Organic LETTERS

Letter

Cite This: Org. Lett. XXXX, XXX, XXX–XXX

pubs.acs.org/OrgLett

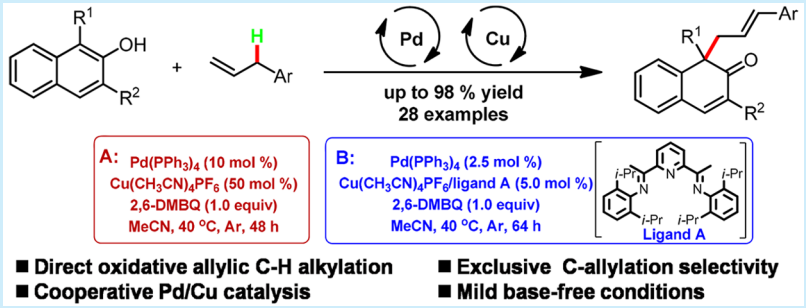
Direct Allylic C(sp3)-H Alkylation with 2-Naphthols via Cooperative Palladium and Copper Catalysis: Construction of Cyclohexadienones with Quaternary Carbon Centers

Ming Jin,[†] Wei Ren,[†] Dang-Wei Qian,[†] and Shang-Dong Yang*[,†,‡]

[†]State Key Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou 730000, P. R. China

[‡]Key Laboratory of Functional Molecular Engineering of Guangdong Province, South China University of Technology, Guangzhou 510640, P. R. China

Supporting Information



ABSTRACT: Oxidative allylic C−H alkylation with 2-naphthols was accomplished with excellent chemoselectivities and broad substrate scope through $Pd(PPh_3)_4/Cu(MeCN)_4PF_6$ cooperative catalysis under mild base-free conditions. Special tolerance was observed with peptides, allowing late-stage modifications of peptides. The transformation provides a general protocol to obtain functionalized cyclohexadienones with quaternary carbon centers under two alternative sets of conditions and serves as a complementary catalysis system for the dearomatization of 2-naphthols.

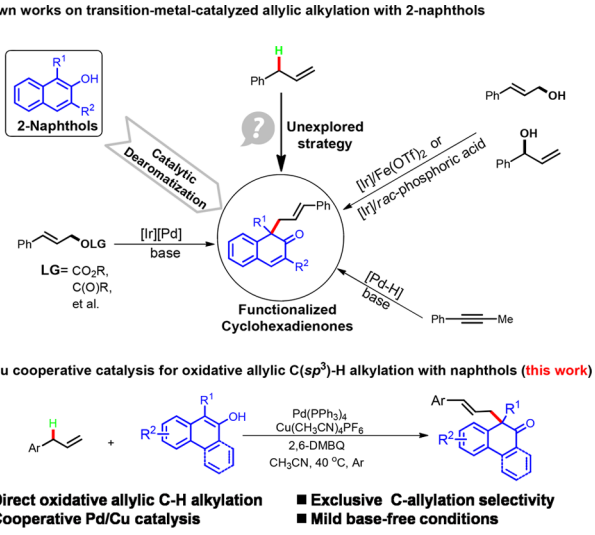
Cyclohexadienones with *ortho*-quaternary carbon centers are pivotal skeletons with special bioactivities[1] for drug discovery, excellent photoelectric performance for material science,[2] and great importance[3] in the total synthesis of natural products. Therefore, the efficient construction of cyclohexadienone motifs has been of significant synthetic interest in the chemical community.[4] Recently, transition-metal-catalyzed asymmetric allylic dearomatization, commonly known as CADA reaction,[5] has proven to be the most effective strategy for preparing the target molecules from simple phenol compounds.[6] Previous work in this area focused largely on preoxidized allylic electrophiles[7] for the dearomatization of naphthols, which required extra steps for prefunctionalization. To overcome this limitation, some elegant transformations have been developed (Scheme 1A), including two reports on iridium-catalyzed allylic dearomatization reaction by directly using allylic alcohols[8] and one example of a palladium-hydride-mediated dearomative allylation process.[9] Although successful, one major constraint that remained is that an alkaline system[6b] is needed for effective dearomatization processes and good C/O-allylation selectivities; this is introduced either through the use of stoichiometric amounts of basic additives or by using preoxidized substrates in situ, which results in poor tolerance with competitive electrophiles in more complex substrates. One way to improve the prospects of these reactions is through the discovery of a new activation mode for phenol dearomatization.

In recent years, transition-metal-catalyzed oxidative allylic C−H activation has witnessed significant breakthroughs and diverse C−H functionalizations have been well established.[10−12] Cooperative catalysis,[13] in which multiple chemical interactions participate in synergy to achieve significant enhancement in catalytic activity and/or selectivity, has also enabled many new and challenging processes. Metal Lewis acid catalysis has long been established as one of the most powerful tools in organic synthesis.[13e,14] Inspired by these advances, we hypothesized that Lewis acids might be efficient to activate naphthols for dearomatization as bases and to ensure good C/O-allylation selectivities by changing the properties[15] of phenolic hydroxyl groups synchronously through coordination. With the advantage of a cooperative Lewis acid catalyst, transition-metal-catalyzed allylic C−H activation may allow direct allylic C−H dearomatization to be conducted under mild base-free conditions, allowing good chemical selectivities and functional-group tolerance. On the basis of our endeavors, a new method for the direct allylic C−H alkylation with 2-naphthols through palladium/copper cooperative catalysis

Received: September 11, 2018

DOI: 10.1021/acs.orglett.8b02910
Org. Lett. XXXX, XXX, XXX−XXX

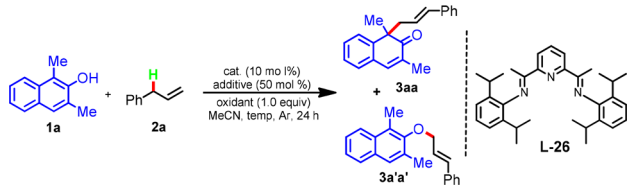
Scheme 1. Strategies for Transition-Metal-Catalyzed Allylic Dearomatization of 2-Naphthols



under base-free conditions with high C-allylation selectivity was developed (Scheme 1B). The novel chemistry enables effective preparation of diverse cyclohexadienones with *ortho*-quaternary carbon centers and shows special tolerance with peptides.

Initially, naphthol **1a** and allylbenzene **2a** were chosen as model substrates for the allylic dearomatization reaction. To our delight, a palladium-BQ combination in acetonitrile was found to catalyze the reaction, albeit in low yield of dearomative product **3aa** (Table 1, entry 1) after preliminary screening. Subsequent control experiments indicated the significance of palladium catalyst (entry 2) and BQ (entry 3) for the reaction. With these initial results in hand, an extensive exploration of additives, catalysts and ligands, oxidants, and temperature was conducted (entries 4−28). The examination of Lewis acids revealed that Ag_2CO_3, $Sc(OTf)_3$, and $CeCl_3$ were ineffective in the reaction, and the yield was greatly improved to 42% with $Cu_2(OH)_2CO_3$ (entries 4−7). $Cu(CH_3CN)_4BF_4$ showed a comparable effect (entry 8) to $Cu_2(OH)_2CO_3$, and the best copper salt screened was $Cu(CH_3CN)_4PF_6$ (49% yield; entry 9). Elevated or reduced amounts of copper salts all provided diminished yields (entries 7−9). The catalyst was then evaluated. The combinations of PPh_3 and palladium salts such as $Pd(OAc)_2$, $Pd(acac)_2$, and $Pd(dba)_2$ displayed reduced reactivity (entries 10−12). Palladium chlorides failed to catalyze the reaction (entries 13−14). An extensive screening of phosphine ligands gave no improved results (see Supporting Information (SI) for details). Therefore, readily available $Pd(PPh_3)_4$ was chosen for further screening. Subsequently, the effects of a series of benzoquinone-type oxidants were investigated (entries 15−18) and the best result was achieved with 2,6-DMBQ (69% yield; entry 16). Notably, with the assistance of $Cu(CH_3CN)_4PF_6$, the reaction proceeded smoothly at 40 °C with a dramatically improvement on yield (87%; entry 22). Elevated temperatures provided lower yields[16] (entries 19−21), and a reduction in temperature to room temperature significantly decreased the yield with the appearance of byproduct **3a′a′** (entry 23). Furthermore, a diminished yield was observed when the catalyst loading was reduced to 5 mol % (entry 24). Under air, no reaction was detected (entry 25), indicating serious adverse

Table 1. Optimization of Reaction Conditions



entry	cat.	oxidant	additive	temp (°C)	yield (%)[a]
1	$Pd(PPh_3)_4$	BQ	-	100	14
2	-	BQ	-	100	nr
3	$Pd(PPh_3)_4$	-	-	100	nr
4	$Pd(PPh_3)_4$	BQ	Ag_2CO_3	100	nr
5	$Pd(PPh_3)_4$	BQ	$Sc(OTf)_3$	100	nr
6	$Pd(PPh_3)_4$	BQ	$CeCl_3$	100	trace
7	$Pd(PPh_3)_4$	BQ	$Cu_2(OH)_2(CO_3)$	100	42 (24)[b] (45)[c]
8	$Pd(PPh_3)_4$	BQ	$Cu(CH_3CN)_4BF_4$	100	38 (14)[b] (35)[c]
9	$Pd(PPh_3)_4$	BQ	$Cu(CH_3CN)_4PF_6$	100	49 (28)[b] (45)[c]
10	$Pd(OAc)_2/2PPh_3$	BQ	$Cu(CH_3CN)_4PF_6$	100	17
11	$Pd(acac)_2/2PPh_3$	BQ	$Cu(CH_3CN)_4PF_6$	100	28
12	$Pd(dba)_2/2PPh_3$	BQ	$Cu(CH_3CN)_4PF_6$	100	45
13	$PdCl_2/2PPh_3$	BQ	$Cu(CH_3CN)_4PF_6$	100	nr
14	$Pd(PPh_3)_2Cl_2$	BQ	$Cu(CH_3CN)_4PF_6$	100	nr
15	$Pd(PPh_3)_4$	2,5-DMBQ	$Cu(CH_3CN)_4PF_6$	100	63
16	$Pd(PPh_3)_4$	2,6-DMBQ	$Cu(CH_3CN)_4PF_6$	100	69
17	$Pd(PPh_3)_4$	2,6-DTBQ	$Cu(CH_3CN)_4PF_6$	100	69
18	$Pd(PPh_3)_4$	2,5-DTBQ	$Cu(CH_3CN)_4PF_6$	100	30
19	$Pd(PPh_3)_4$	2,6-DMBQ	$Cu(CH_3CN)_4PF_6$	120	59
20	$Pd(PPh_3)_4$	2,6-DMBQ	$Cu(CH_3CN)_4PF_6$	80	76
21	$Pd(PPh_3)_4$	2,6-DMBQ	$Cu(CH_3CN)_4PF_6$	60	80
22[d]	**$Pd(PPh_3)_4$**	**2,6-DMBQ**	**$Cu(CH_3CN)_4PF_6$**	**40**	**87**
23	$Pd(PPh_3)_4$	2,6-DMBQ	$Cu(CH_3CN)_4PF_6$	25	25 (41)[e]
24[f]	$Pd(PPh_3)_4$	2,6-DMBQ	$Cu(CH_3CN)_4PF_6$	40	73
25[g]	$Pd(PPh_3)_4$	2,6-DMBQ	$Cu(CH_3CN)_4PF_6$	40	nr
26	-	2,6-DMBQ	$Cu(CH_3CN)_4PF_6$	40	nr
27	$Pd(PPh_3)_4$	2,6-DMBQ	-	40	nr
28[h]	**$Pd(PPh_3)_4$**	**2,6-DMBQ**	**$Cu(CH_3CN)_4PF_6$**	**40**	**92**

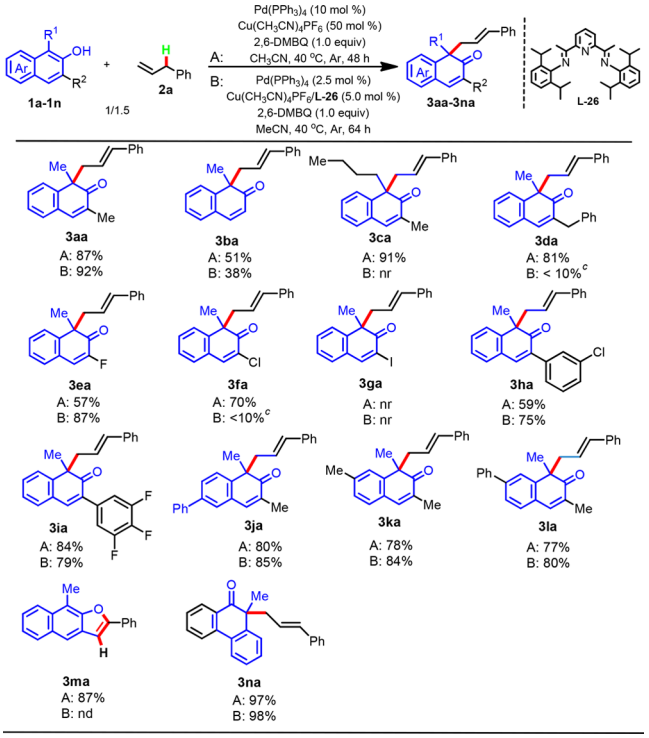
[a]Yield of isolated product **3aa**. [b]Additive (20 mol %) was used. [c]Additive (100 mol %) was used. [d]Conditions A. [e]Yield of isolated byproduct **3a′a′**. [f]Palladium (5 mol %) was used. [g]Under air. [h]Conditions B: Palladium (2.5 mol %), complex of copper and ligand **L-26** (5.0 mol %) was used (see the SI for details). nr = no reaction.

effects of air on the active catalyst. As demonstrated by the control experiments (entries 26−27), palladium catalyst and the copper salt were both essential to the reaction. On the basis of these results, a cooperative role of palladium catalyst and copper additive allowed us to move forward to investigating chirality and reaction optimization. Multiple chiral ligands to control enantioselective C−H dearomatization with palladium or copper catalysts were investigated, and it was found that ligands had a vital effect on the transformation; only racemic products were obtained with the screened ligands (see the SI for details). Further optimization revealed that addition of an achiral ligand **L-26** with copper catalyst dramatically enhanced the catalytic activity and 92% yield of dearomatization product was isolated with only 2.5 mol % $Pd(PPh_3)_4$ (Table 1, entry 28). In all, the optimization studies provided two sets of conditions for the palladium/copper-catalyzed allylic C−H dearomatization reaction: the general conditions (conditions A) and an alternative set of conditions with lower loading of catalysts (conditions B).

With the optimal conditions in hand, we explored the scope of Pd-catalyzed allylic C−H dearomatization of 2-naphthols under conditions A. The scope of the reaction with respect to 2-naphthols was first investigated (Scheme 2, conditions A). 1,3-Dialkyl substituted naphthols were good substrates for allylic alkylation and all gave excellent yields (81−91%, **3aa**,

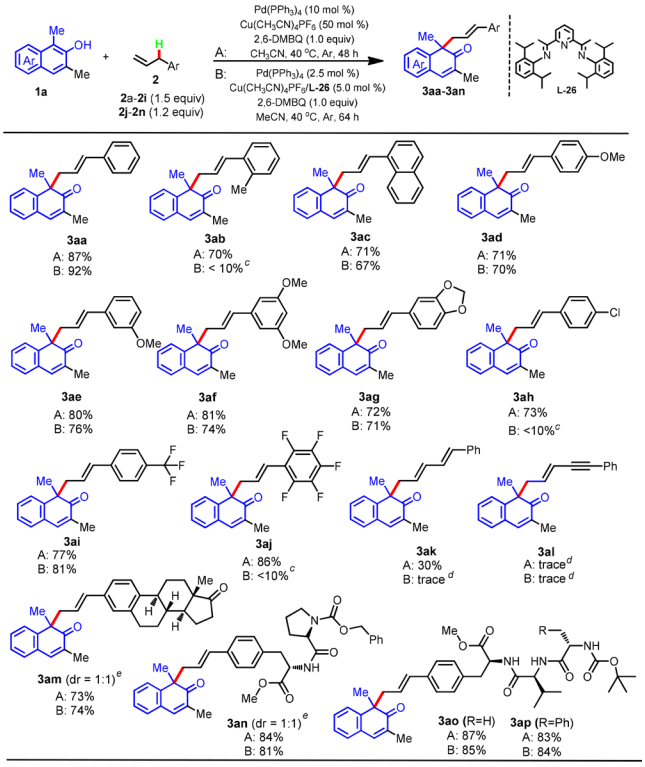
DOI: 10.1021/acs.orglett.8b02910
Org. Lett. XXXX, XXX, XXX−XXX

Scheme 2. Scope of Substituted Naphthols[a,b]



[a]Conditions A: $Pd(PPh_3)_4$ (0.02 mmol), $Cu(CH_3CN)_4PF_6$ (0.10 mmol), **1a**–**n** (0.20 mmol), 2,6-DMBQ (0.20 mmol), **2a** (0.30 mmol), MeCN (1.0 mL), under argon for 48 h. Conditions B: $Pd(PPh_3)_4$ (0.005 mmol), $Cu(CH_3CN)_4PF_6$ (0.01 mmol), ligand **L-26** (0.01 mmol), **1a**–**n** (0.20 mmol), 2,6-DMBQ (0.20 mmol), **2a** (0.30 mmol), MeCN (1.0 mL), under argon for 64 h (see SI). [b]Yield of isolated product. [c]*O*-Allylation byproduct was detected. nr = no reaction. nd = not detected.

Scheme 3. Scope of Allylbenzenes[a,b]



[a]Conditions A: $Pd(PPh_3)_4$ (0.02 mmol), $Cu(CH_3CN)_4PF_6$ (0.10 mmol), **1a** (0.20 mmol), 2,6-DMBQ (0.20 mmol), **2a**–**i** (0.30 mmol) or **2j**–**n** (0.24 mmol), MeCN (1.0 mL), under argon for 48 h. Conditions B: $Pd(PPh_3)_4$ (0.005 mmol), $Cu(CH_3CN)_4PF_6$ (0.010 mmol), ligand **L-26** (0.010 mmol), **1a**–**n** (0.20 mmol), 2,6-DMBQ (0.20 mmol), **2a**–**i** (0.30 mmol) or **2j**–**n** (0.24 mmol), MeCN (1.0 mL), under argon for 64 h (see SI). [b]Yield of isolated product. [c]Byproduct was detected. [d]Complex system was observed. [e]The dr value was determined by HPLC analysis.

3ca–**da**). However, a lack of substituents on the 3-position greatly diminished the yield (51%; **3ba**). In view of the observations noted above, substitutes on the 3-position were examined further. Fluorine and chlorine groups were well tolerated in the reaction, but the more active iodine atom completely restrained the transformation (**3ea**–**ga**). Naphthols with substituted phenyl groups on the 3-position also reacted smoothly with good yields (**3ha**–**ia**). Furthermore, excellent yields (77–80%, **3ja**–**la**) were also observed with methyl and phenyl groups on the other aromatic ring. Notably, alkynyl groups were not compatible with the oxidative procedure and only naphthofuran compound **3ma** was obtained. Phenanthrol **1n**, with weaker aromaticity, gave almost equivalent yield (97%; **3na**).

The scope of the reaction with allylbenzenes was then explored (Scheme 3; conditions A). Various allylbenzenes showed good reactivities to naphthol **1a**, regardless of whether they had electron-donating or -withdrawing substituents (70–86%, **3aa**–**aj**). 1,4-Diene also worked in this reaction, albeit in low yield (**3ak**). In comparison, only a complex system was observed with the reaction of phenyl olefin **2l**. Estrone-derived allylbenene **2m** was a good substrate for this reaction. Notably, substrates **2n**–**p**, with peptide fragments, were well tolerated with the chemistry, and excellent yields were achieved, indicating good tolerance of the Pd/Cu catalytic system and the potential utilities in the late-stage modification of peptides.

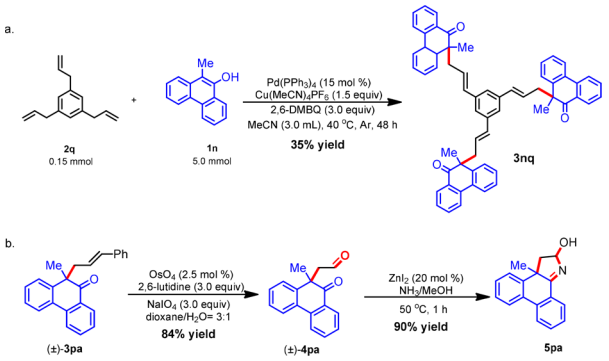
In comparison with conditions A, comparable or better yields were achieved under conditions B for most products (Schemes 2 and 3) and good tolerance with peptides remained (Scheme 3, **3an**–**ap**), indicating the robustness of this catalysis system. However, for naphthol **1c** with a large *n*-Bu group and electron deficient allylbenzene **2j**, the transformations failed when a steric bulky ligand **L-26** was introduced to the reaction. Under conditions B, the catalysis was sensitive to C–Cl bonds and substrates such as **1f** and **2h** were not tolerated any further.

To further demonstrate the potential utilities, transformations based on the methodology and products were made (Scheme 4). Easily accessible 1,3,5-triallylbenzene (**2q**) was applied to the chemistry, and the high molecular weight compound **3nq** was obtained with a slight modification of conditions A (Scheme 4a). The dearomative product **3pa** was also transformed into a rare and stable 5-hydroxy-Δ1-pyrroline **5pa** (Scheme 4b) in good yield through simple transformations; such species are of great synthetic and pharmaceutical importance.[17]

Having established the generality of the methodology, mechanism experiments were conducted to gain insight into the reaction pathway. Under the standard conditions, the byproduct **3a′a′** could not be transformed into product **3aa**, showing that allyl ether **3a′a′** is not a reaction intermediate

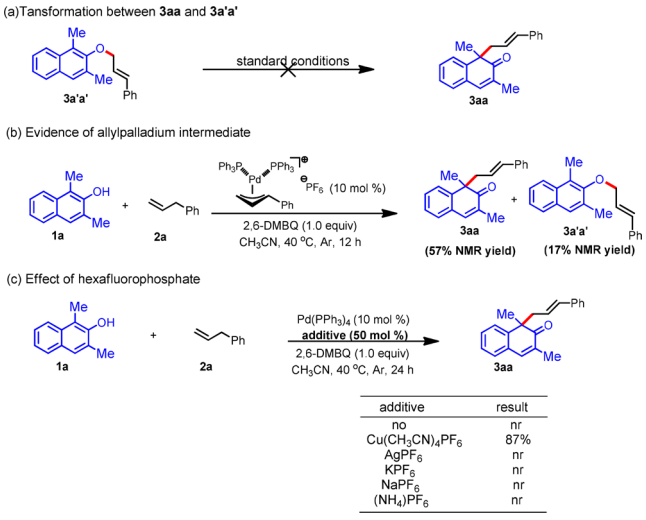
DOI: 10.1021/acs.orglett.8b02910
Org. Lett. XXXX, XXX, XXX–XXX

Scheme 4. Synthetic Applications



(Scheme 5a). Furthermore, to verify the allypalladium intermediate, a π-allylpalladium(II) complex [Pd(η^3-cin)-

Scheme 5. Preliminary Mechanism Investigation

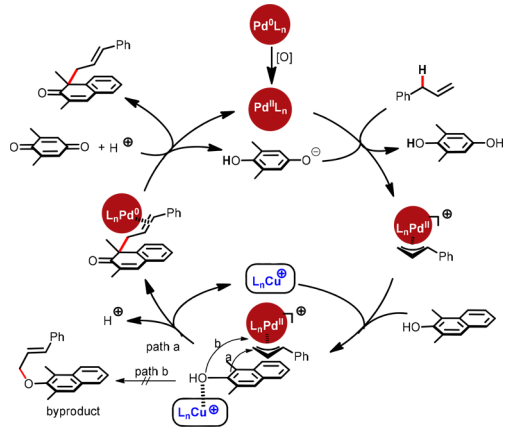


additive	result
no	nr
$Cu(CH_3CN)_4PF_6$	87%
$AgPF_6$	nr
KPF_6	nr
$NaPF_6$	nr
$(NH_4)PF_6$	nr

$(PPh_3)_2PF_6$] was synthesized and used in the reaction. The complex indeed catalyzed the reaction even in the absence of copper(I)-salt, in spite of resulting in a mixture of dearomatization product **3aa** (57% yield) and allylic etherification byproduct **3a′a′** (17% yield) (Scheme 5b), indicating the involvement of a highly electrophilic allypalladium species. Furthermore, the effect of copper salt was investigated (Scheme 5c). The product was obtained in 87% yield under the standard conditions A, whereas no product was detected without $Cu(CH_3CN)_4PF_6$ or with other additives such as $AgPF_6$, KPF_6, or $NaPF_6$, showing the indispensable role of the copper cation for the allylic dearomatization process. The effects of copper additive were further evaluated. During the reaction, $Cu(MeCN)_4PF_6$ may increase the activity of palladium catalyst through anion exchange and act as a Lewis acid to activate naphthols for dearomatization. On the other hand, copper(I) can also be oxidized to Cu^{II} and be involved in the oxidation[18] of palladium(0) to palladium(II) with 2,6-DMBQ. To illustrate these processes, ESR experiments (see SI for details) were conducted to detect a possible Cu^{II} signal. The ESR spectra of the reaction system showed no signal corresponding to Cu^{II},[19] thereby discounting a cooperative oxidation role of copper salt. On the basis of previous reports, a more likely role of copper(I) salt as a Lewis acid[20] for naphthol dearomatization is proposed.

With the results illustrated above in hand, a plausible catalytic pathway was proposed (Scheme 6). Initially, an

Scheme 6. Proposed Catalytic Pathway



electrophilic palladium(II) species is generated in situ through oxidation of palladium(0) precatalyst and subsequent precoordination of palladium(II) to allylbenzene and proton abstraction[21] give rise to a highly active π-allylpalladium(II) electrophile. Synchronously, coordination of copper(I) to oxygen modulates the nucleophilic reactivity of phenolic hydroxyl group in 2-naphthol and activates the naphthol to be a *pro*-3° carbon nucleophile. Next, an electrophonic allylic substitution with naphthol at the carbon center (path a) proceeds. Finally, palladium(0) is oxidized to palladium(II) by 2,6-DMBQ under acidic conditions[18] and the dearomatization product is liberated simultaneously. The byproduct is the result of allylic substitution on the nucleophilic oxygen center (path b), which is an unfavorable process under the current conditions.

In summary, we have disclosed a palladium/copper cooperative catalysis for the direct oxidative allylic C−H dearomatization of 2-naphthols under mild conditions. The introduction of a cooperative copper catalyst allows highly effective and selective C-allylation of naphthols under base-free conditions. The special tolerance of the conditions toward peptides demonstrates the high potential for synthetic applications.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.8b02910.

Experimental details and characterization data for all new compounds (PDF)

Accession Codes

CCDC 1839679 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.

DOI: 10.1021/acs.orglett.8b02910
Org. Lett. XXXX, XXX, XXX−XXX

AUTHOR INFORMATION

Corresponding Author

*E-mail: yangshd@lzu.edu.cn.

ORCID

Shang-Dong Yang: 0000-0002-4486-800X

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

We are grateful for the NSFC (nos. 21472076 and 21532001) and the Open Fund of the Key Laboratory of Functional Molecular Engineering of Guangdong Province (no. 2016B01017) financial support.

REFERENCES

(1) (a) Amand, S.; Vallet, M.; Guedon, L.; Genta-Jouve, G.; Wien, F.; Mann, S.; Dupont, J.; Prado, S.; Nay, B. *Org. Lett.* **2017**, *19*, 4038−4041. (b) Hutchinson, D. K. et al. Anti-infective Agents. US Patent US20050107364. 2005. (c) Decosterd, L. A.; Stoeckli-Evans, H.; Chapuis, J. C.; Sordat, B.; Hostettmann, K. *Helv. Chim. Acta* **1989**, *72*, 1833−1845.

(2) Eiji, Y.; Takashi, A.; Hiroki, K.; Tomoya, K. Polymer Compounds, and Organic Thin Film and Organic Semiconductor Element Containing the Same. Japan Patent JP 2015218291. 2015.

(3) (a) Majetich, G.; Grove, J. L. *Org. Lett.* **2009**, *11*, 2904−2907. (b) Myers, A. G.; Herzon, S. B. *J. Am. Chem. Soc.* **2003**, *125*, 12080−12081. (c) Xu, Z.-R.; Wang, Q.; Zhu, J.-P. *J. Am. Chem. Soc.* **2015**, *137*, 6712−6724.

(4) For examples to synthesize cyclohexadienone structures: (a) Hart, H.; Lange, R. M. *J. Org. Chem.* **1966**, *31*, 3776−3779. (b) Coleman, R. S.; Guernon, J. M.; Roland, J. T. *Org. Lett.* **2000**, *2*, 277−280. (c) Jackson, S. R.; Johnson, M. G.; Mikami, M.; Shiokawa, S.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2001**, *40*, 2694−2697. (d) Liu, P.; Fukui, Y.; Tian, P.; He, Z.-T.; Sun, C.-Y.; Wu, N.-Y.; Lin, G.-Q. *J. Am. Chem. Soc.* **2013**, *135*, 11700−11703. (e) Reddy, R. R.; Gudup, S. S.; Ghorai, P. *Angew. Chem., Int. Ed.* **2016**, *55*, 15115−15119.

(5) For recent reviews on catalytic asymmetric dearomatization reactions: (a) Zhuo, C.-X.; Zhang, W.; You, S.-L. *Angew. Chem., Int. Ed.* **2012**, *51*, 12662−12686. (b) Zhuo, C.-X.; Zheng, C.; You, S.-L. *Acc. Chem. Res.* **2014**, *47*, 2558−2573. (c) Zheng, C.; You, S.-L. *Chem.* **2016**, *1*, 830−857.

(6) For reviews on dearomatization of phenols: (a) Magdziak, D.; Meek, S. J.; Pettus, T. R. R. *Chem. Rev.* **2004**, *104*, 1383−1429. (b) Wu, W.-T.; Zhang, L.-M.; You, S.-L. *Chem. Soc. Rev.* **2016**, *45*, 1570−1580.

(7) For examples of AADC reactions of naphthols with protected allylic alcohols: (a) Nemoto, T.; Ishige, Y.; Yoshida, M.; Kohno, Y.; Kanematsu, M.; Hamada, Y. *Org. Lett.* **2010**, *12*, 5020−5023. (b) Yoshida, M.; Nemoto, T.; Zhao, Z.; Ishige, Y.; Hamada, Y. *Tetrahedron: Asymmetry* **2012**, *23*, 859−866. (c) Zhuo, C.-X.; You, S.-L. *Adv. Synth. Catal.* **2014**, *356*, 2020−2028. (d) Zhuo, C.-X.; You, S.-L. *Angew. Chem., Int. Ed.* **2013**, *52*, 10056−10059. (e) Cheng, Q.; Wang, Y.; You, S.-L. *Angew. Chem., Int. Ed.* **2016**, *55*, 3496−3499.

(8) (a) Tu, H.-F.; Zheng, C.; Xu, R.-Q.; Liu, X.-J.; You, S.-L. *Angew. Chem., Int. Ed.* **2017**, *56*, 3237−3241. (b) Shen, D.; Chen, Q.-L.; Yan, P.-P.; Zeng, X.-F.; Zhong, G.-F. *Angew. Chem., Int. Ed.* **2017**, *56*, 3242−3246.

(9) Fang, X.-X.; Zeng, Y.-Y.; Li, Q.-Y.; Wu, Z.-J.; Yao, H.-Q.; Lin, A.-J. *Org. Lett.* **2018**, *20*, 2530−2533.

(10) For palladium-catalyzed C−H functionalizations: (a) Chen, M. S.; White, M. C. *J. Am. Chem. Soc.* **2004**, *126*, 1346−1347. (b) Reed, S. A.; White, M. C. *J. Am. Chem. Soc.* **2008**, *130*, 3316−3318. (c) Lin, S.; Song, C.-X.; Cai, G.-X.; Wang, W.-H.; Shi, Z.-J. *J. Am. Chem. Soc.* **2008**, *130*, 12901−12903. (d) Xu, J.; Fu, Y.; Luo, D.-F.; Jiang, Y.-Y.; Xiao, B.; Liu, Z.-J.; Gong, T.-J.; Liu, L. *J. Am. Chem. Soc.* **2011**, *133*, 15300−15303. (e) Parsons, A. T.; Buchwald, S. L. *Angew. Chem.* **2011**, *123*, 9286−9289. (f) Campbell, A. N.; White, P. B.; Guzei, I. A.; Stahl, S. S. *J. Am. Chem. Soc.* **2010**, *132*, 15116−15119. (g) Alam, R.; Pilarski, L. T.; Pershagen, E.; Szabó, K. J. *J. Am. Chem. Soc.* **2012**, *134*, 8778−8781. (h) Braun, M. G.; Doyle, A. G. *J. Am. Chem. Soc.* **2013**, *135*, 12990−12993. (i) Jiang, H.-F.; Yang, W.-F.; Chen, H.-J.; Li, J.-X.; Wu, W.-Q. *Chem. Commun.* **2014**, *50*, 7202−7204. (j) McAtee, J. R.; Yap, G. P. A.; Watson, D. A. *J. Am. Chem. Soc.* **2014**, *136*, 10166−10172. (k) Qi, X.-X.; Chen, P.-H.; Liu, G.-S. *Angew. Chem.* **2017**, *129*, 9645−9649. (l) Trost, B. M.; Hansmann, M. M.; Thaisrivongs, D. A. *Angew. Chem.* **2012**, *124*, 5034−5037. (m) McAtee, J. R.; Yap, G. P. A.; Watson, D. A. *J. Am. Chem. Soc.* **2014**, *136*, 10166−10172. (n) Hu, R.-B.; Wang, C.-H.; Ren, W.; Liu, Z.; Yang, S.-D. *ACS Catal.* **2017**, *7*, 7400−7404.

(11) For rhodium-catalyzed allylic C−H functionalization: (a) Cochet, T.; Bellosta, V.; Roche, D.; Ortholand, J.; Greiner, A.; Cossy, J. *Chem. Commun.* **2012**, *48*, 10745−10747. (b) Archambeau, A.; Rovis, T. *Angew. Chem., Int. Ed.* **2015**, *54*, 13337−13340. (c) Shibata, Y.; Kudo, E.; Sugiyama, H.; Uekusa, H.; Tanaka, K. *Organometallics* **2016**, *35*, 1547−1552. (d) Burman, J. S.; Blakey, S. B. *Angew. Chem., Int. Ed.* **2017**, *56*, 13666−13669.

(12) For cobalt-catalyzed allylic C−H functionalization: Michigami, K.; Mita, T.; Sato, Y. *J. Am. Chem. Soc.* **2017**, *139*, 6094−6097.

(13) For reviews on cooperative catalysis: (a) Kim, D.; Park, W.; Jun, C. H. *Chem. Rev.* **2017**, *117*, 8977−9015. (b) Afewerki, S.; Córdova, A. *Chem. Rev.* **2016**, *116*, 13512−13570. (c) Jindal, G.; Kisan, H. K.; Sunoj, R. B. *ACS Catal.* **2015**, *5*, 480−503. (d) Wang, M. H.; Scheidt, K. A. *Angew. Chem., Int. Ed.* **2016**, *55*, 14912−14922. (e) Peters, R. *Cooperative Catalysis: Designing Efficient Catalysts for Synthesis*; Wiley-VCH: Weinheim, 2015.

(14) Bolm, M. B. C. *Transition Metals for Organic Synthesis: Building Blocks and Fine Chemicals*; Wiley-VCH: Weinheim, 2004.

(15) For an review on allylic alkylation with soft and hard nucleophiles: Trost, B. M.; Van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395−422.

(16) Silvery metal was observed on the tube at high temperature, resulting from deactivation of partial palladium catalyst.

(17) (a) Dvorko, M. Y.; Shabalin, D. A.; Schmidt, E. Y.; Ushakov, I. A.; Trofimov, B. A. *Eur. J. Org. Chem.* **2017**, *2017*, 4609−4616. (b) Zhang, L.; Ang, G. Y.; Chiba, S. *Org. Lett.* **2011**, *13*, 1622−1625. (c) Rostovskii, N. V.; Sakharov, P. A.; Novikov, M. S.; Khlebnikov, N. V.; Starova, G. L. *Org. Lett.* **2015**, *17*, 4148−4151. (d) Alizadeh, A.; Moafi, L. *Helv. Chim. Acta* **2016**, *99*, 306−309. (e) Clark, V. C.; Raxworthy, C. J.; Rakotomalala, V.; Sierwald, P.; Fisher, B. L. *Proc. Natl. Acad. Sci. U. S. A.* **2005**, *102*, 11617−11622.

(18) (a) Stahl, S. S. *Angew. Chem., Int. Ed.* **2004**, *43*, 3400−3420. (b) Piera, J.; Bäckvall, J. E. *Angew. Chem., Int. Ed.* **2008**, *47*, 3506−3523. (c) Gligorich, K. M.; Sigman, M. S. *Chem. Commun.* **2009**, 3854−3867. (d) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094−5115. (e) Beccalli, E. M.; Broggini, G.; Martinelli, M.; Sottocornola, S. *Chem. Rev.* **2007**, *107*, 5318−5365. (f) Ma, X.-T.; Xu, H.; Xiao, Y.-L.; Su, C.-L.; Liu, J.-P.; Xu, Q. *Chin. Chem. Lett.* **2017**, *28*, 1336−1339.

(19) The ESR spectra of reaction system (g = 1.999) displayed the signal of Pd^{II} (g = 2.000) and no signal of Cu^{II} (g = 2.178) was detected. See Supporting Information for details.

(20) For selected examples of lewis acid-catalyzed Aza-Friedel−Crafts reaction of phenols with aldimines: (a) Niu, L.-F.; Xin, Y.-C.; Wang, R.-L.; Jiang, F.; Xu, P.-F.; Hui, X.-P. *Synlett* **2010**, *2010*, 765−768. (b) Bai, S.; Liao, Y.-T.; Lin, L.-L.; Luo, W.-W.; Liu, X.-H.; Feng, X.-M. *J. Org. Chem.* **2014**, *79*, 10662−10668. (c) Montesinos-Magraner, M.; Cantón, R.; Vila, C.; Blay, G.; Fernández, I.; Muñoz, M. C.; Pedro, J. R. *RSC Adv.* **2015**, *5*, 60101−60105.

(21) Engelin, C.; Jensen, T.; Rodriguez-Rodriguez, S.; Fristrup, P. *ACS Catal.* **2013**, *3*, 294−302.

DOI: 10.1021/acs.orglett.8b02910
Org. Lett. XXXX, XXX, XXX−XXX