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# Acid- and Base-Switched Palladium-Catalyzed $\gamma$-C($sp^3$)–H Alkylation and Alkenylation of Neopentylamine

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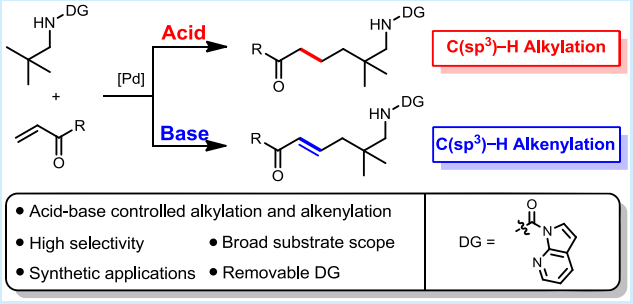
**ABSTRACT:** The functionalization of remote unactivated C-($sp^3$)–H and the reaction selectivity are among the core pursuits for transition-metal catalytic system development. Herein, we report Pd-catalyzed $\gamma$-C($sp^3$)–H-selective alkylation and alkenylation with removable 7-azaindole as a directing group. Acid and base were found to be the decisive regulators for the selective alkylation and alkenylation, respectively, on the same single substrate under otherwise the same reaction conditions. Various acrylates were compatible for the formation of C($sp^3$)–C($sp^3$) and C($sp^3$)–C($sp^2$) bonds. The alkenylation protocol could be further extended to acrylates with natural product units and $\alpha,\beta$-unsaturated ketones. The preliminary synthetic manipulation of the alkylation and alkenylation products demonstrates the potential of this strategy for structurally diverse aliphatic chain extension and functionalization. Mechanistic experimental studies showed that the acidic and basic catalytic transformations shared the same six-membered dimer palladacycle.

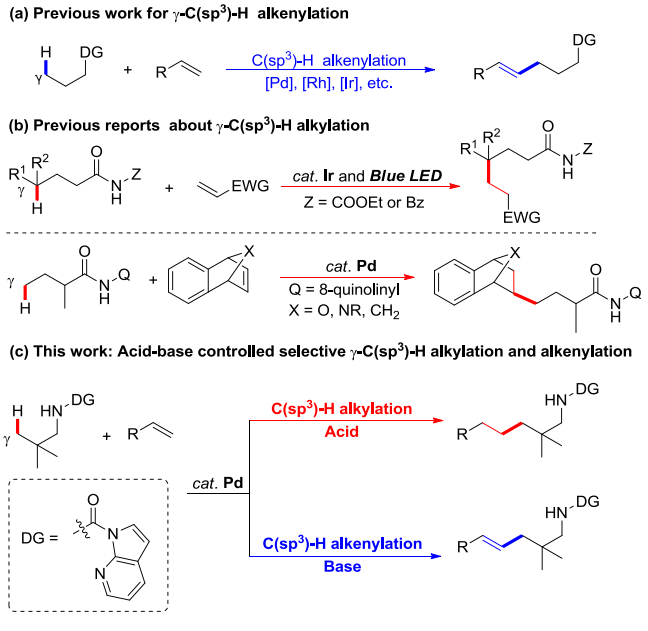





Saturated aliphatic carbon, the basic unit of organic molecules, makes the environmentally benign C($sp^3$)–H manipulation strategy conducive to enrich molecular diversity and complexity.[1] The transition-metal catalysis technique developed in the past decade has rapidly become a promising and powerful tool for C($sp^3$)–H functionalization.[2] Hence, in this study, transition-metal-catalyzed C–H activation was investigated for C($sp^3$)–H alkenylation[3] (Scheme 1a), and the results demonstrate the potential of this approach for realizing C($sp^3$)–C($sp^3$) bond formation, besides the metal-locarbene- and photoassisted alkylation approaches. The alkylation of relatively more active $\alpha$-C($sp^3$)–H was realized when olefin derivatives and other coupling partners were used,[4] and $\beta$-C($sp^3$)–H alkylation was also achieved.[5] However, the remote alkylation of stable $\gamma$- and $\delta$-C($sp^3$)–H is more challenging and rarely reported due to the kinetically less favored formation of transition-metal intermediate complexes. Rovis and Knowles demonstrated the $\delta$-C($sp^3$)–H alkylation with the assistance of iridium complex and blue light-emitting diode.[6] Rovis applied the same strategy to realize $\gamma$-C($sp^3$)–H alkylation (Scheme 1b).[7] Recently, Shi reported the $\gamma$-C($sp^3$)–H alkylation of aliphatic carboxamides using strained bicyclic olefins as the coupling agent (Scheme 1b).[8] Because of the inert property of aliphatic C–H bond, it remains a challenge to develop selective transition-metal catalytic systems for the remote functionalization of unactivated C($sp^3$)–H bonds.

The functionalization of remote unactivated $\gamma$-C($sp^3$)–H, which is attractive in organic chemistry, has always been a challenge. Though C($sp^2$)–H switchable alkylation and

**Scheme 1. $\gamma$-C($sp^3$)–H Alkylation and Alkenylation**

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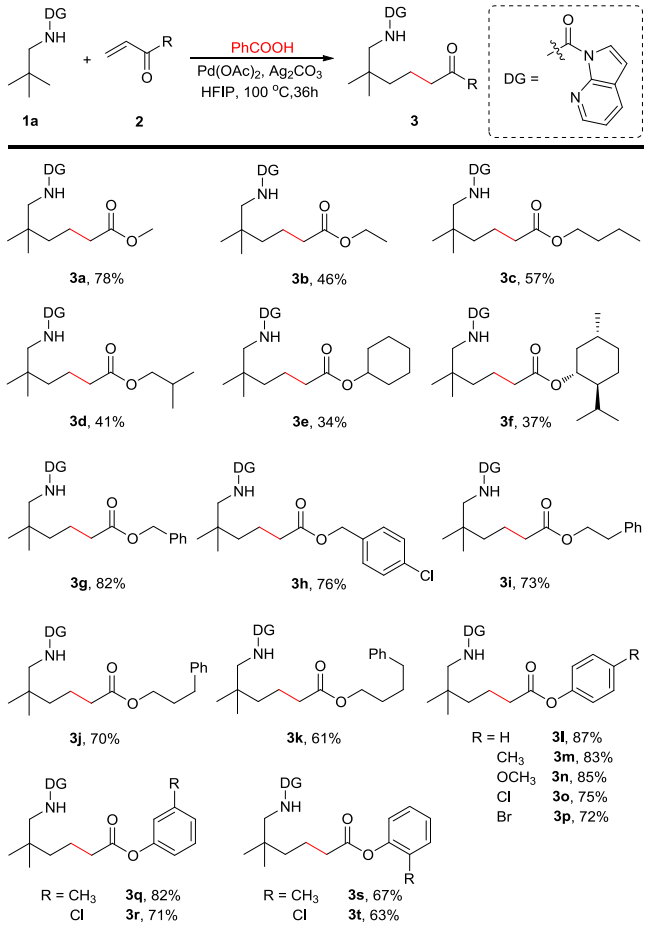
alkenylation has been reported,[9] no substrate has been demonstrated capable of concurrently initiating both γ-C(sp$^3$)−H alkylation and alkenylation via a palladium catalytic system. Following our previous report on temperature-switched arylation of C(sp$^3$)−H and C(sp$^2$)−H and catalytic indole manipulation,[10] herein we report an acid/base-modulated selective alkylation and alkenylation of remote γ-C(sp$^3$)−H bond (Scheme 1c). Here, 7-azaindole was used as the *N*,*N*′-bidentate DG under a palladium catalytic system. Moreover, γ-C(sp$^3$)−H alkylation was realized with the assistance of benzoic acid, while γ-C(sp$^3$)−H alkenylation was realized with the assistance of the organic base 1,4-diazabicyclo[2.2.2]octane (DABCO) under otherwise the same reaction conditions. A wide range of acrylates with various alkyl chains and substituted benzene rings were tested for these transformations, as well as α,β-unsaturated ketones or acrylates with natural product units as the olefin coupling partner. The synthetic utility of this protocol was further investigated for structurally diverse alkanes from the alkylated and alkenylated products. Experimental studies were performed to further elucidate the underlying selective reaction mechanism.

We began our reaction investigations with *N*-neopentyl-1*H*-pyrrolo[2,3-*b*]pyridine-1-carboxamide (**1a**) and methyl acrylate (**2a**) under the $Pd(OAc)_2$ catalytic system with $Ag_2CO_3$ as an additive in the presence of acids or bases (see the Supporting Information for details). Different reaction temperature, various acids and bases as well as their amount were tested. The results showed that 100 °C with 3 equiv. of benzoic acid and 30 °C with 3 equiv. of triethylenediamine (DABCO) were proved to be the most favorable conditions for alkylation and alkenylation reactions, respectively.

With the optimal acid and base reaction conditions established, we evaluated the substrate scope of C(sp$^3$)−H alkylation products (Scheme 2). The results showed that this reaction could tolerate a wide range of acrylates with different lengths of alkyl chains (**2a**−**2d**), cyclohexyl derivatives (**2e**, **2f**), phenyl-substituted alkyl chains (**2g**−**2k**), and substituted benzenes (**2l**−**2t**). The linear or cyclo-alkane coupled acrylates produced similarly moderate yields of the alkylation products (**3b**−**3f**). A clear trend was observed for **3g**−**3k**: the longer the alkyl chain between the phenyl group and the oxygen atom, the lower the yield of the alkylated product **3**, ranging from 61 to 82%. The acrylates with the same substituents on the para-position of benzenes (**3m**, **3o**) showed higher conversion rates than those with ortho- (**3s**, **3t**) or meta-substituents (**3q**, **3r**). The electron-donating groups (**3m**, **3n**) at the phenyl para-position was preferred to the electron-withdrawing groups (**3o**, **3p**). The relatively deficient behaviors of **3s** and **3t** with ortho-methyl and chloro group might be due to their steric hindrance against intermediate complex formation.

The scope of C(sp$^3$)−H alkenylation was also investigated (Scheme 3). Acrylates with different alkyl chains successfully reacted with **1a** to give alkenylation products in moderate to good isolated yields (**4a**−**4e**). The results showed that the longer chain length led to less yields of products (**4b**−**4e**), and the transformation rate on the branched alkyl substrates (**4c**, **4e**) was slightly lower than the corresponding unbranched alkylsubstrates (**4b**, **4d**). The cyclohexyl and adamantyl group further reduced the reaction productivity (**4f** and **4g**). The phenyl alkyl substituents also successfully produced moderate to good isolated yields of products (**4h**−**4l**), whereas the substituted benzenes with an electron-donating group

**Scheme 2. Scope of for γ-C(sp$^3$)−H Alkylation**[a,b]




[a]Conditions: 0.2 mmol of **1a**, 0.5 mmol of **2a**, 0.02 mmol of $Pd(OAc)_2$, 0.6 mmol of $Ag_2CO_3$, 0.6 mmol of acid, 1 mL of HFIP, 100 °C reaction temperature, and 36 h reaction time. [b]Isolated yields.

produced relatively lower yields (**4m**−**4o**). However, acrylates with a substituted benzene ring containing an electron-withdrawing group failed to yield the product. Interestingly, α,β-unsaturated ketones could also form corresponding alkenylation products (**4p**−**4r**).

Given the appealing results so far, we applied the C(sp$^3$)−H alkenylation system to natural products (Scheme 3). Acrylates with cholesterol (**4s**), fenchyl alcohol (**4t**), citronellol (**4u**), isopulegol (**4v**), perillyl alcohol (**4w**), and L-menthol (**4w**) were all well tolerated. These results demonstrate the successful application of this catalytic protocol to perform late-stage C(sp$^3$)−H alkenylation of hydroxyl-containing natural products.

The manipulation of aliphatic chains is a major pursuit in organic chemistry. To showcase the synthetic utility of the C(sp$^3$)−H alkylation and alkenylation reactions, scale-up (2.0 mmol) reactions of **1a** and **2a** were conducted. Products **3a** and **4a** were selectively obtained with 55 and 62% yields, respectively, confirming the catalytic system efficiency (Scheme 4a). Moreover, the DG deprotection of **3a** and **4a** was accompanied by hydrolysis to obtain free acid. In the presence of an acid group, the benzoyl protection of the free amine was conducted for easy purification and analysis. Hence, the removal of DG from **3a** led to amine hexanoate derivative **6**, with 63% yield, whereas the newly formed amine after **4a**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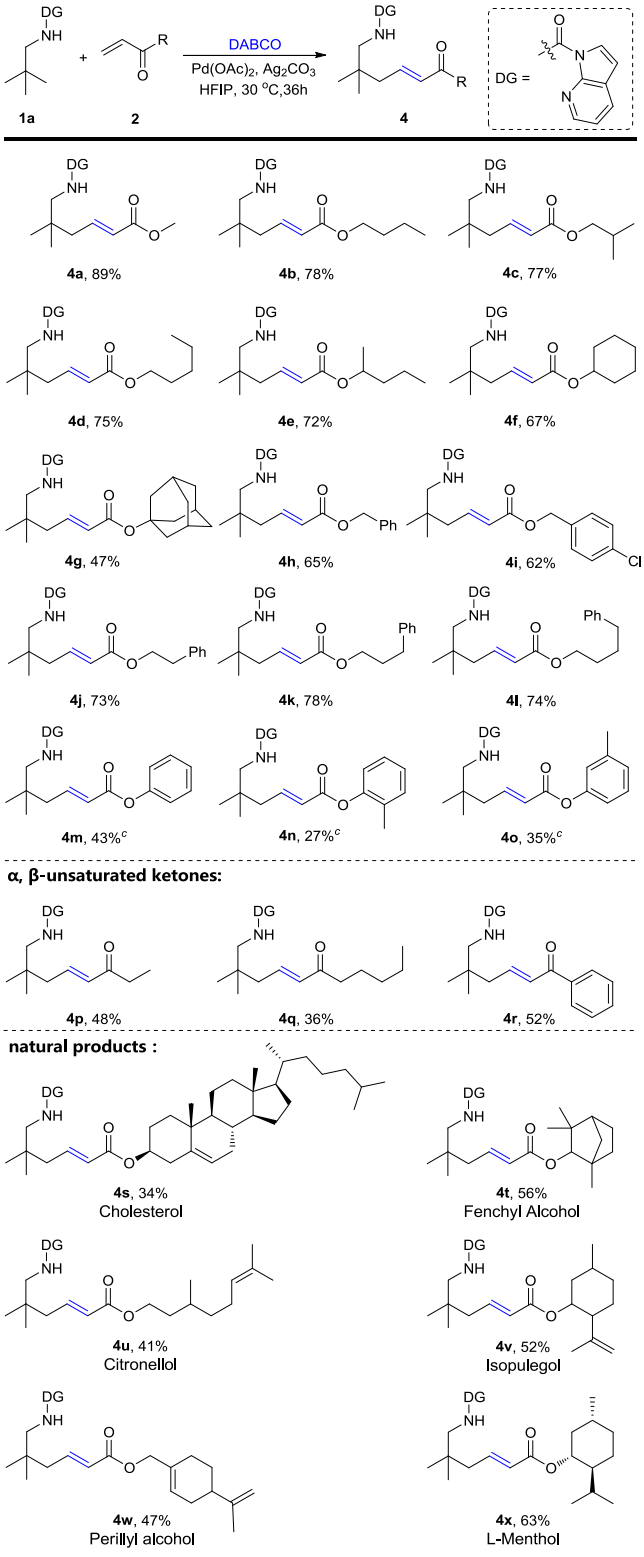
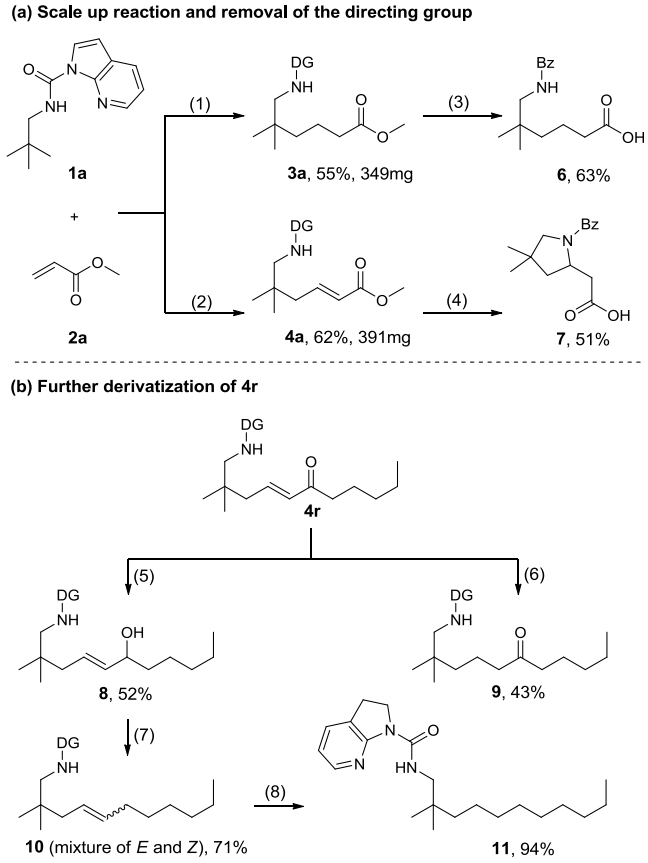
**Scheme 3. Scope for γ-C(sp$^3$)−H Alkenylation**[a,b]




[a]Conditions: 0.2 mmol of **1a**, 0.5 mmol of **2**, 0.02 mmol of $Pd(OAc)_2$, 0.6 mmol of $Ag_2CO_3$, 0.6 mmol of DABCO, 1 mL of HFIP, 30 °C reaction temperature, 36 h reaction time. [b]Isolated yields. [c]0.6 mmol of $Et_3N$ as base.

DG cleavage simultaneously underwent nucleophilic cycloaddition to olefin, affording the tetrahydropyrrole derivative **7** with 51% yield (Scheme 4a). The reduction of **4r** using $NaBH_4$ provided the hydroxyl alkene product **8** with 52% yield, while the hydrogenation of double bond of **4r** with Zn/AcOH enabled the formation of **9** with 43% yield (Scheme 4b). The further treatment of **8** with $B(C_6F_5)_3$ and *n*-butylsilane afforded the olefin derivative **10**. The following Pd/C reduction of **10** afforded the saturated long-chain undecylamine **11** in almost quantity yield, along with the hydrogenation of active double bond from DG (Scheme 4b). These transformations from the alkylated or alkenylated products demonstrate the great potential of this selective γ-C(sp$^3$)−H functionalization for the further efficient construction of diversified alkanes.

**Scheme 4. Synthetic Applications**[a]




[a]Legend: (1) $Pd(OAc)_2$, $Ag_2CO_3$, PhCOOH, HFIP, 100 °C, 36 h, 55%; (2) $Pd(OAc)_2$, $Ag_2CO_3$, DABCO, HFIP, 30 °C, 36 h, 62%; (3) $K_2CO_3$, MeOH, $H_2O$, BzCl, 63%; (4) $K_2CO_3$, MeOH, $H_2O$, BzCl, 51%; (5) $NaBH_4$, MeOH, 52%; (6) Zn, AcOH, 43%; (7) $B(C_6F_5)_3$, *n*-butylsilane, $CH_2Cl_2$, 71%; (8) Pd/C, MeOH, $H_2$, 94%.

To gain insights into the reaction mechanism, we conducted mechanistic study experiments (Scheme 5). Initially, indole derivative **1b**, instead of 7-azaindole, was reacted with **2a** under C(sp$^3$)−H alkylation condition. Only the C(sp$^2$)−H alkenylation product (**5b**) was formed, indicating that N7 on 7-azaindole was vital to initiate these C(sp$^3$)−H alkylation and alkenylation reactions (Scheme 5a). To further delineate the reaction process, we performed a stoichiometric reaction to obtain the intermediate palladium complex **12**. Through X-ray crystallography, the structure of **12** was confirmed to be a six-membered palladacycle dimer (CCDC: 2058757), showing that the palladium chelated with N7 and the alkyl nitrogen (Scheme 5b). This result also proves that the N7 of 7-azaindole was involved in the catalytic system. A further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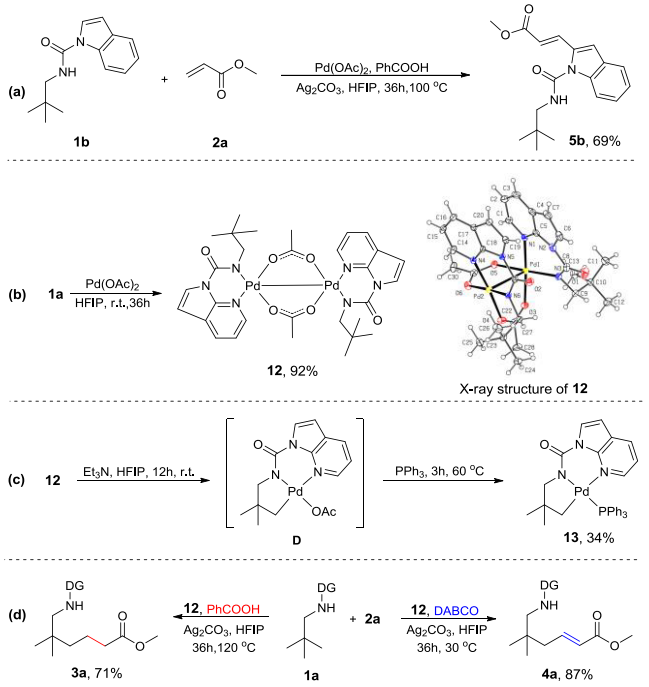
**Scheme 5. Mechanistic Studies**

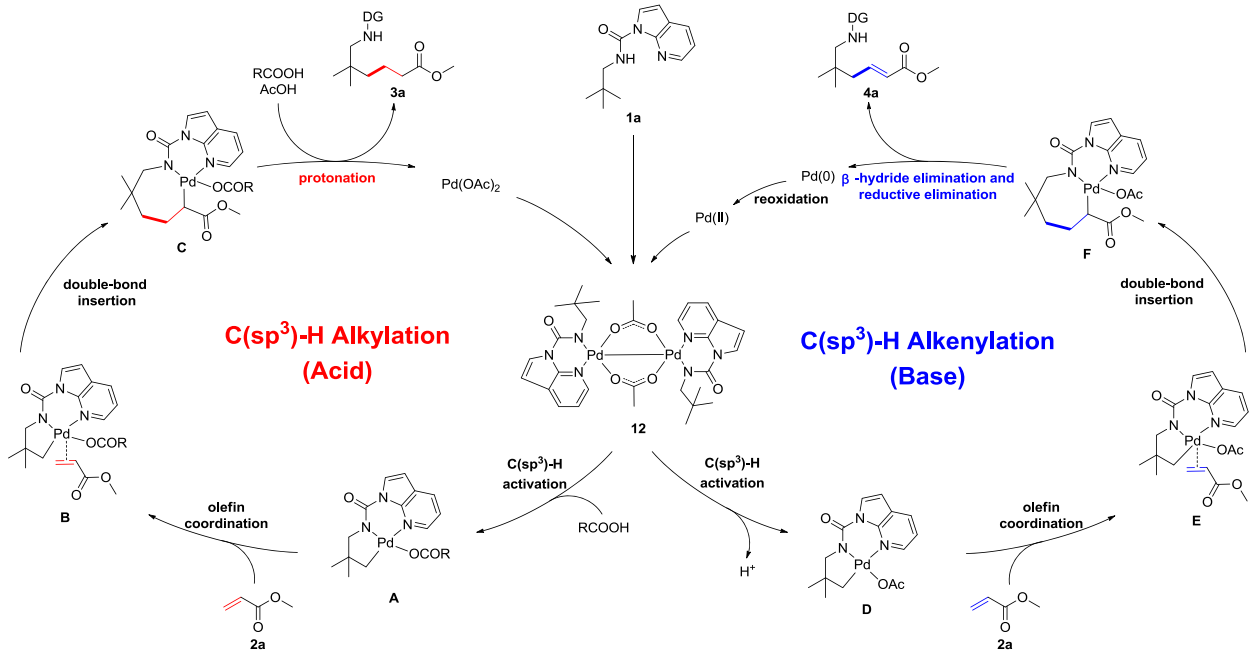



attempt to the C−H insertion palladacycle from **12** failed to get the plausible intermediate **D**, possibly due to its instability. $PPh_3$ was then used to trap the unstable **D** to afford complex **13** for the basic C($sp^3$)−H alkenylation (Scheme 5c).[11] However, a similar strategy failed to afford the acidic catalytic intermediate. To confirm the role of **12** in these transformations, we used a catalytic amount of **12** to replace $Pd(OAc)_2$, forming **3a** (71%) from benzoic acid and **4a** (87%) from DABCO (Scheme 5d). These findings suggest that **12** is a shared key originating intermediate for C($sp^3$)−H alkylation and alkenylation.

On the basis of our experiments and previous research reports on C($sp^3$)−H functionalization,[12] we propose a plausible mechanism (Scheme 6). The initial coordination of **1a** with $Pd(OAc)_2$ forms a dimer of six-membered palladacycle intermediate **12**, which is further converted to [6,5]-fused palladacycle **A** with the assistance of RCOOH (RCOOH = AcOH or PhCOOH) or **D** under basic conditions after C($sp^3$)−H activation. The following coordination of **A** and **D** to olefin leads to the corresponding complexes **B** and **E**, and the subsequent double-bond insertion leads to the intermediates **C** and **F**, respectively. Finally, the C($sp^3$)−H alkylation product **3a** is obtained after protonation in the presence of $H^+$, whereas $\beta$-hydride elimination and reductive elimination give the C($sp^3$)−H alkenylation product **4a**.

In summary, we demonstrate the first example of $\gamma$-C($sp^3$)−H selective alkylation and alkenylation reactions controlled by acid and base, respectively, using 7-azaindole as the DG and $Pd(OAc)_2$ as a catalyst. Benzoic acid selectively initiated the C($sp^3$)−H alkylation, while the organic base DABCO exclusively provided the alkenylation products. The results of the mechanistic study showed that the acidic and basic catalytic cycle shared the same palladacycle dimer as the originating intermediate. Acrylates with various alkyl chains and substituted benzene rings were well tolerated in the selective alkylation and alkenylation reactions and the gram-scale reaction. Moreover, $\alpha,\beta$-unsaturated ketones were also compatible with the C($sp^3$)−H alkenylation. Furthermore, the reaction demonstrated tolerance to acrylates derived from natural alcohols, indicating the potential application of the manipulation strategy to natural products. Preliminary simple DG removal or one-step reaction could convert the alkylation and alkenylation products into structurally diverse molecules. This transition metal−catalyzed selective $\gamma$-C($sp^3$)−H activation can allow for further potential extension and derivatization of certain alkyl chains. This study results might also encourage researchers to discover more promising strategies enriching C($sp^3$)−H functionalization.

**Scheme 6. Proposed Catalytic Cycle**



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## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.1c00903.

Experimental procedures, characterization data for all products, crystal data, and NMR spectra (PDF)

### Accession Codes

CCDC 2058757 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

†J. Z. and S. Z. contributed equally to this work.


### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

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## ■ REFERENCES


(1) (a) Chen, Z.; Rong, M.; Nie, J.; Zhu, X.; Shi, B.; Ma, J. Catalytic Alkylation of Unactivated C(sp3)−H Bonds for C(sp3)−C(sp3) Bond Formation. *Chem. Soc. Rev.* **2019**, *48*, 4921−4942. (b) Sterckx, H.; Morel, B.; Maes, B. U. W. Catalytic Aerobic Oxidation of C(sp3)−H Bonds. *Angew. Chem., Int. Ed.* **2019**, *58*, 7946−7970.

(2) (a) He, J.; Wasa, M.; Chan, K. S. L.; Shao, Q.; Yu, J. Palladium-Catalyzed Transformations of Alkyl C−H Bonds. *Chem. Rev.* **2017**, *117*, 8754−8786. (b) Saint-Denis, T. G.; Zhu, R.; Chen, G.; Wu, Q.; Yu, J. Enantioselective C(sp3)−H Bond Activation by Chiral Transition Metal Catalysts. *Science* **2018**, *359*, eaao4798. (c) Xu, Y.; Dong, G. sp3 C−H Activation via Exo-Type Directing Groups. *Chem. Sci.* **2018**, *9*, 1424−1432. (d) Yang, K.; Song, M.; Liu, H.; Ge, H. Palladium-Catalyzed Direct Asymmetric C−H Bond Functionalization Enabled by the Directing Group Strategy. *Chem. Sci.* **2020**, *11*, 12616−12632. (e) Trowbridge, A.; Walton, S. M.; Gaunt, M. J. New Strategies for the Transition-Metal Catalyzed Synthesis of Aliphatic Amines. *Chem. Rev.* **2020**, *120*, 2613−2692.

(3) (a) Park, H.; Li, Y.; Yu, J. Utilizing Carbonyl Coordination of Native Amides for Palladium-Catalyzed C(sp3)−H Olefination. *Angew. Chem., Int. Ed.* **2019**, *58*, 11424−11428. (b) Park, H. S.; Fan, Z.; Zhu, R.; Yu, J. Distal γ-C(sp3)−H Olefination of Ketone Derivatives and Free Carboxylic Acids. *Angew. Chem., Int. Ed.* **2020**, *59*, 12853−12859. (c) Fan, Z.; Zhao, S.; Liu, T.; Shen, P.; Cui, Z.; Zhuang, Z.; Shao, Q.; Chen, J. S.; Ratnayake, A. S.; Flanagan, M. E.; Kölmel, D. K.; Piotrowski, D. W.; Richardson, P.; Yu, J. Merging C(sp3)−H Activation with DNA-Encoding. *Chem. Sci.* **2020**, *11*, 12282−12288.

(4) (a) Nako, A. E.; Oyamada, J.; Nishiura, M.; Hou, Z. Scandium-Catalysed Intermolecular Hydroaminoalkylation of Olefins with Aliphatic Tertiary Amines. *Chem. Sci.* **2016**, *7*, 6429−6434. (b) Tran, A. T.; Yu, J. Practical Alkoxythiocarbonyl Auxiliaries for Iridium(I)-Catalyzed C−H Alkylation of Azacycles. *Angew. Chem., Int. Ed.* **2017**, *56*, 10530−10534. (c) Yamauchi, D.; Nishimura, T.; Yorimitsu, H. Hydroxoiridium-Catalyzed Hydroalkylation of Terminal Alkenes with Ureas by C(sp3)−H Bond Activation. *Angew. Chem., Int. Ed.* **2017**, *56*, 7200−7204. (d) Edwards, P. M.; Schafer, L. L. Early Transition-Metal-Catalyzed C−H Alkylation: Hydroaminoalkylation for Csp3−Csp3 Bond Formation in the Synthesis of Selectively Substituted Amines. *Chem. Commun.* **2018**, *54*, 12543−12560. (e) Verma, P.; Richter, J. M.; Chekshin, N.; Qiao, J. X.; Yu, J. Iridium(I)-Catalyzed α-C(sp3)−H Alkylation of Saturated Azacycles. *J. Am. Chem. Soc.* **2020**, *142*, 5117−5125.

(5) (a) Chen, K.; Shi, B. Sulfonamide-Promoted Palladium(II)-Catalyzed Alkylation of Unactivated Methylene C(sp3)−H Bonds with Alkyl Iodides. *Angew. Chem., Int. Ed.* **2014**, *53*, 11950−11954. (b) Zhu, R.; He, J.; Wang, X.; Yu, J. Ligand-Promoted Alkylation of C(sp3)−H and C(sp2)−H Bonds. *J. Am. Chem. Soc.* **2014**, *136*, 13194−13197. (c) Wu, X.; Zhao, Y.; Ge, H. Nickel-Catalyzed Site-Selective Alkylation of Unactivated C(sp3)−H Bonds. *J. Am. Chem. Soc.* **2014**, *136*, 1789−1792. (d) Wang, C.; Dong, G. Direct β-Alkylation of Ketones and Aldehydes via Pd-Catalyzed Redox Cascade. *J. Am. Chem. Soc.* **2018**, *140*, 6057−6061.

(6) (a) Choi, G. J.; Zhu, Q.; Miller, D. C.; Gu, C. J.; Knowles, R. R. Catalytic Alkylation of Remote C−H Bonds Enabled by Proton-Coupled Electron Transfer. *Nature* **2016**, *539*, 268−271. (b) Chu, J. C. K.; Rovis, T. Amide-Directed Photoredox-Catalysed C−C Bond Formation at Unactivated sp3 C−H Bonds. *Nature* **2016**, *539*, 272−275.

(7) Chen, D.; Chu, J. C. K.; Rovis, T. Directed γ-C(sp3)−H Alkylation of Carboxylic Acid Derivatives through Visible Light Photoredox Catalysis. *J. Am. Chem. Soc.* **2017**, *139*, 14897−14900.

(8) Li, Y.; Zhang, P.; Liu, Y.; Yu, Z.; Shi, B. Remote γ-C(sp3)−H Alkylation of Aliphatic Carboxamides via an Unexpected Regiodetermining Pd Migration Process: Reaction Development and Mechanistic Study. *ACS Catal.* **2020**, *10*, 8212−8222.

(9) Pradhan, S.; Mishra, M.; De, P. B.; Banerjee, S.; Punniyamurthy, T. Weak Coordination Enabled Switchable C4-Alkenylation and Alkylation of Indoles with Allyl Alcohols. *Org. Lett.* **2020**, *22*, 1720−1725.

(10) (a) Zhang, J.; Xie, H.; Zhu, H.; Zhang, S.; Reddy Lonka, M.; Zou, H. Chameleon-like Behavior of the Directing Group in the Rh(III)-Catalyzed Regioselective C−H Amidation of Indole: An Experimental and Computational Study. *ACS Catal.* **2019**, *9*, 10233−10244. (b) Gogula, T.; Zhang, J.; Lonka, M. R.; Zhang, S.; Zou, H. Temperature-Modulated Selective C(sp3)−H or C(sp2)−H Arylation Through Palladium Catalysis. *Chem. Sci.* **2020**, *11*, 11461−11467. (c) Zhang, J.; Zhang, S.; Gogula, T.; Zou, H. Versatile Regioselective Deuteration of Indoles via Transition-Metal-Catalyzed H/D Exchange. *ACS Catal.* **2020**, *10*, 7486−7494.

(11) Zhu, R.; Liu, L.; Yu, J. Highly Versatile β-C(sp3)−H Iodination of Ketones Using a Practical Auxiliary. *J. Am. Chem. Soc.* **2017**, *139*, 12394−12397.

(12) (a) Thrimurtulu, N.; Khan, S.; Maity, S.; Volla, C. M. R.; Maiti, D. Palladium Catalyzed Direct Aliphatic γ-C(sp3)−H Alkenylation with Alkenes and Alkenyl Iodides. *Chem. Commun.* **2017**, *53*, 12457−12460. (b) Shibata, K.; Natsui, S.; Chatani, N. Rhodium-Catalyzed Alkenylation of C−H Bonds in Aromatic Amides with Alkynes. *Org. Lett.* **2017**, *19*, 2234−2237. (c) Yang, X.; Sun, R.; Zhang, C.; Zheng,

X.; Yuan, M.; Fu, H.; Li, R.; Chen, H. Iridium-Catalyzed Benzylamine C−H Alkenylation Enabled by Pentafluorobenzoyl as the Directing Group. *Org. Lett.* **2019**, *21*, 1002−1006. (d) Xu, S.; Hirano, K.; Miura, M. Pd-Catalyzed Regioselective C−H Alkenylation and Alkynylation of Allylic Alcohols with the Assistance of a Bidentate Phenanthroline Auxiliary. *Org. Lett.* **2020**, *22*, 9059−9064.



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