Regioselective 1,2-Hydrosilylation of N-Heterocycles Catalyzed by a Ruthenium Olefin Metathesis Catalyst

Xinyuan Maa and Steven P. Nolana\*

aDepartment of Chemistry and Center for Sustainable Chemistry, Ghent University, Krijgslaan 281, S-3, 9000 Ghent, Belgium

Supporting Information Placeholder

ABSTRACT: A first-generation ruthenium-indenylidene olefin metathesis complex catalyzes the 1,2-hydrosilylation reaction to access dihydroquinoline derivatives with high regioselectivity under mild conditions. The ruthenium-indenylidene complex was shown to have excellent catalytic efficiency when the challenging Ph2SiH2 hydride donor is used. The reaction is efficient at 0.25-1 mol% catalyst loadings with a wide range of quinoline derivatives and N-heterocycles. A mechanism for this transformation is proposed based on stoichiometric reactions.

Introduction

Olefin metathesis is considered a highly efficient C−C bond-forming reaction in modern organic chemistry,1 with key applications in materials science2 and chemical biology.3 Its importance was recognized by the 2005 Nobel Prize in chemistry to Grubbs, Schrock, and Chauvin.4 Grubbs-type ruthenium-complex-catalyzed non-metathetical reactions have led to the parallel development of new synthetic strategies.5 Ruthenium alkylidenes such as Grubbs- and Hoveyda-type complexes, which are widely used for olefin metathesis, have been shown to function as pre-catalysts in several types of fundamental organic transformations.6-8 However, first generation indenylidene (Ind) complexes, which are particularly facile to prepare, are commonly used as synthons for the preparation of second-, third-generation metathesis precatalysts9 and related congeners.10 They have rarely been reported as catalysts in non-metathesis reactions. This type of catalyst has proven slower to initiate and therefore more stable in the longer term than other olefin metathesis catalysts.8 As previous reports had extensively examined the catalytic activity of the benzylidene precursors in different types of reactions,5-8 we became interested in the influence of olefin metathesis catalysts bearing an indenylidene moiety, which also exhibit overall catalytic activity equal to or even slightly higher than that of their benzylidene counterparts (Figure 1).10c, 11

The dearomatization of N-heteroarenes affords dihydroquinolines (DHQs), which are important building blocks for a variety of agrochemical and pharmaceutical molecules, find applications in materials science and synthetic chemistry.12 The dearomatization of (hetero)aromatics is considered to be a kinetically unfavorable process, because it requires highly efficient catalytic systems to overcome high resonance stabilization energies.13



**Figure 1.** Selected ruthenium complexes deployed in this study.

Recently, the dearomatization of quinolines, via the use of excess borane14 and silane15, has attracted attention. During this process, harsh reaction conditions are avoided and N-sila or -bora functionalized molecules can be used as key intermediates for further functionalization.16 Despite these recent significant advances in quinoline hydroboration and hydrosilylation, the latter methods are still far from general.

Up to now, a very limited number of examples exist for the 1,2-regioselective hydrosilylation of N-heteroarenes compared to the widely reported 1,4-hydrosilylation reactions.17,18 Early hydrosilylation reactions were catalyzed by Mg,19,20 or Ca21 species, which either led to poor selectivity, or were quite limited in scope. Subsequently, the Chang22 and Nikonov groups23,24 (Scheme 1) developed the 1,2-hydrosilylative dearomatization of N-heteroaromatics to afford N-silyl 1,2-DHQ derivatives using Ir and Zn catalysts, respectively. However, some of these methods are limited to the use of a single and excess silane as reducing agent or require high catalyst loadings to achieve moderate to high yields, even going so far as to require several days of reaction time. Furthermore, the Gunanathan group achieved regioselective dearomatization of N-heteroarenes using [Ru(*p*-cymene)(PCy3)Cl2] as catalyst (Scheme 1).18a We acknowledge that the results of this work largely make up for the deficiencies of the previous studies, however, none of the aforementioned catalytic systems overcome the difficulty of using bulky silanes, such as Ph2SiH2, as hydrogen donors, until now.

Scheme 1. Catalytic Regioselective Hydrosilylation of N-Heteroarenes



While this manuscript was being assembled, Petit and co-workers reported hydrido-cobalt complexes catalyzed hydrosilylation reaction requiring high temperature and long reaction time.25 With the exception of these previous studies, simple synthetic methods are needed, especially considering the importance of the 1,2-dihydroquinoline derivatives.26

Inspired by the reports mentioned above and by our previous experience in ruthenium catalysis, we present here a simple and versatile method for the regioselective 1,2-hydrosilylation using a commercially available ruthenium-indenylidene olefin metathesis catalyst as a hydrosilylation catalyst. Figure 1 presents the structures and acronyms of the complexes used in this study.

Results and Discussion

Initially, the ruthenium-catalyzed 1,2-hydrosilylation of quinoline (**1a**) with diethylsilane (Et2SiH2) was examined under anaerobic conditions (Table 1 and SI, Table S1). A preliminary screening revealed that commercially available olefin metathesis catalyst **M2** (0.25 mol%) allowed the reaction of quinoline and Et2SiH2 to proceed to the desired product in more than 99% yield, with excellent regioselectivity at room temperature (Table 1, entry 1). By comparison to the recently reported protocol that requires 2 mol% of [Ru(PCy3)Cl2(*p*-cymene)]18a and heating at 60 ℃ for 18h, the present system, involving first-generation ruthenium-indenylidene catalyst **M2** not only greatly shortens the reaction time under milder conditions, but also reduces the amount of catalyst by approximately a factor of 10, which represents an important step forward in this hydrosilylation reaction. Subsequently, the activity of a family of metathesis catalysts was examined based on the initial reaction conditions. The results show that the catalytic efficiency of the indenylidene-bearing pre-catalyst precursor **M1** (PPh3) is significantly lower than that displayed by **M2** (PCy3) and **M3** ( *i*Bu-Phoban) (Table 1, entry 2 vs 1 and 3). It appears that more electron-donating supporting ligands facilitate the transformation.27 In this particular case, the first generation indenylidene complex **M2** led to higher yield than reactions using the second-, and third- generation of metathesis pre-catalysts (**M4** and **M5**), indicating that the nature of the leaving group in these ruthenium catalysts has a profound influence on catalyst activity/stability (Table 1, entry 1 vs 4-5), observations not entirely surprising in light of the mechanistic work already performed on olefin metathesis.1,9 The reaction using **M6** or **Caz-1** as the catalysts led to trace and moderate conversions, respectively (Table 1, entries 6-7). For comparison, results obtained with the Grubbs catalysts are also included. The first-generation Grubbs ruthenium catalyst exhibited an exclusive regioselectivity and resulted in higher conversion than when using the second-generation Grubbs ruthenium catalyst (Table 1, entries 8-9). It is worth noting that the indenylidene catalyst **M2** showed slightly higher catalytic efficiency than first-generation Grubbs catalyst within 2h in this case, as monitored by 1H NMR (Table 1, entries 10-11). The former complex (**M2**) is particularly attractive due to its facile preparation and relatively low cost.11

Table 1. Optimization of the Reaction Conditions for Different Silanesa



|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Entry | Cat. | [Si] | T (℃) | Time | Yield (%)*b* |
| 1 | **M2** | Et2SiH2 | rt | 6 | >99 |
| 2 | **M1** | Et2SiH2 | rt | 6 | 29 |
| 3 | **M3** | Et2SiH2 | rt | 6 | 81 |
| 4 | **M4** | Et2SiH2 | rt | 6 | 51 |
| 5 | **M5** | Et2SiH2 | rt | 6 | 94 |
| 6 | **M6** | Et2SiH2 | rt | 6 | trace |
| 7 | **Caz-1** | Et2SiH2 | rt | 6 | 47 |
| 8 | **G**-**I** | Et2SiH2 | rt | 6 | >99 |
| 9 | **G**-**II** | Et2SiH2 | rt | 6 | 40 |
| 10 | **M2** | Et2SiH2 | rt | 2 | 98 |
| 11 | **G-I** | Et2SiH2 | rt | 2 | 95 |
| 12c | **M2** | Ph2SiH2 | 60 | 18 | 93 |
| 13c,d | **M2** | PhSiH3 | 60 | 18 | 99 |
| 14c | **M2** | Et3SiH | 60 | 18 | - |
| 15c | **M2** | Ph3SiH | 60 | 18 | - |

a Reaction conditions: **1a** (0.2 mmol, 1 eq.), **2** (0.3 mmol, 1.5 eq.), Ru catalyst (0.25 mol%), 0.1 ml CDCl3, under Ar. b NMR yields (Cyclohexane as internal standard). c 1 mol% of **M2**. d 1.2 eq. of **2.**

Encouraged by the above results, the use of Ph2SiH2, as a challenging hydrogen source,18a,22,24 was examined in combination with **M2** in the reduction reaction. In addition, diphenylsilane is the optimal candidate because of its low price and stable intermediates.17d The hypothesis here was that larger silanes might lead to higher product selectivity in the hydrosilylation reaction. We were then delighted to see that 1.5 eq. of the bulky Ph2SiH2 reacted with quinoline in the presence of **M2** at 60 ℃, affording 93% of 1,2-dihydroquinoline as the sole regio isomer (Table 1, entry 12). This reagent was examined to probe the limitation of the system in terms of silane stereo-electronic properties. This is the first case where such a bulky silane has been successfully used in the 1,2-hydrosilylation, extending the scope beyond limitations of existing catalytic systems. As we expected, the olefin metathesis catalyst was competent in the 1,2-hydrosilylation using PhSiH3 as hydride donor, giving the corresponding 1-(phenylsilyl)-1,2-dihydroquinoline in 99% NMR yield (Table 1, entry 13). Unfortunately, **M2** is inactive when employing tertiary silanes at 60 ℃ (Table 1, entries 14-15). Here it appears a limit has been reached in terms of steric bulk of the H-delivery agent.

Scheme 2. 1,2-Selective Hydrosilylation of Quinoline Derivativesa



a Reaction conditions: **1** (0.2 mmol, 1 eq.), **2** (0.3 mmol, 1.5 eq.), **M2** (0.25 mol%), 0.1 ml CDCl3 or C6D6, 6h, under Ar. The yield was calculated by 1H NMR analysis using cyclohexane as an internal standard. b **M2** (1 mol%), 60℃, neat, 18h, under Ar. c **2** (0.24 mmol, 1.2 eq.), **M2** (1 mol%), 60℃, neat, 18h. d 0.5 mmol of **1**.

The scope of quinoline derivatives reacting with different silanes by employing **M2** was explored under the optimal conditions. In general, almost all examined substrates led from high to excellent yields. Among these examples, the reaction can be achieved with complete conversion when using 0.25 mol% of **M2** with Et2SiH2 as the hydride donor in a reaction time of 6 hours (Scheme 2, **3a**-**3h**). Quantitative yields of **3a-c** were obtained when increasing the amount of substrate to 0.5 mmol. Compared to current reported catalysts18a,19-20,22-24, **M2** exhibited higher efficiency in the 1,2-hydrosilylation. Notably, when a quinoline derivative substituted with a strongly electron-donating group (-OMe) was used, an 83% yield of **3e** was obtained after 6 hours, while prolonging the time to 18 hours achieved complete conversion, indicating advantageous catalyst lifetime properties. The reaction is sensitive to electronic effects induced by substituents on the quinoline framework. By comparison, unsubstituted quinolines led to higher yields than quinoline derivatives with electron donating or electron withdrawing groups (Scheme 2, **3i** vs **3j**-**3m**). The yield is dramatically eroded when 6-methoxyquinoline was reacted with diphenylsilane, leading to a 35% yield of 1,2-hydrosilylation product. The halogen-substituted quinolines were well tolerated under these reaction conditions, which led to product **3m** in 71% yield. Moreover, various quinolines provided high regioselectivity with Ph2SiH2 at 1 mol% catalyst loading. In addition, quinoline derivatives were also subjected to regioselective 1,2-hydrosilylation with primary silane, which provided 87-99% yields under the optimized reaction conditions (Scheme 2, **3n**-**3p**).

Scheme 3. 1,2-Selective Hydrosilylation of N-heterocyclesa



a Reaction conditions: **1** (0.2 mmol, 1 eq.), **2** (0.3 mmol, 1.5 eq.), **M2** (0.25 mol%), C6D6 (0.1 mL), 6h, under Ar. The yield was calculated by 1H NMR analysis using cyclohexane as an internal standard. b **M2** (1 mol%), 18h. c **2** (0.24 mmol, 1.2 eq.), **M2** (1 mol%). d **2** (0.4 mmol, 2 eq.). e 0.5 mmol of **1**.

Encouraged by this initial success, various N-heteroarenes were subjected to the catalytic 1,2-hydrosilylation with silanes in the presence of **M2** (Scheme 3). Isoquinolines reacted with primary and secondary silanes to quantitatively and selectively give products **4a**-**4d**, respectively. It is worth mentioning that, the double-addition product **4c** was formed instead of the mono-adduct when we employed PhSiH3 as the hydride donor, in a subsequent hydrosilylation of the initial product (1,2-dihydroisoquinoline)SiH2Ph.21 Here the silane selection issue is clearly key in addressing the observed product selectivity. In addition, quinoxaline and quinazoline reacting with Et2SiH2 lead to 82%-99% yield of double-hydrosilylation products **4e-4f** under the optimal conditions, respectively. Unexpectedly, when the hydrosilylation reaction was performed using 1,5-naphthyridine as starting material, a single 1,2-hydrosilylation product **4g** was obtained in complete conversion. We targeted the double-hydrosilylation product by prolonging the reaction time or increasing the catalyst loading, but the single N-sila functionalized compound **4g** remained the main obtained product after 48h. Replacing Et2SiH2 by Ph2SiH2 or PhSiH3 provided **4h**-**4i** in only 46-71% yields at 60℃ and requires longer reaction times. 2-Methyl-benzimidazole and benzothiazole can also undergo hydrosilylation, leading to 41-90% conversion of **4j** and **4k**. Dearomative hydrosilylation of pyrazine resulted in the corresponding 1,2,3,4-tetrahydropyrazine product **4l** in a 50% yield. Likewise, the hydrosilylation of pyridine and 3-chloro pyridine was sluggish under the present conditions, resulting in 19-42% yields after 36h (**4n** and **4m**).

We next turned our attention to the reaction mechanism(Scheme 4). Based on previous reports and experimental results, 6a, 18, 20 we performed a reaction using equal amounts of quinoline and **M2**, observing no reactivity (Scheme 4, a). When **M2** is reacted with 5 equiv. of Et2SiH2 in the absence of quinoline, hydride complexes **5**–**7** are the dominant ruthenium species, formed after a brief induction period by dissociation of free PCy3 and ligand exchange monitored *in situ*. When reducing the amount of silane to 1 equiv., traces of dihydroruthenium complex **6** were still observed. This result suggests that **6** may be an intermediate or active species involved in the catalytic cycle (Scheme 4, b; SI, Scheme S1). Analysis of the stoichiometric reactions by 31P NMR spectroscopy confirms that phosphine dissociation is an important step in the reaction sequence.10b To possibly simplify the reaction system, we employed the less active PPh3-bearing **M1** instead of **M2**. To our surprise, under very simple conditions the η5-indenyl-bearing ruthenium complex **8** was observed as the main compound when the reaction was perform with complex **M1** and 1 equiv. of Et2SiH2, displaying the characteristic two doublet signals at δ 50.57 ppm (d, *J* = 45.3 Hz) and 43.23 ppm (d, *J* = 45.1 Hz) in the 31P NMR spectrum (Scheme 4, c; SI, Scheme S2).9b However, catalyst **8** proved inactive for the hydrosilylation reaction involving Et2SiH2 under standard conditions. This result could explain why only 29% of the quinoline was hydrosilylated when **M1** was used as catalyst, as mentioned above. Here productive catalysis competes with catalyst deactivation yet this outcome could prove beneficial as it offers a simple synthetic route to **8**. Finally, we examined how the reaction proceeded using our model reaction when mediated by **M2**. In addition to the hydrosilylation product, compound **7** was the main entity detected, supporting the fact that it may be the catalyst resting state (Scheme 4, d; SI, Scheme S3). The commercially available complexes [Ru(PPh3)3H2(CO)] and [Ru(PCy3)2ClH(CO)] were employed in the hydrosilylation reaction, and high yields were obtained after 18 hours, using the current conditions, which again suggests the ruthenium hydride intermediate **I** may be the active species in this reaction (Scheme 4, e and f).

Scheme 4. Stoichiometric Experiments and Possible Mechanism



To place these stoichiometric/monitoring experiments in the context of a catalytic cycle, the active species **I** is generated by dissociation of PCy3 and ligand exchange in the presence of silane. According to the experimental results, we propose that a ruthenium dihydride species participates in the cycle as an active intermediate. Quinoline **1a** coordinates to ruthenium species **I**, leading to intermediate **III** via hydrogen transfer. Intermediate **IV** undergoes release of hydrosilylation product **3a** via *σ*‑bond metathesis involving a second Et2SiH2 (Scheme 4, B).

To demonstrate the efficiency of this methodology, we performed a gram-scale experiment using quinoline **1a** that provided the 1,2-hydrosilylation product **3a** in quantitative yield (Scheme 5a). Synthetic applications involving N-silylhydroquinoline and their derivatives were further examined (Scheme 5b). Isolated N-benzoyl derivative **9** was successfully obtained using an *in situ* generated **3a** and **3i** under mild conditions, resulting in high isolated yield. Furthermore, reaction of 2-(diethylsilyl)-1,2-dihydroisoquinoline formed *in situ* with 4-toluenesulfonyl azide (TsN3) **10** resulted in an 86% yield of the desired product **11**. This method exhibiting significantly higher efficiency than the previously reported work.17d

Scheme 5. Gram-scale Reaction and Synthetic Applications



In conclusion, we report a highly regioselective 1,2-hydrosilylation protocol using metathesis active ruthenium complexes as catalysts. The first-generation indenylidene-type catalyst clearly acts as pre-catalyst in a non-metathesis reaction and this with slightly higher efficiency than Grubbs-type congeners. This protocol allows for the efficient dearomatization of a broad scope of substituted quinolines and other N-heteroarenes with a catalyst loading as low as 0.25 mol%, in short reaction time and under mild conditions. This method is not only applicable to primary silanes as hydrogen donors, but also results in good to excellent yields with challenging bulkier secondary silanes. Furthermore, we propose a possible mechanism based on a series of stoichiometric experiments which include the monitoring of ruthenium species involved in the catalytic cycle.

EXPERIMENTAL SECTION

**General Information.** All manipulations were carried out under argon, in vials. Solvents and reagents were used as received without any further purification or distillation. All catalysts, silanes, quinoline and their derivatives were purchased from Umicore, Strem, Sigma, TCI or Fluorochem. 1H NMR and 13C NMR were recorded in CDCl3 or C6D6 at room temperature on Bruker spectrometer (300 MHz or 400 MHz). Chemical shifts (ppm) are referenced to the residual solvent peak. Coupling constants (*J*) are given in Hertz. Abbreviations used in the designation of the signals: s = singlet, br s = broad singlet, d = doublet, br d = broad doublet, dd = doublet of doublets, ddd = doublet of doublets of doublets, m = multiplet, td = triplet of doublets, tt = triplet of triplets, q = quadruplet, qt = quadruplet of triplets, hept = heptet.

**General optimization procedure for 1,2-hydrosilylation of quinoline react with Et2SiH2.** A 4-mL screwcap vial equipped with a septum cap and a stirring bar was charged with quinoline (0.2 mmol, 1 eq.), diethylsilane (0.3 mmol, 1.5 eq.), and **M2** (0.25 mol% in 100 µl CDCl3 or C6D6) in the glovebox. The reaction vial was taken out from the glovebox and stirred at room temperature while being protected from light for 6 hours. Afterwards, the reaction was taken inside the glove box, where the internal standard cyclohexane (0.2 mmol) was added via syringe. Then 100 µl CDCl3 or C6D6 was added into the reaction mixture and stirred for 1 minute. The mixture solution was transferred to a NMR tube and used for NMR analyses. All experimental procedures were conducted inside a glovebox.18a

**General optimization procedure for 1,2-hydrosilylation of quinoline react with different silanes.** A 4-mL screwcap vial equipped with a septum cap and a stirring bar was charged with quinoline (0.2 mmol, 1 eq.), Ph2SiH2 (0.3 mmol, 1.5 eq.) or PhSiH3 (0.24 mmol, 1.2 eq.), and **M2** (1 mol% in 100 µl CDCl3 or C6D6) in the glovebox. The reaction vial was taken out from the glovebox and stirred at 60℃ while protected from light for a given time. The subsequent experimental procedure follows the one above.18a

**General procedure to the synthesis of compound 9.** The 1,2-hydrosilylation product **3a** was prepared according to the optimal condition. Then benzoyl chloride (0.6 mmol, 1.2 equiv) with a catalytic amount of I2 (0.05 mmol, 10 mol%) was slowly added into the above reaction mixture at 0℃. The mixture was allowed to react at room temperature for 6 h and was then quenched by adding Na2SO3 (0.075 mmol, 0.15 equiv.). Subsequently, this quenched crude solution was dried via evaporation under reduced pressure, and purified by column chromatography on silica gel (ethyl acetate/hexane = 1/4) to give the corresponding phenyl(quinolin-1(2*H*)-yl)methanone **9**.22

**General procedure to the synthesis of compound 11.** A 4-mL screwcap vial equipped with a septum cap and a stirring bar was charged with quinoline (0.5 mmol, 1 eq.), Et2SiH2 (0.75 mmol, 1.5 eq.) and **M2** (0.25 mol% in 100 µl C6D6) in the glovebox. The reaction vial was taken out from the glovebox and stirred at room temperature while being protected from light for 6 hours. Then to the crude solution was added tosyl azide at room temperature inside the glovebox and a NMR spectrum recorded after 2 h. The resulting mixtures were quenched by MeOH addition, silica filter, and wash with DCM. The resulting crude mixture was purified by column chromatography (ethyl acetate/hexane = 1/4) to give the corresponding 4-methyl-N-(quinolin-2(1*H*)-ylidene)benzenesulfonamide **11**.17d

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Experimental procedures, additional optimization experiments, mechanistic experiments, compound characterization data and copies of the NMR spectra. (PDF)

AUTHOR INFORMATION

Corresponding Author

\* Steven P. Nolan − Department of Chemistry and Center for Sustainable Chemistry, Ghent University, 9000Gent, Belgium; orcid.org/0000-0001-9024-2035; Email: Steven.Nolan@ Ugent.be

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REFERENCES

(1) (a) Grubbs, R. H.; Wenzel, A. G.; O’Leary, D. J.; Khosravi, E.; Eds.; Handbook of Metathesis, 2nd ed.; Wiley-VCH: Weinheim, **2015.** (b) Kajetanowicz, A.; Grela, K. Nitro and Other Electron Withdrawing Group Activated Ruthenium Catalysts for Olefin Metathesis Reactions. *Angew. Chem. Int. Ed.* **2021**, *60*, 13738–13756. (c) Vecchio, A. D.; Smallman, H. R.; Morvan, J.; McBride, T.; Browne, D. L.; Mauduit, M. Challenges Arising from Continuous-Flow Olefin Metathesis. *Angew. Chem. Int. Ed.* **2022**, *61*, e20220956. (d) Blanco, C. O.; Fogg, D. E. Water-Accelerated Decomposition of Olefin Metathesis Catalysts, *ACS Catal*. **2023**, 13, 1097−1102.

(2) (a) Sathe, D.; Zhou, J.; Chen, H.; Su, H.-W.; Xie, W.; Hsu, T.-G.; Schrage, B. R.; Smith, T.; Ziegler, C. J.; Wang, J. Olefin Metathesis-based Chemically Recyclable Polymers Enabled by Fusedring Monomers. *Nat. Chem.* **2021**, *13*, 743−750 (b) Berger, O.; Battistella, C.; Chen, Y.; Oktawiec, J.; Siwicka, Z. E.; Tullman-Ercek, D.; Wang, M.; Gianneschi, N. C. Mussel Adhesive-Inspired Proteomimetic Polymer. *J. Am. Chem. Soc.* **2022**, *144*, 4383−4392.

(3) (a) Higman, C. S.; Lummiss, J. A. M.; Fogg, D. E. Olefin Metathesis at the Dawn of Implementation in Pharmaceutical and Specialty-Chemicals Manufacturing. *Angew. Chem. Int. Ed.* **2016**, *55*, 3552–3565. (b) Schunck, N. S.; Mecking, S. In vivo Olefin Metathesis in Microalgae Upgrades Lipids to Building Blocks for Polymers and Chemicals. *Angew. Chem. Int. Ed.* **2022**, *61*, e202211285. (c) Fischer, S.; Ward, T. R.; Liang, A. D. Engineering a Metathesis-Catalyzing Artificial Metalloenzyme Based on HaloTag. *ACS Catal.* **2021**, *11*, 6343−6347.

(4) (a) Grubbs, R. H. Olefin-Metathesis Catalysts for the Preparation of Molecules and Materials, *Angew. Chem. Int. Ed.* **2006**, *45*, 3760–3765. (b) Schrock, R. R. Multiple Metal–Carbon Bonds for Catalytic Metathesis Reactions. *Angew. Chem. Int. Ed.* **2006**, *45*, 3748–3759. (c) Chauvin, Y. Olefin Metathesis: The Early Days. A*ngew. Chem. Int. Ed*. **2006**, *45*, 3741–3747.

(5) Alcaide, B.; Almendros, P.; Luna, A. Grubbs’ Ruthenium-Carbenes Beyond the Metathesis Reaction: Less Conventional Non-Metathetic Utility. *Chem. Rev.* **2009**, *109*, 3817–3858.

(6) (a) Bokka, A.; Hua, Y.; Berlin, A. S.; Jeon, J. Mechanistic Insights into Grubbs-Type Ruthenium-Complex-Catalyzed Intramolecular Alkene Hydrosilylation: Direct *σ*-Bond Metathesis in the Initial Stage of Hydrosilylation. *ACS Catal.* **2015**, *5*, 3189−3195. (b) Dragutan, V.; Dragutan, I.; Delaude, L.; Demonceau, A. NHC–Ru Complexes—Friendly Catalytic Tools for Manifold Chemical Transformations. *Coord. Chem. Rev.* **2007**, *251*, 765–794. (c) Bokka, A.; Jeon, J. Regio- and Stereoselective Dehydrogenative Silylation and Hydrosilylation of Vinylarenes Catalyzed by Ruthenium Alkylidenes. *Org. Lett.* **2016**, *18*, 5324−5327.

(7) (a) Fustero, S.; Lázaro, R.; Herrera, L.; Rodríguez, E.; Mateu, N.; Barrio, P. Asymmetric Allylation/Ring Closing Metathesis: One-Pot Synthesis of Benzo-fused Cyclic Homoallylic Amines. Application to the Formal Synthesis of Sertraline Derivatives. *Org. Lett.* **2013**, *15*, 3770-3773. (b) Renom-Carrasco, M.; Gajewski, P.; Pignataro, L.; de Vries, J. G.; Piarulli, U.; Gennari, C.; Lefort, L. Asymmetric Transfer Hydrogenation of Ketones with Modified Grubbs Metathesis Catalysts: On the Way to a Tandem Process. *Adv. Synth. Catal.* **2016**, *358*, 515–519.

(8) (a) Kusy, R.; Grela, K. E- and Z‑Selective Transfer Semihydrogenation of Alkynes Catalyzed by Standard Ruthenium Olefin Metathesis Catalysts. *Org. Lett.* **2016**, *18*, 6196−6199. (b) Koduri, N. D.; Wang, Z.; Cannell, G.; Cooley, K.; Lemma, T. M.; Miao, K.; Nguyen, M.; Frohock, B.; Castaneda, M.; Scott, H.; Albinescu, D.; Hussaini, S. R. Enaminones via Ruthenium-Catalyzed Coupling of Thioamides and *α*‑Diazocarbonyl Compounds. *J. Org. Chem.* **2014**, *79*, 7405−7414.

(9) (a) Manzini, S.; Fernández-Salas, J. A.; Nolan. S. P. From a Decomposition Product to an Efficient and Versatile Catalyst: The [Ru(η5‑indenyl)(PPh3)2Cl] Story. *Acc. Chem. Res.* **2014,** *47*, 3089−3101. (b) Manzini, S.; Urbina-Blanco, C. A.; Poater, A.; Slawin, A. M. Z.; Cavallo, L.; Nolan, S. P. From Olefin Metathesis Catalyst to Alcohol Racemization Catalyst in One Step. *Angew. Chem. Int. Ed.* **2012**, *124*, 1066–1069.

(10) (a) Boeda, F.; Clavier, H.; Nolan, S. P. Ruthenium–indenylidene Complexes: Powerful Tools for Metathesis Transformations. *Chem. Commun.* **2008**, 2726–2740. (b) Urbina-Blanco, C. A.; Manzini, S.; Gomes, J. P.; Doppiu, A.; Nolan, S. P. Simple Synthetic Routes to Ruthenium–indenylidene Olefin Metathesis Catalysts. *Chem. Commun.* **2011**, *47*, 5022–5024. (c) Lozano-Vila, A. M.; Monsaert, S.; Bajek, A.; Verpoort, F. Ruthenium-Based Olefin Metathesis Catalysts Derived from Alkynes, *Chem. Rev.* **2010**, *110*, 4865–4909.

(11) (a) Fürstner, A.; Guth, O.; Düffels, A.; Seidel, G.; Liebl, M.; Gabor, B.; Mynott, R. Indenylidene Complexes of Ruthenium: Optimized Synthesis, Structure Elucidation, and Performance as Catalysts for Olefin Metathesis–Application to the Synthesis of the ADE-Ring System of Nakadomarin A. *Chem. Eur. J.* **2001**, *7*, 4811-4820. (b) Schotten, C.; Plaza, D.; Manzini, S.; Nolan, S. P.; Ley, S. V.; Browne, D. L.; Lapkin, A. Continuous Flow Metathesis for Direct Valorization of Food Waste: An Example of Cocoa Butter Triglyceride. *ACS Sustainable Chem. Eng.* **2015**, *3*, 1453−1459.

(12) (a) Bull, J. A.; Mousseau, J. J.; Pelletier, G.; Charette, A. B. Synthesis of Pyridine and Dihydropyridine Derivatives by Regio- and Stereoselective Addition to N-Activated Pyridines. *Chem. Rev.* **2012**, *112*, 2642−2713. (b) Jeong, J.; Heo, J.; Kim, D.; Chang, S. NHC-Catalyzed 1,2-Selective Hydroboration of Quinolines. *ACS Catal.* **2020**, *10*, 5023−5029. (c) Zhang, Y.; Sim, J. H.; MacMillan, S. N.; Lambert, T. H. Synthesis of 1,2-Dihydroquinolines via Hydrazine-catalyzed Ring-closing Carbonyl-olefin Metathesis. *Org. Lett.* **2020**, *22*, 6026−6030.

(13) (a) Krygowski, T. M.; Cryănski, M. K. Structural Aspects of Aromaticity. *Chem. Rev.* **2001**, *101*, 1385. (b) McLaughlin, M. F.; Massolo, E.; Liu, S.; Johnson, J. S. Enantioselective Phenolic *α*‑Oxidation Using H2O2 via an Unusual Double Dearomatization Mechanism. *J. Am. Chem. Soc.* **2019**, *141*, 2645−2651. (c) Zeng, Z.; Liu, Y.; Huang, W.; Shreeve, J. M.; Tang, Y. Radical-mediated C–N Bond Activation in 3,5-Diamino-4-nitro-1*H*-pyrazole Towards High-energy and Insensitive Energetic Materials. *J. Mater. Chem. A* **2022**, *10*, 8268–8272. (d) Roche, S. P.; Porco Jr., J. A. Dearomatization Strategies in the Synthesis of Complex Natural Products. *Angew. Chem. Int. Ed.* **2011**, *50*, 4068-4093.

(14) (a) Dudnik, A. S.; Weidner, V. L.; Motta, A.; Delferro, M.; Marks, T. J. Atom-efficient Regioselective 1,2-Dearomatization of Functionalized Pyridines by an Earth-abundant Organolanthanide Catalyst. *Nat. Chem.* **2014**, *6*, 1100-1107. (b) Liu, J.; Chen, J.-Y.; Jia, M.; Ming, B.; Jia, J.; Liao, R.-Z.; Tung, C.-H.; Wang, W. Ni–O Cooperation versus Nickel(II) Hydride in Catalytic Hydroboration of N-Heteroarenes. *ACS Catal.* **2019**, *9*, 3849-3857.

(15) (a) Lee, S.-H.; Gutsulyak, D. V.; Nikonov, G. I. Chemo- and Regioselective Catalytic Reduction of N-Heterocycles by Silane. *Organometallics* **2013**, *32*, 4457-4464. (b) Bähr, S.; Simonneau, A.; Irran, E.; Oestreich, M. An Air-Stable Dimeric Ru–S Complex with an NHC as Ancillary Ligand for Cooperative Si–H Bond Activation. *Organometallics* **2016**, *35*, 925-928. (c) Bahr, S.; Oestreich, M. A Neutral RuII Hydride Complex for the Regio- and Chemoselective Reduction of N-Silylpyridinium Ions. *Chem. Eur. J.* **2018**, *24*, 5613-5622. (d) Petrushko, W. D.; Nikonov, G. I. Mono(hydrosilylation) of N-Heterocycles Catalyzed by B(C6F5)3 and Silylium Ion.  *Organometallics* **2020**, *39*, 4717-4722.

(16) (a) Luo, L.; Tang, J.; Sun, R.; Li, W.; Zheng, X.; Yuan, M.; Li, R.; Chen, H.; Fu, H. Direct C–H Sulfonylimination of Pyridinium Salts. *Org. Lett.* **2022**, *24*, 2821−2825. (b) Jo, D. G.; Kim, C.; Lee, S.; Yun, S.; Joung, S. Synthesis of Cyclic N-Acyl Amidines by [3 + 2] Cycloaddition of N-Silyl Enamines and Activated Acyl Azides. *Molecules* **2022**, *27*, 1696. (c) Cao, V. D.; Kim, H.; Kwak, J.; Joung, S. (3 + 2) Cycloaddition Reaction of the Endocyclic N-Silyl Enamine and N,N’-Cyclic Azomethine Imine. *Org. Lett.* **2022**, *24*, 1974−1978.

(17) (a) Königs, C. D. F.; Klare, H. F. T.; Oestreich, M. Catalytic 1,4-Selective Hydrosilylation of Pyridines and BenzannulatedCongeners. *Angew. Chem. Int. Ed.* **2013**, *52*, 10076-10079. (b) Gutsulyak, D. V.; van der Est, A.; Nikonov, G. I. Facile Catalytic Hydrosilylation of Pyridines. *Angew. Chem. Int. Ed.* **2011**, *50*, 1384-1387. (c) Osakada, K. 1,4-Hydrosilylation of Pyridine by Ruthenium Catalyst: A New Reaction and Mechanism. *Angew. Chem. Int. Ed.* **2011**, *50*, 3845-3846. (d) Cao, V. D.; Mun, S. H.; Kim, S. H.; Kim, G. U.; Kim, H. G.; Joung, S. Synthesis of Cyclic Amidines from Quinolines by a Borane-Catalyzed Dearomatization Strategy. *Org. Lett.* **2020**, *22*, 515−519.

(18) (a) Behera, D.; Thiyagarajan, S.; Anjalikrishna, P. K.; Suresh, C. H.; Gunanathan, C. Ruthenium(II)-Catalyzed Regioselective 1,2-Hydrosilylation of N-Heteroarenes and Tetrel Bonding Mechanism. *ACS Catal.* **2021**, *11*, 5885-5893. (b) Bories, C. C.; Barbazanges, M.; Derat, E.; Petit, M. Implication of a Silyl Cobalt Dihydride Complex as a Useful Catalyst for the Hydrosilylation of Imines. *ACS Catal.* **2021**, *11*, 14262-14273.

(19) (a) Ashby, E. C.; Goel, A. B. The Preparation of HMgX Compounds. *J. Am. Chem. Soc.* **1977**, *99*, 310– 311. (b) Ashby, E. C.; Goel, A. B. Preparation and Characterization of Alkylmagnesium Hydrides. *J. Chem. Soc. Chem. Commun.* **1977**, 169 –169.

(20) (a) Hill, M. S.; MacDougall, D. J.; Mahon, M. F. Magnesium Hydride-promoted Dearomatisation of Pyridine. *Dalton Trans.* **2010**, *39*, 11129–11131. (b) Hill, M. S.; Kociok-Kçhn, G.; MacDougall, D. J.; Mahon, M. F.; Weetman, C. Magnesium Hydrides and the Dearomatisation of Pyridine and Quinoline Derivatives. *Dalton Trans.* **2011**, *40*, 12500–12509.

(21) Intemann, J.; Bauer, H.; Pahl, J.; Maron, L.; Harder, S. Calcium Hydride Catalyzed Highly 1,2-Selective Pyridine Hydrosilylation. *Chem. Eur. J.* **2015**, *21*, 11452-11461.

(22) Jeong, J.; Park, S.; Chang, S. Iridium-catalyzed Selective 1,2-Hydrosilylation of N-Heterocycles. *Chem. Sci.* **2016**, *7*, 5362-5370.

(23) (a) Lortie, J. L.; Dudding, T.; Gabidullin, B. M.; Nikonov, G. I. Zinc-catalyzed Hydrosilylation and Hydroboration of N-Heterocycles. *ACS Catal.* **2017**, *7*, 8454−8459. (b) Wang, X.; Zhang, Y.; Yuan, D.; Yao, Y. Regioselective Hydroboration and Hydrosilylation of N-Heteroarenes Catalyzed by a Zinc Alkyl Complex. *Org. Lett.* **2020**, *22*, 5695−5700.

(24) Sahoo, R. K.; Sarkar, N.; Nembenna, S. Intermediates, Isolation and Mechanistic Insights into Zinc HydrideCatalyzed 1,2-Regioselective Hydrofunctionalization of N‑Heteroarenes. *Inorg. Chem.* **2023**, *62*, 304−317.

(25) Bories, C. C.; Gontard, G.; Barbazanges, M.; Derat, E.; Petit, M. Hydrido-Cobalt Complexes for the Chemo- and Regioselective 1,2- Silylative Dearomatization of N‑Heteroarenes. doi.org/10.1021/acs.orglett.3c00022.

(26) (a) Park, S. Recent Advances in Catalytic Dearomative Hydroboration of N-Heteroarenes. *ChemCatChem* **2020**, *12*, 3170− 3185. (b) Park, S.; Chang, S. Catalytic Dearomatization of N-Heteroarenes with Silicon and Boron Compounds. *Angew. Chem. Int. Ed.* **2017**, *56*, 7720−7738. (d) Liu, Z.; Chen, L.; Li, J.; Liu, K.; Zhao, J.; Xu, M.; Feng, L.; Wan, R.-z.; Li, W.; Liu, L. Oxidative C−H Functionalization of N-Carbamoyl 1,2-Dihydroquinolines. *Org. Biomol. Chem.* **2017**, *15*, 7600−7606. (e) Jeong, E.; Heo, J.; Jin, S.; Kim, D.; Chang, S. KOtBu-Catalyzed 1,2-Silaboration of N‑Heteroarenes to Access 2‑Silylheterocycles: A Cooperative Model for the Regioselectivity. *ACS Catal.* **2022**, *12*, 4898−4905.

(27) Manzini, S.; Poater, A.; Nelson, D. J.; Cavallo, L.; Slawin, A. M. Z.; Nolan, S. P. Insights into the Decomposition of Olefin Metathesis Precatalysts. *Angew. Chem. Int. Ed.* **2014**, *53*, 8995 –8999.

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