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Rhodium(III)-Catalyzed Alkenyl C−H Functionalization to Dienes and Allenes

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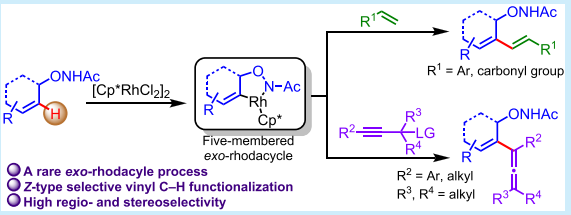
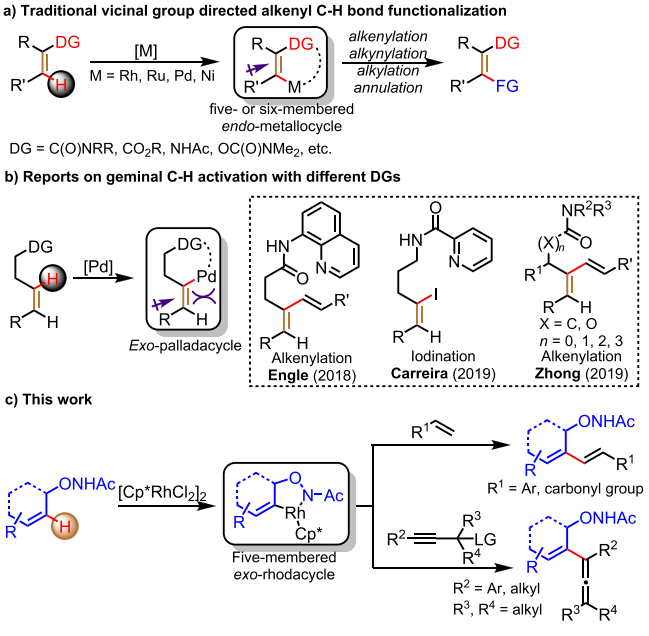
ABSTRACT: An oxyacetamide-directed Rh(III)-catalyzed *Z*-type alkenyl C−H functionalization through a rare *exo*-rhodacyle intermediate is described, forming multisubstituted dienes and allenes. A variety of alkenes and propargylic carbonate coupling partners are suitable for this transformation with high regio- and stereoselectivity. The synthetic utility is demonstrated by the selective late-stage modification of the *Z*-type natural products as well as the synthesis of the unnatural *β*-amino acid.



Since dienes and allenes are critical synthetic blocks to numerous important compounds, development of efficient approaches to synthesize functional alkenes is of great significance in the field of organic synthesis.[1] These compounds are traditionally synthesized by a Suzuki−Miyaura coupling reaction, Wittig reaction, or Horner−Wadsworth−Emmons reaction relying on prefunctionalized synthetic building blocks.[2] These methods suffered from disadvantages such as multistep syntheses, limited substrate scopes, and poor regioselectivity. Recently, transition-metal-catalyzed C−H functionalization has emerged as an effective approach in organic synthesis and medicinal chemistry by minimizing byproducts and prefunctionalization steps, and a series of C−C or C−X (O, N, S, etc.) bonds have been constructed efficiently.[3] Metallocycles are the key intermediates in selective transformations primarily formed via C−H bond activation with the aid of directing groups, consisting of *endo*- and *exo*-metallocycles depending on the position of the *π*-bonds.[4] In spite of the progress in direct alkenyl C−H bond functionalization directed by the vicinal groups, such as alkenylation,[5] alkynylation,[6] annulation,[7] and others,[8] most of those prefer the *endo*-metallocycles process of *E*-type olefins via the vicinal groups (Scheme 1a). However, the more challenging *Z*-type selective functionalization of alkenyl C−H bond via metallocycle process remains elusive.[9]

Z-type olefins to form the *endo*-metallocycle structure can increase the conformational free energy, which results in greater distortion of the C=C bond *π*-system during the formation process and reduced stability;[10] therefore, the alkenyl C−H bond functionalization for *Z*-type olefins is more likely through the *exo*-metallocycle process. To date, most of the alkenyl C−H activation was carried out by a five- or six-membered metallacycle pathway; a further size enlargement will make the bonds more rotatable, thus reducing the stability.[5−9] Besides, the propensity for *exo*-metallacycle formation can be increased by either eliminating the potential formation sites of *endo*-metallocycle or incorporating a suitable coordinating entity to promote chelation (formation of an extra 5- or 6-membered *exo*-metallocycle will restrain the *endo*-metallocycle and increase *exo*-metallocycle structural rigidity).[4c] As far as we are concerned, only a few reports with *exo*-metallocycle mechanisms have been revealed.[11−15] Dong and

Scheme 1. Alkenyl C−H Bond Functionalization



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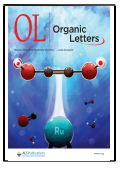

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others revealed outstanding strategies by using oxime as the *exo*-directing groups for the selective C(sp^3)−H acetoxylation, intramolecular alkoxylation, amidation, and fluorination via a five-membered *exo*-palladacycle.[12] Engle's group reported a C(sp^2)−H functionalization via a palladium-involved six-membered *exo*-palladacycle directed by *N,N*-bidentate auxiliary which was then removed by a nickel-catalyzed methanolysis to provide the corresponding ester.[13] Carreira et al. demonstrated the palladium-catalyzed C−H iodination and alkynylation of unactivated olefins by picolinamide as the directing group.[14] Zhong et al. have achieved alkenyl C−H bond functionalization of amides, carbamates, and alkenyl alcohols through weakly *O*-monodentate coordination (Scheme 1b).[15]

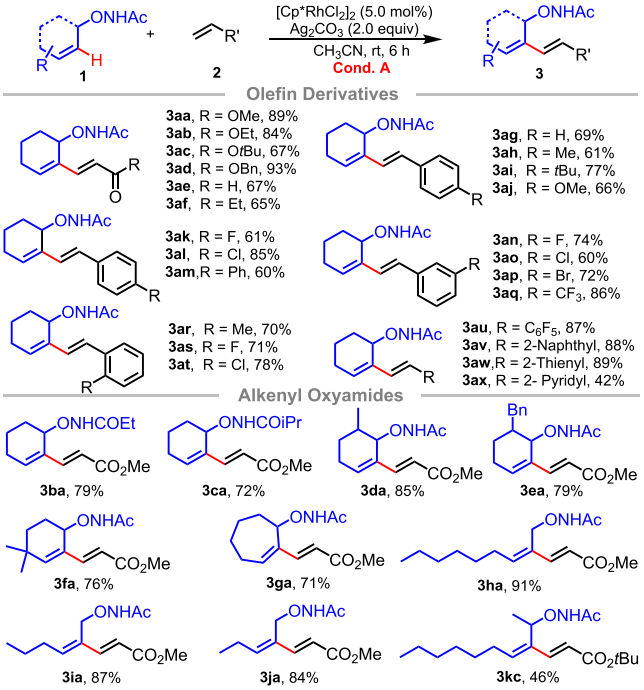
Oxyacetamide (−ONHAc) has been widely used as a directing group in the functionalization of aryl C(sp^2)−H bonds by Lu,[16] Wang,[17] You,[18] Glorius,[19] Yi,[20] and others.[21] Our group has also been committed to the application of −ONHAc group in the field of C−H activation and achieved selective synthesis of both *ortho*- and *para*-functional phenols.[22] Considering the importance of selective alkenyl C−H bond functionalization, we reported a facile and efficient −ONHAc-directed Rh(III)-catalyzed regio- and stereoselective alkenyl *β*-position C−H bond functionalization to synthesize dienes and allenes through a rare five-membered *exo*-rhodacycle process (Scheme 1c).

This work was commenced by investigating the coupling of 2-cyclohexen-1-oxyacetamide **1a** and methyl acrylate **2a** (see Table S1). The use of 5 mol % $[Cp^*RhCl_2]_2$ as a catalyst, 2.0 equiv of Ag_2CO_3 as an oxidant, and **2a** (3.0 equiv) as the coupling partner at room temperature in 1,2-dichloroethane (DCE) gave 1,3-diene **3aa** in the yield of 31%. After solvent screening, CH_3CN was found as a superior solvent by improving the yield to 89%. No reaction was proceeded without oxidant or catalyst.

With the optimized reaction conditions in hand, we went on to explore the scope of the substrates and coupling partners for the synthesis of trisubstituted 1,3-dienes (Scheme 2). All reaction afforded the desired dienes in good to excellent yields (42−93%) with high regio- and stereoselectivity. For acrylate coupling partners (**2b**−**2d**), the desired dienes were obtained in yields of 67%−93%. It is worth noting that acrolein **2e** and ethyl alkenyl ketone **2f** also succeeded in giving the conjugated dienes in 67% and 65% yields, respectively. For styrene coupling partners, this transformation showed good tolerance for a variety of substitutions at either *para*- (**3ag**−**3am**), *meta*- (**3an**−**3aq**), or *ortho*- (**3ar**−**3at**) positions, providing the dienes with 60−86% yields. Interestingly, − CF_3 substituted styrene and pentafluorostyrene proceeded smoothly, giving **3aq** and **3au** in 86% and 87% yield, respectively. For heterocyclic alkenyl coupling partners, the electronic property was critical for the reactivity: the electron-rich thiophene was quite reactive to afford **3aw** in 89% yield, while the electron-deficient pyridine only gave 42% yield (**3ax**).

Subsequently, different alkenyl oxyamide substrates were tested under the standard conditions. When substrates with propionyl and isobutyryl substituents were used, the target products **3ba** and **3ca** were obtained in the yield of 79% and 72%, respectively. Substrates with methyl and benzyl groups provided the corresponding 1,3-dienes **3da** and **3ea** with 85% and 79% yield, respectively. Notably, cyclohexene containing a quaternary carbon, which was widely presented in galantamine and drug molecules, gave the corresponding product **3fa** in 76% yield. Substrate with seven-membered ring gave the

Scheme 2. Variations of Alkenyl Oxyamides and Alkenes[a]



[a]Reaction conditions: 0.2 mmol of **1**, **2** (3.0 equiv), 5 mol % of $[Cp^*RhCl_2]_2$, and Ag_2CO_3 (2.0 equiv) in CH_3CN (1 mL) at rt for 6 h under N_2, isolated yield.

desired product **3ga** with 71% yield. When using acyclic alkenyl oxyamides, the reactions were also carried out smoothly to give the desired products **3ha**−**3ja** and **3kc** in yields of 46−91%.

Considering the similarity of reactivity between olefins and propargylic carbonates, we examined the coupling reaction of **1a** with propargylic carbonate **4a**. To our delight, after a detailed screening of additives, solvents, and temperatures (see Table S2), the optimized conditions were identified as 5.0 mol % $[Cp^*RhCl_2]_2$ with 2.0 equiv of KOAc in 1,2-dichloroethane (DCE) at 50 °C, giving **5aa** in 86% yield. A range of propargylic carbonates showed good reactivity under the optimized conditions, providing the corresponding tetra-substituted allenes in 41%−86% yields, as shown in Scheme 3. In general, propargylic carbonates with electron-donating substituents (**5ab**, **5ac**, and **5ai**) on the aryl moiety exhibited better reactivity than those with electron-withdrawing ones (**5ad**−**5ah**, **5aj**, and **5ak**). It is worth noting that when a strong electron-withdrawing substituent was applied a much lower yield of 41% was obtained (**5ah**). Heteroaryl-bearing propargylic carbonate **4m** gave the corresponding allene **5am** in 47% yield. The sterically hindered methyl and ethyl groups on the tertiary carbon of the propargylic carbonates depressed the reaction yields to 57% (**5an**) and 42% (**5ao**), respectively. Interestingly, alkyl propionate carbonate worked well and gave the corresponding allene **5ap** in 67% yield. Subsequently, a variety of alkenyl oxyamide substrates were tested, presenting good group tolerance to afford the desired allenes (**5ba**−**5fa**) in yields of 74−82%. Acyclic alkenyl oxyamides gave the corresponding allenes **5ha**−**5ja** in yields of 43%−51%. The results showed that the cyclic oxyamides has a higher rigid structure and is more stable when combined with the rhodium catalyst, which promotes the activity of the substrate under the

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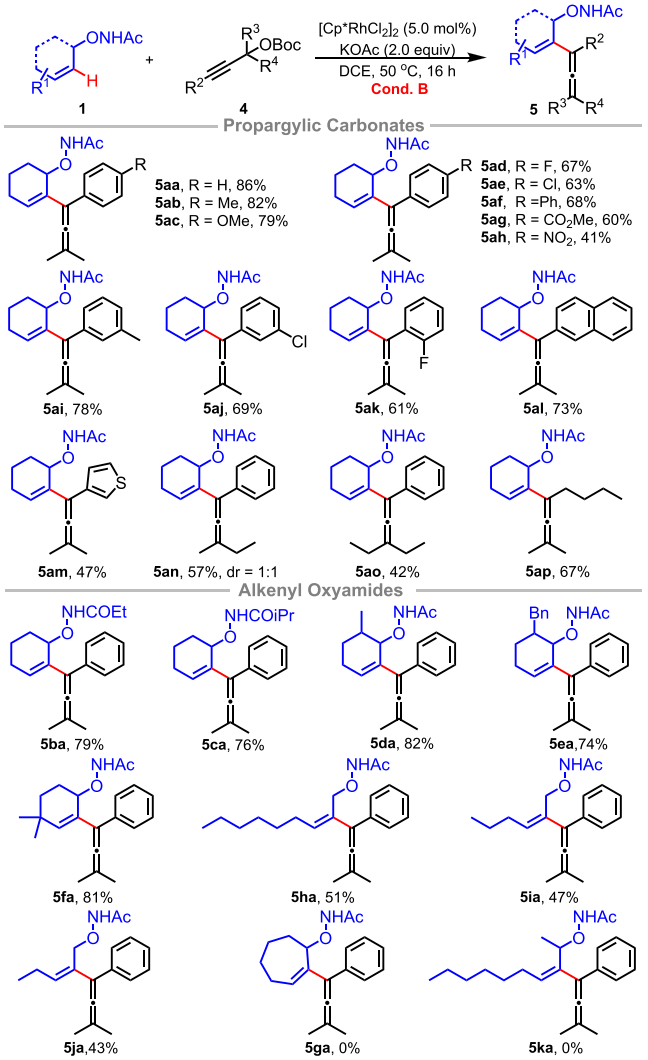
Scheme 3. Variations of Alkenyl Oxyamides and Propargylic Carbonates[a]



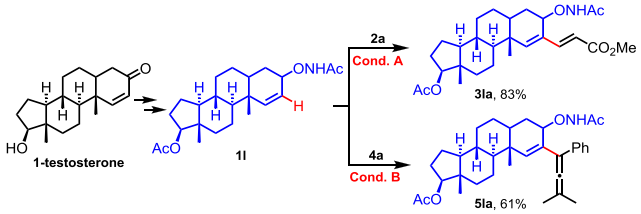
[a]Reaction conditions: 0.2 mmol of **1**, **4** (1.2 equiv), 5 mol % of $[Cp^*RhCl_2]_2$ and KOAc (2.0 equiv) in DCE (1 mL) at 50 °C for 16 h, isolated yield.

reaction conditions. However, no reaction was observed for the seven-membered cycloheptene substrate **1g** and acyclic alkenyl oxyamide **1k** under the optimized condition, probably due to the steric hindrance.

The mild reaction conditions and good substrate compatibility prompted us to apply this transformation to modify the existing clinical drugs and natural products. 1-Testosterone is used for treating male endogenous androgen deficiency or female functional uterine bleeding.[23] Steroid-derived oxyacetamide **1l** was synthesized from 1-testosterone as a representative molecule for diversified modifications. The desired 1,3-dienes **3la** and allene **5la** were successfully obtained in 83% and 61% yields, respectively (Scheme 4), revealing potential application in the late-stage modification of natural products.

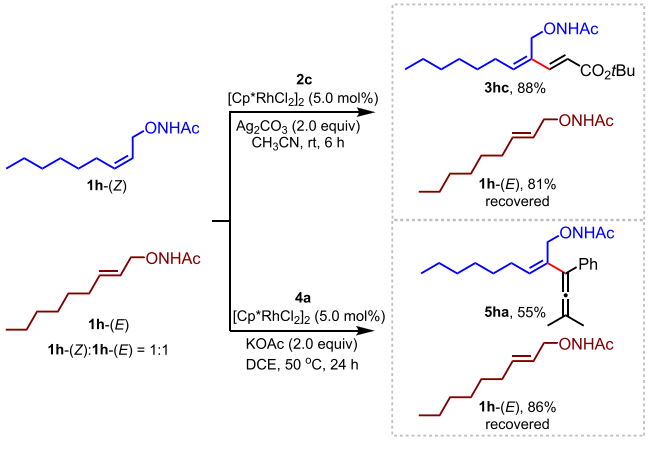
Given the ubiquity of olefins, their structure−activity relationship plays an important role in pharmacological research. To further explore the application of this transformation, we applied the standard reaction condition to an inseparable mixture of *Z*- and *E*-olefins **1h**. The *Z*-olefins

Scheme 4. Alkenyl C−H Modifications of 1-Testosterone Derivative



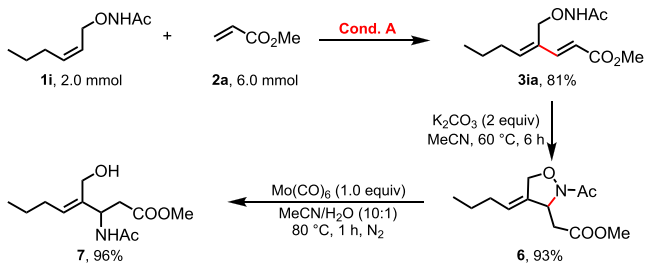
reacted smoothly and gave the desired diene **3hc** with 88% yield, while the unreacted *E*-isomers was successfully recovered in 81% yield. When the mixed olefins **1h** reacted with **4a**, 55% allene **5ha** was obtained by extending reaction time while 86% *E*-isomers was recovered, which can be applied to the selective separation of *Z*/*E* olefins as well (Scheme 5).

Scheme 5. *Z*/*E*-Selective Reaction of Olefins



Because of the success in producing the dienolates with −ONHAc group through our developed method, we designed a strategy for the efficient synthesis of *β*-amino acid (Scheme 6): **3ia** was obtained in high yield through this method and

Scheme 6. *β*-Amino Acid Synthesis



then cyclized by a one-pot intramolecular Michael addition to result in a unique structure isoxazolidine **6** which was converted to *β*-amino acid **7** in 96% yield by the reduction of the N−O bond with $Mo(CO)_6$.[24] Therefore, this method can be further expanded to be used in the synthesis of *β*-amino acids.

Control experiments were conducted to identify the reaction process (Scheme 7). First of all, η^3-rhodium complex **A** was isolated and its structure was confirmed by the X-ray diffraction. However, there was no reaction occurred when **A** was used as the catalyst, ruling out the possibility that the η^3-

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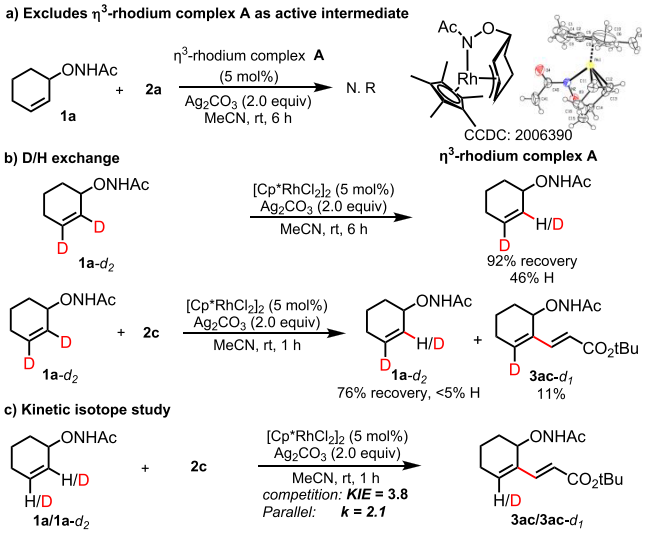
Scheme 7. Mechanistic Experiments



rhodium complex was the active intermediate in this reaction (Scheme 7a). Second, deuterated **1a**-d_2 was performed under standard conditions without alkene substrate, 54% deuterium on the β-carbon was retained, indicated that C−H activation was reversible in the absence of alkene coupling partner. However, < 5% protonation of **1a**-d_2 was observed when **2c** was added, suggesting that the C−H activation step may be the turnover-limiting step (Scheme 7b). Third, the competition and parallel experiment of **1a** and **1a**-d_2 with **2c** were conducted to measure the kinetic isotope effect, which gave the KIE value of 3.8 and k value of 2.1, indicating that the C−H cleavage might be the rate-determining step (Scheme 7c).

In summary, we have developed a Cp*Rh(III)-catalyzed Z-type alkenyl C−H functionalization to prepare multisubstituted dienes and allenes with −ONHAc as the directing group through a rare *exo*-rhodacycle process. This method was applied to a variety of alkenes and propargylic carbonates coupling partners featuring high regio- and stereoselectivity and good functional group compatibility. Such a method can also be utilized to the modification of drug molecules and the selective separation of olefin compounds with Z/E structure. Furthermore, the dienoate products can be converted to the corresponding β-amino acids efficiently, providing a new strategy for the synthsis of β-amino acids.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c03126.

Experimental procedures, characterization, and spectral data (PDF)

Accession Codes

CCDC 2006390 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Author Contributions

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Konno, T. *Stereoselective Synthesis of Drugs and Natural Products*; Wiley, 2013; Vol. 1, p 769. (b) Ma, S. *Chem. Rev.* **2005**, *105*, 2829. (c) Wu, S.; Huang, X.; Wu, W.; Li, P.; Fu, C.; Ma, S. *Nat. Commun.* **2015**, *6*, 7946.

(2) (a) Davidson, A. H.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1976**, 639. (b) Taylor, D. R. *Chem. Rev.* **1967**, *67*, 317.

(3) For selected reviews and examples, see: (a) Ackermann, L. *Acc. Chem. Res.* **2020**, *53*, 84. (b) Dong, Z.; Ren, Z.; Thompson, S. J.; Xu, Y.; Dong, G. *Chem. Rev.* **2017**, *117*, 9333. (c) Gandeepan, P.; Muller, T.; Zell, D.; Cera, G.; Warratz, S. *Chem. Rev.* **2019**, *119*, 2192.

(d) Gao, D. W.; Gu, Q.; Zheng, C.; You, S. L. *Acc. Chem. Res.* **2017**, *50*, 351. (e) Giri, R.; Shi, B. F.; Engle, K. M.; Maugel, N.; Yu, J. Q. *Chem. Soc. Rev.* **2009**, *38*, 3242. (f) Kim, H.; Chang, S. *Acc. Chem. Res.* **2017**, *50*, 482. (g) Park, Y.; Kim, Y.; Chang, S. *Chem. Rev.* **2017**, *117*, 9247. (h) Sambiagio, C.; Schonbauer, D.; Blieck, R.; Dao-Huy, T.; Pototschnig, G.; Schaaf, P.; Wiesinger, T.; Zia, M. F.; Wencel-Delord, J.; Besset, T.; Maes, B. U. W.; Schnurch, M. *Chem. Soc. Rev.* **2018**, *47*, 6603. (i) Wang, F.; Yu, S.; Li, X. *Chem. Soc. Rev.* **2016**, *45*, 6462. (j) Yang, L.; Huang, H. *Chem. Rev.* **2015**, *115*, 3468. (k) He, J.; Wasa, M.; Chan, K. S. L.; Shao, Q.; Yu, J.-Q. *Chem. Rev.* **2017**, *117*, 8754.

(4) (a) Gensch, T.; Hopkinson, M. N.; Glorius, F.; Wencel-Delord, J. *Chem. Soc. Rev.* **2016**, *45*, 2900. (b) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147. (c) Xu, Y.; Dong, G. *Chem. Sci.* **2018**, *9*, 1424.

(5) (a) Jiang, B.; Zhao, M.; Li, S. S.; Xu, Y. H.; Loh, T. P. *Angew. Chem., Int. Ed.* **2018**, *57*, 555. (b) Liang, Q. J.; Yang, C.; Meng, F. F.; Jiang, B.; Xu, Y. H.; Loh, T. P. *Angew. Chem., Int. Ed.* **2017**, *56*, 5091. (c) Meng, K.; Sun, Y.; Zhang, J.; Zhang, K.; Ji, X.; Ding, L.; Zhong, G. *Org. Lett.* **2019**, *21*, 8219. (d) Sun, Y.; Meng, K.; Zhang, J.; Jin, M.; Huang, N.; Zhong, G. *Org. Lett.* **2019**, *21*, 4868. (e) Tang, S.; Liu, K.; Liu, C.; Lei, A. *Chem. Soc. Rev.* **2015**, *44*, 1070.

(6) (a) Feng, C.; Loh, T. P. *Angew. Chem., Int. Ed.* **2014**, *53*, 2722. (b) Tan, E.; Quinonero, O.; Elena de Orbe, M.; Echavarren, A. M. *ACS Catal.* **2018**, *8*, 2166. (c) Zhao, T.; Qin, D.; Han, W.; Yang, S.; Feng, B.; Gao, G.; You, J. *Chem. Commun.* **2019**, *55*, 6118.

(7) (a) Kuppusamy, R.; Muralirajan, K.; Cheng, C.-H. *ACS Catal.* **2016**, *6*, 3909. (b) Shi, Z.; Koester, D. C.; Boultadakis-Arapinis, M.; Glorius, F. *J. Am. Chem. Soc.* **2013**, *135*, 12204. (c) Zhao, Y.; Li, S.; Zheng, X.; Tang, J.; She, Z.; Gao, G.; You, J. *Angew. Chem., Int. Ed.* **2017**, *56*, 4286. (d) Zhou, S.; Yan, B. W.; Fan, S. X.; Tian, J. S.; Loh, T. P. *Org. Lett.* **2018**, *20*, 3975. (e) Xu, Y.; Zheng, G.; Kong, L.; Li, X. *Org. Lett.* **2019**, *21*, 3402.

(8) (a) Chang, X. H.; Wang, Z. L.; Zhao, M.; Yang, C.; Li, J. J.; Ma, W. W.; Xu, Y. H. *Org. Lett.* **2020**, *22*, 1326. (b) Jiang, Y.; Li, P.; Wang, J.; Zhao, J.; Li, Y.; Zhang, Y.; Chang, J.; Liu, B.; Li, X. *Org. Lett.* **2020**, *22*, 438. (c) Liu, R. H.; Shen, Z. Y.; Wang, C.; Loh, T. P.; Hu, X. H. *Org. Lett.* **2020**, *22*, 944. (d) Shen, Z.-Y.; Cheng, J.-K.; Wang, C.; Yuan, C.; Loh, T.-P.; Hu, X.-H. *ACS Catal.* **2019**, *9*, 8128. (e) Yatabe, T.; Jin, X.; Mizuno, N.; Yamaguchi, K. *ACS Catal.* **2018**, *8*, 4969. (f) Yu, D. G.; Gensch, T.; de Azambuja, F.; Vasquez-Cespedes, S.; Glorius, F. *J. Am. Chem. Soc.* **2014**, *136*, 17722. (g) Parella, R.; Babu, S. A. *J. Org. Chem.* **2015**, *80*, 12379. (h) Parella, R.; Babu, S. A. *J. Org. Chem.* **2017**, *82*, 6550. (i) Wu, Z.; Fatuzzo, N.; Dong, G. *J. Am. Chem. Soc.* **2020**, *142*, 2715.

(9) (a) Aihara, Y.; Chatani, N. *J. Am. Chem. Soc.* **2013**, *135*, 5308. (b) Feng, C.; Loh, T. P. *Angew. Chem., Int. Ed.* **2013**, *52*, 12414. (c) Ilies, L.; Asako, S.; Nakamura, E. *J. Am. Chem. Soc.* **2011**, *133*, 7672. (d) Morimoto, M.; Miura, T.; Murakami, M. *Angew. Chem., Int. Ed.* **2015**, *54*, 12659. (e) Piou, T.; Rovis, T. *J. Am. Chem. Soc.* **2014**, *136*, 11292. (f) Wang, D.; Wang, F.; Song, G.; Li, X. *Angew. Chem., Int. Ed.* **2012**, *51*, 12348. (g) Wang, K.; Hu, F.; Zhang, Y.; Wang, J. *Sci. China: Chem.* **2015**, *58*, 1252. (h) Wu, L.; Wang, F.; Chen, P.; Liu, G. *J. Am. Chem. Soc.* **2019**, *141*, 1887. (i) Xie, F.; Qi, Z.; Yu, S.; Li, X. *J. Am. Chem. Soc.* **2014**, *136*, 4780. (j) Yu, C.; Zhang, J.; Zhong, G. *Chem. Commun.* **2017**, *53*, 9902. (k) Zhou, B.; Hu, Y.; Wang, C. *Angew. Chem., Int. Ed.* **2015**, *54*, 13659. (l) Yang, X.; Zheng, G.; Li, X. *Angew. Chem., Int. Ed.* **2019**, *58*, 322.

(10) (a) Mawo, R. Y.; Mustakim, S.; Jr, V. G. Y.; Hoffmann, M. R.; Smoliakova, I. P. *Organometallics* **2007**, *26*, 1801. (b) Makino, T.; Itoh, K. *J. Org. Chem.* **2004**, *69*, 395.

(11) (a) Kong, W. J.; Liu, Y. J.; Xu, H.; Chen, Y. Q.; Dai, H. X.; Yu, J. Q. *J. Am. Chem. Soc.* **2016**, *138*, 2146. (b) Tsai, H. C.; Huang, Y. H.; Chou, C. M. *Org. Lett.* **2018**, *20*, 1328. (c) Wang, Y.; Huang, Y.; Tsai, H.; Basha, R. S.; Chou, C. *Org. Lett.* **2020**, *22*, 6765.

(12) (a) Kang, T.; Kim, H.; Kim, J. G.; Chang, S. *Chem. Commun.* **2014**, *50*, 12073. (b) Mao, Y. J.; Lou, S. J.; Hao, H. Y.; Xu, D. Q. *Angew. Chem., Int. Ed.* **2018**, *57*, 14085. (c) Ren, Z.; Mo, F.; Dong, G. *J. Am. Chem. Soc.* **2012**, *134*, 16991. (d) Thompson, S. J.; Thach, D. Q.; Dong, G. *J. Am. Chem. Soc.* **2015**, *137*, 11586.

(13) Liu, M.; Yang, P.; Karunananda, M. K.; Wang, Y.; Liu, P.; Engle, K. M. *J. Am. Chem. Soc.* **2018**, *140*, 5805.

(14) (a) Schreib, B. S.; Carreira, E. M. *J. Am. Chem. Soc.* **2019**, *141*, 8758. (b) Schreib, B. S.; Fadel, M.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2020**, *59*, 7818.

(15) Meng, K.; Li, T.; Yu, C.; Shen, C.; Zhang, J.; Zhong, G. *Nat. Commun.* **2019**, *10*, 5109.

(16) (a) Hu, Z.; Tong, X.; Liu, G. *Org. Lett.* **2016**, *18*, 1702. (b) Liu, G.; Shen, Y.; Zhou, Z.; Lu, X. *Angew. Chem., Int. Ed.* **2013**, *52*, 6033. (c) Shen, Y.; Liu, G.; Zhou, Z.; Lu, X. *Org. Lett.* **2013**, *15*, 3366. (d) Zhou, Z.; Liu, G.; Chen, Y.; Lu, X. *Org. Lett.* **2015**, *17*, 5874. (e) Zhou, Z.; Liu, G.; Shen, Y.; Lu, X. *Org. Chem. Front.* **2014**, *1*, 1161.

(17) (a) Hu, F.; Xia, Y.; Ye, F.; Liu, Z.; Ma, C.; Zhang, Y.; Wang, J. *Angew. Chem., Int. Ed.* **2014**, *53*, 1364. (b) Zhang, H.; Wang, K.; Wang, B.; Yi, H.; Hu, F.; Li, C.; Zhang, Y.; Wang, J. *Angew. Chem., Int. Ed.* **2014**, *53*, 13234.

(18) Li, B.; Lan, J.; Wu, D.; You, J. *Angew. Chem., Int. Ed.* **2015**, *54*, 14008.

(19) (a) Lerchen, A.; Knecht, T.; Daniliuc, C. G.; Glorius, F. *Angew. Chem., Int. Ed.* **2016**, *55*, 15166. (b) Wang, X.; Gensch, T.; Lerchen, A.; Daniliuc, C. G.; Glorius, F. *J. Am. Chem. Soc.* **2017**, *139*, 6506. (c) Wang, X.; Lerchen, A.; Daniliuc, C. G.; Glorius, F. *Angew. Chem., Int. Ed.* **2018**, *57*, 1712. (d) Wang, X.; Lerchen, A.; Gensch, T.; Knecht, T.; Daniliuc, C. G.; Glorius, F. *Angew. Chem., Int. Ed.* **2017**, *56*, 1381. (e) Wang, X.; Li, Y.; Knecht, T.; Daniliuc, C. G.; Houk, K. N.; Glorius, F. *Angew. Chem., Int. Ed.* **2018**, *57*, 5520.

(20) (a) Chen, W.; Liu, F.-X.; Gong, W.; Zhou, Z.; Gao, H.; Shi, J.; Wu, B.; Yi, W. *Adv. Synth. Catal.* **2018**, *360*, 2470. (b) Chen, W.; Liu, F. X.; Bian, M.; Li, L.; Zhou, Z.; Yi, W. *J. Org. Chem.* **2019**, *84*, 15557. (c) Gao, H.; Sun, M.; Zhang, H.; Bian, M.; Wu, M.; Zhu, G.; Zhou, Z.; Yi, W. *Org. Lett.* **2019**, *21*, 5229. (d) Liu, F. X.; Chen, W.; Zhu, G.; Zhou, Z.; Gao, H.; Yi, W. *Adv. Synth. Catal.* **2019**, *361*, 3980. (e) Yi, W.; Chen, W.; Liu, F.-X.; Zhong, Y.; Wu, D.; Zhou, Z.; Gao, H. *ACS Catal.* **2018**, *8*, 9508. (f) Zheng, G.; Zhou, Z.; Zhu, G.; Zhai, S.; Xu, H.; Duan, X.; Yi, W.; Li, X. *Angew. Chem., Int. Ed.* **2020**, *59*, 2890. (g) Zhou, J.; Shi, J.; Liu, X.; Jia, J.; Song, H.; Xu, H. E.; Yi, W. *Chem. Commun.* **2015**, *51*, 5868. (h) Zhou, J.; Shi, J.; Qi, Z.; Li, X.; Xu, H. E.; Yi, W. *ACS Catal.* **2015**, *5*, 6999. (i) Zhou, Z.; Bian, M.; Zhao, L.; Gao, H.; Huang, J.; Liu, X.; Yu, X.; Li, X.; Yi, W. *Org. Lett.* **2018**, *20*, 3892.

(21) (a) Li, M.; Wang, J. H.; Li, W.; Wen, L. R. *Org. Lett.* **2018**, *20*, 7694. (b) Mei, Y. L.; Zhou, W.; Huo, T.; Zhou, F. S.; Xue, J.; Zhang, G. Y.; Ren, B. T.; Zhong, C.; Deng, Q. H. *Org. Lett.* **2019**, *21*, 9598. (c) Pan, J. L.; Liu, C.; Chen, C.; Liu, T. Q.; Wang, M.; Sun, Z.; Zhang, S. Y. *Org. Lett.* **2019**, *21*, 2823. (d) Pan, J. L.; Xie, P.; Chen, C.; Hao, Y.; Liu, C.; Bai, H. Y.; Ding, J.; Wang, L. R.; Xia, Y.; Zhang, S. Y. *Org. Lett.* **2018**, *20*, 7131. (e) Wu, Y.; Chen, Z.; Yang, Y.; Zhu, W.; Zhou, B. *J. Am. Chem. Soc.* **2018**, *140*, 42. (f) Xie, Y. *Chem. Commun.* **2016**, *52*, 12372. (g) Xiong, F.; Zuo, Y.; Song, Y.; Zhang, L.; Zhang, X.; Xu, S.; Ren, Y. *Org. Lett.* **2020**, *22*, 3799. (h) Yuan, W. K.; Zhu, M. H.; Geng, R. S.; Ren, G. Y.; Zhang, L. B.; Wen, L. R.; Li, M. *Org. Lett.* **2019**, *21*, 1654. (i) Zhou, W.; Mei, Y. L.; Li, B.; Guan, Z. Y.; Deng, Q. H. *Org. Lett.* **2018**, *20*, 5808. (j) Zhu, Y.; Zhao, X.; Wu, Q.; Chen, Y.; Zhao, J. *Wuli Huaxue Xuebao* **2019**, *35*, 989.

(22) (a) Chen, Y.; Wang, D.; Duan, P.; Ben, R.; Dai, L.; Shao, X.; Hong, M.; Zhao, J.; Huang, Y. *Nat. Commun.* **2014**, *5*, 4610. (b) Wu, Q.; Chen, Y.; Yan, D.; Zhang, M.; Lu, Y.; Sun, W. Y.; Zhao, J. *Chem. Sci.* **2017**, *8*, 169. (c) Wu, Q.; Yan, D.; Chen, Y.; Wang, T.; Xiong, F.; Wei, W.; Lu, Y.; Sun, W. Y.; Li, J. J.; Zhao, J. *Nat. Commun.* **2017**, *8*, 14227. (d) Xiong, F.; Lu, L.; Sun, T. Y.; Wu, Q.; Yan, D.; Chen, Y.; Zhang, X.; Wei, W.; Lu, Y.; Sun, W. Y.; Li, J. J.; Zhao, J. *Nat. Commun.* **2017**, *8*, 15912. (e) Yan, D.; Wang, G.; Xiong, F.; Sun, W. Y.; Shi, Z.; Lu, Y.; Li, S.; Zhao, J. *Nat. Commun.* **2018**, *9*, 4293. (f) Zhu, Y.; Chen, F.; Zhao, X.; Yan, D.; Yong, W.; Zhao, J. *Org. Lett.* **2019**, *21*, 5884.

(23) Sawin, C. T.; Ryan, R. J.; Longcope, C.; Fisher, L. E. *J. Clin. Endocrinol. Metab.* **1978**, *46*, 911.

(24) Zhao, G.-L.; Lin, S.; Korotvička, A.; Deiana, L.; Kullberg, M.; Córdova, A. *Adv. Synth. Catal.* **2010**, *352*, 2291.

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