).

*1,7-Dimethyl-8-phenylimidazo[1,2-a]pyridin-1-ium Iodide (**3f**).* Yield = 83%. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 9.43 (d, J = 6.9 Hz, 1H), 9.04 (d, J = 2.2 Hz, 1H), 8.08 (d, J = 2.2 Hz, 1H), 7.59−7.55 (m, 3H), 7.38−7.34 (m, 2H), 7.31 (d, J = 6.9 Hz, 1H), 3.39 (s, 3H), 2.25 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 144.9, 137.5, 131.8, 130.1, 129.4, 129.2, 129.1, 128.0, 124.7, 120.1, 115.4, 37.7, 20.2. HRMS (ESI, positive ion): M^+ = 223.1235 (calculated 223.1230 for $[C_{15}H_{15}N_2]^+$).

*7-Ethyl-1-methyl-8-phenylimidazo[1,2-a]pyridin-1-ium Iodide (**3g**).* Yield = 87%. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 9.38 (d, J = 6.9 Hz, 1H), 8.90 (d, J = 2.2 Hz, 1H), 8.14 (d, J = 2.1 Hz, 1H), 7.57−7.52 (m, 3H), 7.40−7.36 (m, 2H), 7.34 (d, J = 7.0 Hz, 1H), 3.37 (s, 3H), 2.51 (q, J = 7.6 Hz, 2H), 1.12 (t, J = 7.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 150.5, 131.3, 130.3, 130.1, 129.5, 129.3, 129.0, 128.4, 128.1, 124.2, 118.7, 115.2, 37.8, 26.4, 15.0. HRMS

DOI: 10.1021/acs.organomet.6b00530
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(ESI, positive ion): M^+ = 237.1393 (calculated 237.1386 for $[C_{16}H_{17}N_2]^+$).

*1-Methyl-7,8-dipropylimidazo[1,2-a]pyridin-1-ium Iodide (**3h**).* Yield = 31%. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 9.15 (d, J = 6.9 Hz, 1H), 8.75 (s (broad), 1H), 8.30 (d, J = 1.7 Hz, 1H), 7.19 (d, J = 6.9 Hz, 1H), 4.41 (s, 3H), 3.08−3.00 (m, 2H), 2.79−2.71 (m, 2H), 1.67 (dd, J = 15.6, 7.9 Hz, 4H), 1.12 (t, J = 7.3 Hz, 3H), 1.03 (t, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 148.2, 138.8, 128.6, 127.8, 124.3, 119.8, 114.9, 38.7, 34.4, 28.5, 25.4, 24.0, 14.2, 14.0. HRMS (ESI, positive ion): M^+ = 217.1704 (calculated 217.1699 for $[C_{14}H_{21}N_2]^+$).

*1-Methyl-6,7,8-triphenylimidazo[1,2-a]pyridin-1-ium Trifluoromethanesulfonate (**3i**).* Yield = 88%. ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) = 8.66 (s, 1H), 8.11 (d, J = 2.1 Hz, 1H), 7.75 (d, J = 2.1 Hz, 1H), 7.41−7.31 (m, 5H), 7.28−7.23 (m, 3H), 7.18 (dd, J = 7.7, 1.6 Hz, 2H), 7.08−7.00 (m, 3H), 6.96 (dd, J = 7.5, 1.9 Hz, 2H), 3.24 (s, 3H). ^{13}C NMR (101 MHz, CD_3CN): δ (ppm) = 148.1, 136.4, 133.5, 132.9, 132.1, 131.2, 130.9, 130.1, 129.6, 129.1, 129.1, 129.0, 128.5, 128.3, 126.7, 115.3, 38.0. ^{19}F NMR (376 MHz, CD_3CN): δ (ppm) = −79.31. HRMS (ESI, positive ion): M^+ = 361.1717 (calculated 361.1699 for $[C_{26}H_{21}N_2]^+$).

*1-Methyl-6-phenyl-7,8-dipropylimidazo[1,2-a]pyridin-1-ium Trifluoromethanesulfonate (**3j**).* Yield = 86%. ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) = 8.26 (s, 1H), 7.87 (d, J = 2.2 Hz, 1H), 7.68 (d, J = 2.1 Hz, 1H), 7.55−7.50 (m, 3H), 7.38 (dd, J = 6.6, 2.9 Hz, 2H), 4.19 (s, 3H), 3.13−3.07 (m, 2H), 2.73−2.67 (m, 2H), 1.74−1.66 (m, 2H), 1.38−1.29 (m, 2H), 1.13 (t, J = 7.3 Hz, 3H), 0.75 (t, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, CD_3CN): δ (ppm) = 148.2, 136.8, 135.8, 133.5, 129.6, 128.7, 128.6, 128.4, 126.3, 125.1, 113.8, 37.6, 31.1, 28.3, 24.8, 23.5, 13.4, 13.0. ^{19}F NMR (376 MHz, CD_3CN): δ (ppm) = −78.43. HRMS (ESI, positive ion): M^+ = 293.2022 (calculated 293.2012 for $[C_{20}H_{25}N_2]^+$).

*5-Methyl-2,3,4-triphenylbenzo[4,5]imidazo[1,2-a]pyridin-5-ium Trifluoromethanesulfonate (**3k**).* Yield = 86%. ^{1}H NMR (400 MHz, CDCl3): δ (ppm) = 9.00 (s, 1H), 8.32 (d, J = 8.4 Hz, 1H), 7.76−7.70 (m, 2H), 7.61 (t, J = 8.2 Hz, 1H), 7.42−7.36 (m, 2H), 7.33−7.32 (3H), 7.27−7.20 (m, 5H), 7.03−6.96 (m, 3H), 6.91 (dd, J = 7.7, 1.5 Hz, 2H), 3.41 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 152.4, 140.2, 135.0, 134.9, 134.3, 132.7, 131.9, 131.4, 130.3, 130.2, 130.0, 129.5, 128.6, 128.4, 128.4, 128.0, 127.7, 126.3, 126.2, 125.7, 125.6, 120.8, 113.7, 112.2, 77.2, 33.4. ^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = −78.33. HRMS (ESI, positive ion): M^+ = 411.1866 (calculated 411.1856 for $[C_{30}H_{23}N_2]^+$).

*3-Methyl-4,5-diphenyl-6,7,8,9-tetrahydroimidazo[1,2-a]quinolin-3-ium Trifluoromethanesulfonate (**3l**).* Yield = 64%. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.62 (d, J = 2.1 Hz, 1H), 7.41 (d, J = 2.0 Hz, 1H), 7.22−7.16 (m, 8H), 7.02−7.00 (m, 2H), 5.86−5.83 (m, 1H), 5.34−5.29 (m, 1H), 3.09 (s, 3H), 2.90−2.86 (m, 1H), 2.33−2.28 (m, 1H), 2.12−2.08 (m, 1H), 2.00−1.88 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 147.5, 139.7, 139.3, 135.0, 132.4, 131.0, 129.6, 129.1, 128.0 (two peaks overlapping), 127.4, 125.7, 120.4, 120.9, 118.8, 59.2, 55.4, 37.9, 26.8, 25.7, 19.9. ^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = −78.30. HRMS (ESI, positive ion): M^+ = 339.1840 (calculated 339.1856 for $[C_{24}H_{23}N_2]^+$).

*1,7,8-Triphenyl-1H-imidazo[1,2-a]pyridin-4-ium Trifluoromethanesulfonate and 4,5-Diphenyl-3-vinylimidazo[1,2-a]quinolin-3-ium Trifluoromethanesulfonate (**3m** + **3n** (1:2.6)).* Yield = 68%. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 9.38 (d, J = 2.1 Hz, 1H), 9.34 (d, J = 6.9 Hz, 0.4H), 8.89 (d, J = 2.0 Hz, 0.4H), 8.75 (d, J = 8.6 Hz, 1H), 8.16 (d, J = 2.2 Hz, 1H), 8.02−7.93 (m, 1H), 7.69 (d, J = 2.0 Hz, 1H), 7.63 (t, J = 7.6 Hz, 1H), 7.60−7.56 (m, 1H), 7.52 (d, J = 6.9 Hz, 0.4H), 7.36−7.28 (m, 6.4H), 7.25−7.20 (m, 2.4H), 7.19−7.17 (m, 0.1.4H), 7.13 (dd, J = 6.6, 2.9 Hz, 2.0H), 7.10−7.00 (m, 2.7H), 6.95 (t, J = 7.4 Hz, 0.4H), 6.83 (t, J = 7.7 Hz, 0.8H), 6.76 (d, J = 7.1 Hz, 0.8H), 6.11 (dd, J = 15.2, 8.3 Hz, 1H), 5.61 (dd, J = 15.2, 2.4 Hz, 1H), 4.97 (dd, J = 8.3, 2.4 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) = 148.4, 148.1, 136.7, 135.6, 135.4, 134.0, 133.1, 131.7, 131.1, 130.9, 130.8, 130.3, 129.8, 129.7, 129.6, 129.6, 129.5, 129.3, 129.7, 129.0, 128.9, 128.7, 128.7, 128.6, 128.5, 128.4, 128.0, 127.9, 126.7, 124.5, 124.5, 124.3, 122.9, 122.5, 120.8, 119.3, 117.5, 116.6, 116.2, 112.2. ^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) = −78.27. HRMS (ESI, positive ion): M^+ = 347.1542 (calculated 347.1543 for $[C_{25}H_{19}N_2]^+$).

*4,5-Diphenyl-3-vinyl-3H-imidazo[1,2-a][1,6]naphthyridin-10-ium Chloride (**3o**).* Yield = 79%. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 10.63 (d, J = 1.8 Hz, 1H), 9.54 (d, J = 5.9 Hz, 1H), 9.05 (d, J = 5.7 Hz, 1H), 8.88 (s, 1H), 8.64 (d, J = 1.9 Hz, 1H), 7.35 (dd, J = 11.2, 4.1 Hz, 6H), 7.29 (dd, J = 7.7, 1.5 Hz, 2H), 7.18 (dd, J = 6.5, 2.9 Hz, 2H), 6.14 (dd, J = 15.2, 8.3 Hz, 1H), 5.93 (dd, J = 15.2, 2.4 Hz, 1H), 5.05 (dd, J = 8.3, 2.4 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) = 152.1, 151.4, 146.7, 136.3, 135.8, 132.5, 131.2, 131.1, 130.0, 129.9, 129.2, 129.1, 128.6, 128.5, 125.4, 124.7, 118.7, 113.5, 112.4. HRMS (ESI, positive ion): M^+ = 348.1508 (calculated 348.1495 for $[C_{24}H_{18}N_3]^+$).

*5,6,10,11-Tetraphenylpyrido[1′,2′:3,4]imidazo[1,2-a][1,6]-naphthyridin-13-ium Chloride (**3p**).* Yield = 53%. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 9.39 (s, 1H), 9.04−8.99 (m, 2H), 8.96 (s, 1H), 7.51 (d, J = 7.0 Hz, 2H), 7.49−7.38 (m, 8H), 7.34−7.30 (m, 3H), 7.25−7.18 (m, 5H), 7.15 (d, J = 7.7 Hz, 1H), 7.08 (dd, J = 7.7, 1.5 Hz, 2H), 6.89 (d, J = 7.7 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) = 152.1, 150.4, 142.4, 137.5, 136.7, 134.7, 133.6, 133.1, 132.5, 131.3, 130.5, 130.4, 130.4, 130.2, 129.8, 129.6, 129.5, 129.5, 129.5, 129.4, 129.0, 128.6, 128.5, 128.5, 125.2, 122.2, 120.7, 120.3, 112.2, 108.9. HRMS (ESI, positive ion): M^+ = 524.2123 (calculated 524.2121 for $[C_{38}H_{26}N_3]^+$).

D. Synthesis and Characterization of the Cyclometalated Rh(III) Intermediates Complex 4 and Complex 5. A mixture of $[Cp^*RhCl_2]_2$ (0.025 mmol) and NaOAc (0.4 mmol) was stirred in degassed $ClCH_2CH_2Cl$ (5 mL) for 10 min in a Schlenk tube. Then **1a** (for complex **4**) or **1d** (for complex **5**) (0.05 mmol) was added to the reaction mixture, and stirring was continued for a further 24 h at 80 °C. After cooling the reaction mixture to room temperature, the resulting solution was filtered through a Celite plug and the filtrate was reduced to a minimum volume under vacuum. The product was purified by precipitating it with diethyl ether. Then the precipitate was collected and dried in vacuo to obtain the desired products, complex **4** (72%) or **5** (75%).

*Characterization data of **4**.* ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 7.50 (dd, J = 5.0, 2.2 Hz, 1H), 7.04 (d, J = 1.9 Hz, 1H), 6.81 (d, J = 1.9 Hz, 1H), 6.80−6.79 (m, 1H), 3.83 (s, 3H), 1.88 (s, 15H). ^{13}C NMR (176 MHz, $CDCl_3$): δ (ppm) = 181.4 (d, $J_{Rh-C(NHC)}$ = 54.7), 151.7(d, $J_{Rh-C(vinyl)}$ = 34.6),126.6, 120.1, 116.6, 97.2 (d, $J_{Rh-C(Cp^*)}$ = 4.7), 37.5, 10.6. HRMS (ESI, positive ion): M+ = 345.0840 (calculated 345.0833 for $[C_{16}H_{22}N_2Rh]^+$). Anal. Calcd for $C_{16}H_{22}N_2RhI$: C, 40.68; H, 4.70; N, 5.93. Found: C, 40.93; H, 4.61; N, 5.74.

*Characterization data of **5**.* ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.51 (d, J = 7.2 Hz, 2H), 7.23 (d, J = 7.7 Hz, 2H), 7.14 (t, J = 7.3 Hz, 1H), 7.09 (d, J = 1.7 Hz, 1H), 6.83 (d, J = 1.7 Hz, 1H), 6.60 (d, J = 1.8 Hz, 1H), 3.85 (s, 3H), 1.61 (s, 15H). ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) = 181.4 (d, $J_{Rh-C(NHC)}$ = 54.8), 163.2 (d, $J_{Rh-C(vinyl)}$ = 34.2), 146.6, 128.0, 127.8, 125.6, 122.7, 120.8, 116.8, 97.8 (d, $J_{Rh-C(Cp^*)}$ = 4.9), 37.9, 10.1. HRMS (ESI, positive ion): M^+ = 421.1150 (calculated 421.1146 for $[C_{22}H_{26}N_2Rh]^+$). Anal. Calcd for $C_{22}H_{26}N_2RhI$: C, 48.17; H, 4.78; N, 5.11. Found: C, 48.01; H, 5.03; N, 5.10.

E. Stoichiometric Annulation Reaction with the Rh(III) Complex 4. In an oven-dried Schlenk tube, a mixture of complex **4** (0.1 mmol), $Cu(OAc)_2{\cdot}H_2O$ (0.25 mmol), and **2a** (0.12 mmol) was loaded, and then the tube was kept under vacuum for 15 min and backfilled with argon gas. Then dry and degassed MeOH (3.0 mL) was added to it, and the reaction mixture was left stirring at 80 °C for 12 h. After cooling to room temperature, the whole reaction mixture was passed through a short Celite pad, which was subsequently washed with acetonitrile (3 × 5 mL). The combined filtrate was concentrated under reduced pressure, and the residue was absorbed onto a small amount of alumina. Final product was separated by column chromatography (neutral alumina), eluted with a MeOH/$CHCl_3$ (5% MeOH in $CHCl_3$) solvent system, affording pure **3a** (yield 77%).

F. Catalytic Reaction with the Rh(III) Complex 4. To an oven-dried Schlenk tube were loaded **1a** (0.1 mmol), complex **4** (0.0025 mmol), $Cu(OAc)_2{\cdot}H_2O$ (0.25 mmol), and **2a** (0.12 mmol), and then

DOI: 10.1021/acs.organomet.6b00530
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the tube was kept under vacuum for 15 min and backfilled with argon gas. To this mixture was added dry and degassed MeOH (3.0 mL), and the reaction mixture was left stirring at 80 °C for 12 h. After cooling to room temperature, the whole reaction mixture was passed through a short Celite pad, which was subsequently washed with acetonitrile (3 × 5 mL). The combined filtrate was collected and concentrated under reduced pressure, and the residue was absorbed onto a small amount of alumina. Final product was separated by column chromatography (neutral alumina), eluted with a MeOH/$CHCl_3$ (5% MeOH in $CHCl_3$) solvent system, affording pure **3a** (yield 78%).

G. H/D Exchange Experiment. To an oven-dried Schlenk tube were loaded **1d** (0.1 mmol), NaOAc (0.4 mmol), $[RhCp^*Cl_2]_2$ (0.0025 mmol), and AgOTf (0.3 mmol), and then the tube was kept under vacuum for 10 min. After that, the tube was filled with argon gas. To this mixture were added dry and degassed $ClCH_2CH_2Cl$ (2 mL) and then D_2O (1 mL), and the reaction mixture was left stirring at 100 °C under dark for 12 h. After cooling to room temperature, the whole reaction mixture was passed through a short Celite pad, which was subsequently washed with acetonitrile (3 × 5 mL). The combined filtrate was collected, and the solvent was removed under reduced pressure. To the crude residue was added mesitylene (0.1 mmol) as an internal standard, and it was subjected to ^1H NMR spectroscopy in CD_3CN.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.organomet.6b00530.

Additional experimental details and spectra (PDF)
Crystallographic data (CIF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

IISER Bhopal is gratefully acknowledged for funding. R.T. thanks the UGC for a doctoral fellowship, and H.T. thanks the DST for a BS-MS INSPIRE fellowship.

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DOI: 10.1021/acs.organomet.6b00530
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