OL | Organic Letters

Letter

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

pubs.acs.org/OrgLett

Palladium-Catalyzed Hydrocarbonylative Cyclization of 1,5-Dienes

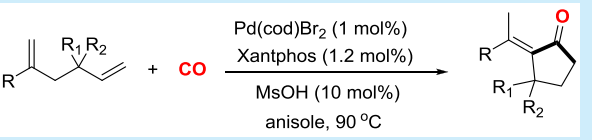
Suchen Zou,[†] Bao Gao,[†] Yao Huang,[†] Tianze Zhang,[†] and Hanmin Huang*[,†,‡]

[†]Hefei National Laboratory for Physical Sciences at the Microscale and Department of Chemistry, Center for Excellence in Molecular Synthesis, University of Science and Technology of China, Chinese Academy of Sciences, Hefei, 230026, People's Republic of China

[‡]State Key Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou, 730000, People's Republic of China

Supporting Information

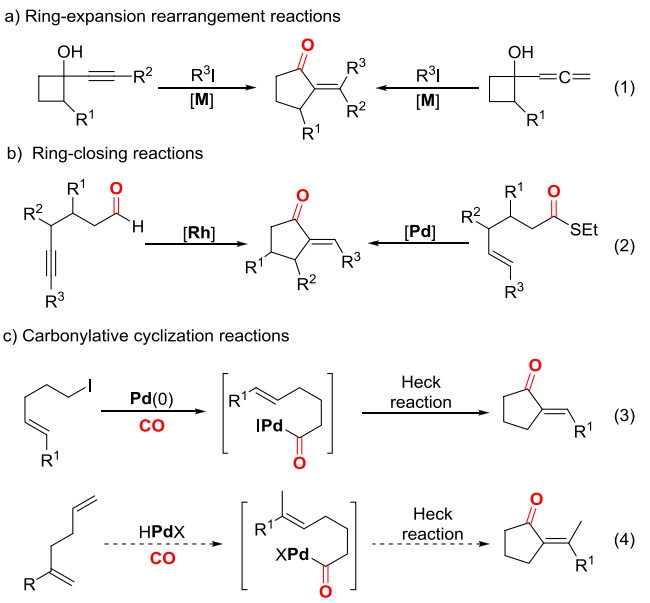
ABSTRACT: A novel and atom-economic palladium-catalyzed isomerization-hydrocarbonylative cyclization reaction of 1,5-dienes to 2-alkylidenecyclopentanones has been developed, which provides a rapid and straightforward approach to 2-alkylidenecyclopentanones with high stereoselectivity. The reaction was found to proceed via alkene isomerization and selective hydrocarbonylative cyclization to generate 2-alkylidenecyclopentanones with high selectivity.



The cyclopentanones are valuable core structures of a plethora of nature products and bioactive compounds, as well as versatile intermediates in the synthesis of complex molecules.[1] In particular, 2-alkylidenecyclopentanones have been identified as versatile building blocks for the synthesis of various pharmaceuticals and bioactive molecules.[2,3] Consequently, general strategies for the efficient and selective synthesis of cyclopentanones are highly desirable but remain underdeveloped. During the past few decades, extensive efforts have been devoted to the ring expansion reactions. Among them, transition-metal-catalyzed ring expansion of functionalized cyclobutanol is particularly attractive for the synthesis of 2-alkylidenecyclopentanones. However, the tedious procedure for the synthesis of cyclobutanol limited the large-scale synthesis (Scheme 1a).[4] Alternatively, ring-closing reactions of alkynals and thioester olefins under the catalysis of transition metals have also been established for the generation of 2-alkylidenecyclopentanones, but the relative higher catalyst loading and stoichiometric amount of additive required significant reduce the synthetic practice (Scheme 1b).[5,6] For all of these approaches, the step and atom economies are imperfect, because of the requirement for prefunctionalization and/or the need for additional reagents in the coupling step.

Although intramolecular carbonylative cyclization reactions, such as the Pauson−Khand reaction, have been studied extensively,[7] the preparation of 2-alkylidenecyclopentanones through analogous cyclization reactions finds considerable less precedent. In this context, Alexanian and co-workers developed a Pd-catalyzed carbonylative Heck-type reaction of alkenyl iodides in the presence of a base. In that reaction, the key acylpalladium species was produced via sequential oxidative addition and CO insertion with alkyl iodides as starting materials, resulting in lower atom economy (see Scheme 1c).[8] Transition-metal-catalyzed hydrocarbonylation reactions that allow the direct use of simple alkenes as starting materials have emerged as atom-economic methods to install carbonyl groups.[9] In this context, one could establish a cyclization reaction with

Scheme 1. Background of the Development Method



1,5-dienes initiated via hydrocarbonylation to form 2-alkylidenecyclopentanones in the presence of CO that possesses complete atom economy (Scheme 1c). A conventional mechanism would include hydropalladation of alkene, CO insertion, and intramolecular alkene insertion.

However, the realization of such a process is challenging, since the site-selective hydropalladation of one alkene moiety among the two reactive alkene moieties is difficult. Moreover, the intramolecular Heck reaction initiated via the hydropalladation may occur to compete with the desired carbonylation reaction.

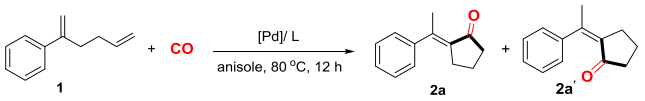
Received: June 28, 2019

DOI: 10.1021/acs.orglett.9b02230
Org. Lett. XXXX, XXX, XXX−XXX

In continuation of our efforts on the hydrocarbonylation reactions,[10] herein we report a palladium-catalyzed selective hydrocarbonylative cyclization of 1,5-dienes, leading to the efficient synthesis of 2-alkylidenecyclopentanones.

Initially, we commenced our studies by attempting the proposed carbonylative cyclization of 2-phenyl-1,5-diene **1a** in anisole at 80 °C under CO (20 atm). With $Pd(COD)Br_2$ as a catalyst precursor, CH_3SO_3H as an additive, a variety of commercially available ligands, including diphosphine and monophosphine, were evaluated, and the results revealed that some commonly used ligands, such as DPPB, DPPP, and DPPF (Table 1, entries 1−3), were ineffective for this carbonylation.

Table 1. Optimization of Reaction Conditions[b]



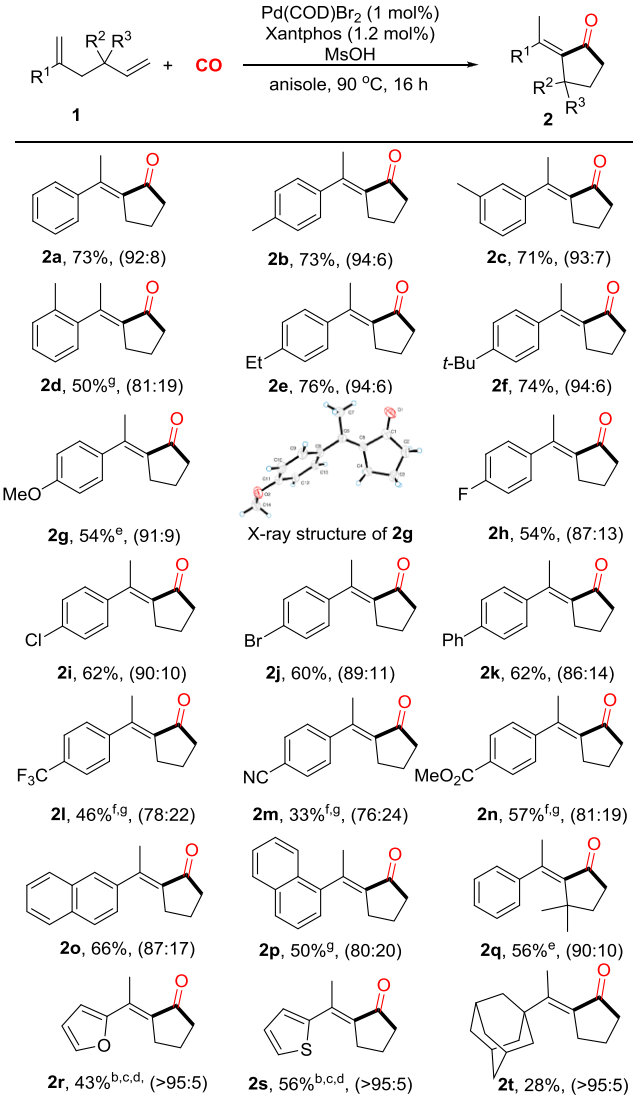
entry	[Pd]	ligand	acid[a]	yield, 2a+2a′ (%)	2a:2a′
1	$Pd(COD)Br_2$	DPPB	MsOH	0	–
2	$Pd(COD)Br_2$	DPPP	MsOH	0	–
3	$Pd(COD)Br_2$	DPPF	MsOH	0	–
4	$Pd(COD)Br_2$	DPEPhos	MsOH	15	88:12
5[c]	$Pd(COD)Br_2$	PPh_3	MsOH	21	88:12
6	$Pd(COD)Br_2$	Xantphos	MsOH	78	91:9
7	$PdCl_2$	Xantphos	MsOH	58	90:10
8	$Pd(PhCN)_2Cl_2$	Xantphos	MsOH	65	88:12
9	$PdBr_2$	Xantphos	MsOH	62	89:11
10[d]	$Pd_2(dba)_3$	Xantphos	MsOH	trace	–
11	$Pd(COD)Br_2$	Xantphos	–	0	–
12	$Pd(COD)Br_2$	Xantphos	NMP·HCl	trace	–
13	$Pd(COD)Br_2$	Xantphos	$PhSO_3H$	73	91:9
14	$Pd(COD)Br_2$	Xantphos	CF_3CO_2H	22	93:7
15	$Pd(COD)Br_2$	Xantphos	TsOH	54	91:9
16[e]	$Pd(COD)Br_2$	Xantphos	MsOH	81	92:8

[a]MsOH = methanesulfonic acid; TsOH = *p*-toluenesulfonic acid. [b]Reaction conditions: **1a** (0.4 mmol), [Pd] (0.02 mmol, 5 mol %), ligand (0.024 mmol, 6 mol %), acid (0.04 mmol, 10 mol %), anisole (1.0 mL), CO (20 atm), 80 °C, 12 h, the combined yield based on the diene and the ratio (**2a**:**2a′**) of the crude reaction mixture was determined by GC and GC-MS analysis using *n*-dodecane as the internal standard. [c]Ligand (0.048 mmol, 12 mol %). [d][Pd] (0.01 mmol, 2.5 mol %). [e]**1a** (1.0 mmol), $Pd(COD)Br_2$ (0.01 mmol, 1 mol %), Xantphos (0.012 mmol, 1.2 mol %), acid (0.1 mmol, 10 mol %), anisole (2.0 mL), CO (30 atm), 90 °C, 16 h.

To our delight, the desired 2-alkylidenecyclopentanone (**2a** + **2a′**) was obtained in a combined yield of 15% with good stereoselectivity when DPEPhos (Table 1, entry 4) was introduced into the catalytic system. Further optimization of the ligands disclosed that Xantphos (Table 1, entry 6) could deliver the carbonylative adducts in a combined yield of 78% with higher stereoselectivity. Examination of palladium precursors revealed that $Pd(COD)Br_2$/Xantphos created the most reactive catalyst for this transformation to give the carbonylation product with high stereoselectivity, and other palladium precursors showed lower activity (Table 1, entries 7−10). No desired product formed in the absence of acid (Table 1, entry 11), and we also found that sulfonic acids such as methanesulfonic acid (MsOH) were superior to other acids. Moreover, the reaction temperature, solvent, and CO pressure were assessed as well, yet variation of these parameters could not deliver better results (see the Supporting Information (SI)). Finally, we were pleased to find that the combined yield could be increased to 81% in the presence of MsOH and 1 mol % of catalyst under 30 atm of CO at 90 °C (Table 1, entry 16).

With the optimized reaction conditions established, we examined the scope of this new reaction with a variety of substituted dienes. As summarized in Table 2, in all cases, 2-phenyl-1,5-dienes bearing both electron-donating and electron-withdrawing groups on the aromatic rings were all smoothly converted to the corresponding (*E*)-2-alkylidenecyclopentanones in moderate to good yields (33%−76%) with good to excellent stereoselectivities. Obviously, the 2-phenyl-1,5-dienes with electron-donating groups provided the desired products with good yields (50%−76%, **2a**−**2g**) and higher selectivities.

Table 2. Substrate Scope[a]



[a]Reaction conditions: **1** (1.0 mmol), $Pd(COD)Br_2$ (1.0 mol %), Xantphos (1.2 mol %), MsOH (0.1 mmol), CO (30 atm), anisole (2.0 mL), 90 °C, 16 h. The isolated yield based on the diene and the ratio (*E*/*Z*) of the crude reaction mixture was determined by GC and GC-MS. [b]$Pd(COD)Br_2$ (5.0 mol %), Xantphos (6 mol %). [c]120 °C. [d]$PhSO_3H$ (0.02 mmol). [e]$PhSO_3H$ (0.1 mmol). [f]MsOH (0.3 mmol). [g]24 h.

DOI: 10.1021/acs.orglett.9b02230
Org. Lett. XXXX, XXX, XXX−XXX

The structure of the desired product **2g** was unambiguously confirmed by single-crystal X-ray diffraction (XRD) analysis. In contrast, 2-phenyl-1,5-dienes substituted by electron-withdrawing groups such as $-CF_3$ (**2l**), $-CN$ (**2m**), and $-CO_2Me$ (**2n**), led to relative lower yields (33%−57%) and selectivities. The steric effect was observed in the transformation. The carbonylation reaction of *ortho*-substituted dienes, such as **1d** and **1p**, gave relative lower yields and selectivities. Pleasingly, the reaction performed well for the diene substituted with 2-naphthyl (**2o**, 66% yield). Substituents could be incorporated into the tether-backbone of the dienes to give the corresponding adduct (**2q**). In addition, heteroaromatic-ring-substituted 1,5-dienes provided corresponding product in moderate yields with excellent stereoselectivities (**2r** and **2s**). Encouraged by our success with aromatic diene, aliphatic diene was then explored. Under the optimized reaction conditions, the large steric 2-adamantyl substituted diene (**1t**) can be applied to this protocol, delivering the desired product (**2t**) in 28% yield with *trans*-configuration. The analogue 1,6-dienes were also tested, but no desired carbonylative cyclization reactions were observed. To our great delight, the target reaction proceeded smoothly at a lower catalyst loading (0.1 mol %), affording the desired 2-alkylidenecyclopentanone **2a** in 49% yield with excellent stereoselectivity (see the SI).

To gain some insight into the mechanism of the present carbonylation reaction, some control experiments were conducted. Treatment of diene **1a** with MsOH at 90 °C for 16 h, the 1,4-diene (**3a**) was obtained in 93.3% yield with *E*:*Z* = 87:13. The 1,4-dienes can be converted to the corresponding product in 60% yield under the standard reaction conditions (Figure 1). The reaction was monitored using substrate **1a** to

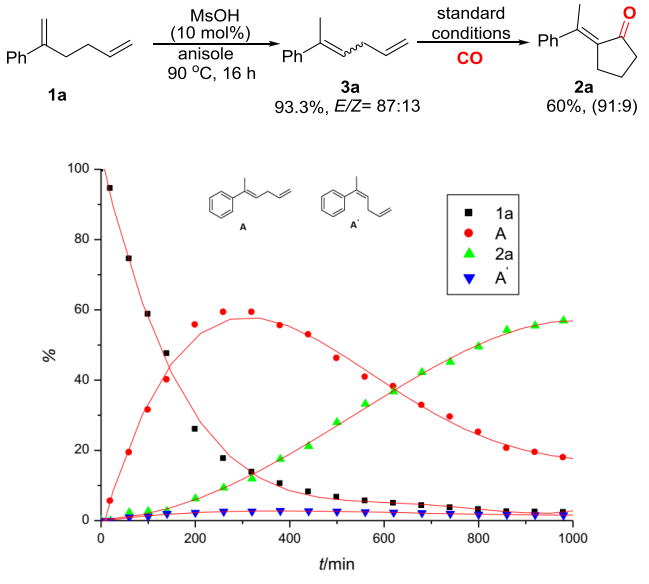
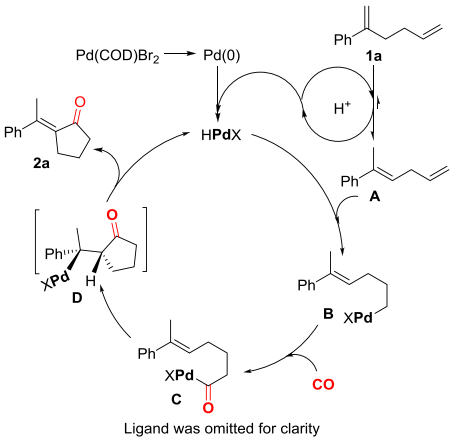


Figure 1. Reaction profile of Pd-catalyzed hydrocarbonylative cyclization of **1a**.

detect whether the diene isomerization occurred. It illustrated that the 1,5-diene **1a** was transformed to 1,4-dienes **A** and **A′** from the beginning of the process and then the 1,4-diene was slowly transformed to the desired product **2a** (Figure 1). Based on these studies, it can be reasoned that selective isomerization of 1,5-diene occurred first to form thermodynamic stable (*E*)-1,4-diene, which was subsequently converted to the desired 2-alkylidenecyclopentanone **2a** via hydrocarbonylation and Heck reaction.

On the basis of precedent results[10] and the above experimental data, a tentative catalytic cycle is proposed in Scheme 2. The reaction begins with the generation of palladium

Scheme 2. Plausible Reaction Mechanism



hydride species from the reaction of Pd(0) and MsOH. Next, intermolecular hydropalladation of the 1,4-diene **A**, which is produced from the isomerization of 1,5-diene under the acidic condition,[11] generated the intermediate **B**. Subsequent insertion of CO into the alkyl−palladium bond affords the acyl palladium complex **C**, followed by the intramolecular C=C double bond insertion to afford the intermediate **D**. Finally, β-hydride elimination leads to the desired product and regenerates the palladium hydride species for the next catalytic cycle.

In summary, we have developed an atom-economic protocol for the synthesis of 2-alkylidenecyclopentanones via Pd-catalyzed isomerization−cyclocarbonylation of 1,5-dienes. The reaction proceeded well to furnish the desired products with good functional-group compatibility and high stereoselectivity, which provided a rapid and reliable approach to 2-alkylidenecyclopentanones. Mechanistic studies suggested that the selective isomerization of 1,5-dienes occurred first to form 1,4-dienes, which subsequently were converted to the desired products through hydrocarbonylation and intramolecular Heck reaction. Further studies to apply this strategy are in progress in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.9b02230.

Experimental details and full spectroscopic data for all new compounds (PDF)

Accession Codes

CCDC 1937070 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.9b02230
Org. Lett. XXXX, XXX, XXX−XXX

AUTHOR INFORMATION

Corresponding Author

*E-mail: hanmin@ustc.edu.cn.

ORCID

Hanmin Huang: 0000-0002-0108-6542

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This research was supported by the National Natural Science Foundation of China (Nos. 21790333, 21702197, and 21672199) and the Fundamental Research Funds for the Central Universities (No. WK2060190086).

REFERENCES

(1) (a) Wang, J.; Zhao, L.; Wang, R.; Lu, M.; Chen, D.; Jing, Y. Synthesis and Anticancer Activity of 2-alkylaminomethyl-5-diarylmethylenecyclopentanone Hydrochlorides and Related Compounds. *Bioorg. Med. Chem.* **2005**, *13*, 1285. (b) Heng, R.; Zard, S. Z. A Flexible Route to Substituted Hydroxy-Cyclopentanones from Cyclobutanones. *Tetrahedron Lett.* **2015**, *56*, 3679. (c) Costanzo, P.; Cariati, L.; Desiderio, D.; Sgammato, R.; Lamberti, A.; Arcone, R.; Salerno, R.; Nardi, M.; Masullo, M.; Oliverio, M. Design, Synthesis, and Evaluation of Donepezil-Like Compounds as AChE and BACE-1 Inhibitors. *ACS Med. Chem. Lett.* **2016**, *7*, 470. (d) Simeonov, S. P.; Nunes, J. P. M.; Guerra, K.; Kurteva, V. B.; Afonso, C. A. M. Synthesis of Chiral Cyclopentenones. *Chem. Rev.* **2016**, *116*, 5744.

(2) (a) Liebeskind, L. S.; Chidambaram, R.; Mitchell, D.; Foster, B. S. Metal Mediated Routes to 5-membered Rings. *Pure Appl. Chem.* **1988**, *60*, 27. (b) Sun, H. D.; Huang, S. X.; Han, Q. B. Diterpenoids from Isodon Species and Their Biological Activities. *Nat. Prod. Rep.* **2006**, *23*, 673.

(3) (a) Gibson, S. E.; Lewis, S. E.; Mainolfi, N. Transition Metal-Mediated Routes to Cyclopentenones. *J. Organomet. Chem.* **2004**, *689*, 3873. (b) Deng, R.; Tang, J.; Xia, L.-P.; Li, D.-D.; Zhou, W.-J.; Wang, L.-L.; Feng, G.-K.; Zeng, Y.-X.; Gao, Y.-H.; Zhu, X.-F. Excisanin A, a Diterpenoid Compound Purified from Isodon Macrocalyxin D, Induces Tumor Cells Apoptosis and Suppresses Tumor Growth Through Inhibition of PKB/AKT Kinase Activity and Blockade of its Signal Pathway. *Mol. Cancer Ther.* **2009**, *8*, 873. (c) Li, C.; Dian, L.; Zhang, W.; Lei, X. Biomimetic Syntheses of (−)-Gochnatiolides A−C and (−)-Ainsliadimer B. *J. Am. Chem. Soc.* **2012**, *134*, 12414.

(4) (a) Larock, R. C.; Reddy, C. K. Synthesis of 2-Alkylidenecyclopentanones via Palladium-Catalyzed Cross-Coupling of 1-(1-Alkynyl)-Cyclobutanols and Aryl or Vinylic Halides. *Org. Lett.* **2000**, *2*, 3325. (b) Larock, R. C.; Reddy, C. K. Synthesis of 2-Alkylidenecyclopentanones via Palladium-Catalyzed Carbopalladation/Ring Expansion of 1-(1-Alkynyl)cyclobutanols. *J. Org. Chem.* **2002**, *67*, 2027. (c) Markham, J. P.; Staben, S. T.; Toste, F. D. Gold(I)-Catalyzed Ring Expansion of Cyclopropanols and Cyclobutanols. *J. Am. Chem. Soc.* **2005**, *127*, 9708. (d) Leemans, E.; D'hooghe, M.; De Kimpe, N. Ring Expansion of Cyclobutylmethylcarbenium Ions to Cyclopentane or Cyclopentene Derivatives and Metal-Promoted Analogous Rearrangements. *Chem. Rev.* **2011**, *111*, 3268. (e) Seiser, T.; Saget, T.; Tran, D. N.; Cramer, N. Cyclobutanes in Catalysis. *Angew. Chem., Int. Ed.* **2011**, *50*, 7740.

(5) (a) Sato, Y.; Oonishi, Y.; Mori, M. A New Method for the Synthesis of Cycloheptenones by Rh^{I}-Catalyzed Intramolecular Hydroacylation of 4,6-Dienals. *Angew. Chem., Int. Ed.* **2002**, *41*, 1218. (b) Takeishi, K.; Sugishima, K.; Sasaki, K.; Tanaka, K. Rhodium-Catalyzed Intramolecular Hydroacylation of 5- and 6-alkynals: Convenient Synthesis of α-Alkylidenecycloalkanones and Cycloalkenones. *Chem. - Eur. J.* **2004**, *10*, 5681.

(6) Thottumkara, A. P.; Kurokawa, T.; Du Bois, J. Carbocyclization of Unsaturated Thioesters under Palladium Catalysis. *Chem. Sci.* **2013**, *4*, 2686.

(7) (a) Brewis, S.; Hughes, P. R. The Carbonylation of Dienes with Palladium Catalysts. *Chem. Commun.* **1965**, 489 (b) Brewis, S.; Hughes, P. R. The Transannular Addition of Carbon Monoxide to cyclo-octa-1,5-Diene. *Chem. Commun.* **1966**, *6*, 6. (c) Blanco-Urgoiti, J.; Añorbe, L.; Pérez-Serrano, L.; Domínguez, G.; Pérez-Castells, J. The Pauson−Khand Reaction, A powerful Synthetic Tool for the Synthesis of Complex Molecules. *Chem. Soc. Rev.* **2004**, *33*, 32. (d) Kitagaki, S.; Inagaki, F.; Mukai, C. [2 + 2+1] Cyclization of Allenes. *Chem. Soc. Rev.* **2014**, *43*, 2956.

(8) Bloome, K. S.; Alexanian, E. J. Palladium-Catalyzed Carbonylative Heck-Type Reactions of Alkyl Iodides. *J. Am. Chem. Soc.* **2010**, *132*, 12823.

(9) (a) Hebrard, F.; Kalck, P. Cobalt-Catalyzed Hydroformylation of Alkenes: Generation and Recycling of the Carbonyl Species, and Catalytic Cycle. *Chem. Rev.* **2009**, *109*, 4272. (b) Wu, X.; Neumann, H.; Beller, M. Synthesis of Heterocycles via Palladium-Catalyzed Carbonylations. *Chem. Rev.* **2013**, *113*, 1. (c) Chiou, W.-H.; Wang, Y.-W.; Kao, C.-L.; Chen, P.-C.; Wu, C.-C. Rhodium-Catalyzed Hydrocarbonylation of a Homoallylamine via N−H Activation and Application for Synthesis of Yohimbane Alkaloids. *Organometallics* **2014**, *33*, 4240. (d) Li, H.; Dong, K.; Neumann, H.; Beller, M. Palladium-Catalyzed Hydroamidocarbonylation of Olefins to Imides. *Angew. Chem. Int. Ed.* **2015**, *54*, 10239. (e) Xu, T.; Sha, F.; Alper, H. Highly Ligand-Controlled Regioselective Pd-Catalyzed Aminocarbonylation of Styrenes with Aminophenols. *J. Am. Chem. Soc.* **2016**, *138*, 6629. (f) Liu, J.; Yang, J.; Ferretti, F.; Jackstell, R.; Beller, M. Pd-Catalyzed Selective Carbonylation of gem-Difluoroalkenes: A Practical Synthesis of Difluoromethylated Esters. *Angew. Chem., Int. Ed.* **2019**, *58*, 4690.

(10) (a) Zhang, G.; Gao, B.; Huang, H. Palladium-Catalyzed Hydroaminocarbonylation of Alkenes with Amines: A Strategy to Overcome the Basicity Barrier Imparted by Aliphatic Amines. *Angew. Chem., Int. Ed.* **2015**, *54*, 7657. (b) Hu, Y.; Shen, Z.; Huang, H. Palladium-Catalyzed Intramolecular Hydroaminocarbonylation to Lactams: Additive-Free Protocol Initiated by Palladium Hydride. *ACS Catal.* **2016**, *6*, 6785. (c) Hu, Y.; Huang, H. Highly Selective Construction of Medium-Sized Lactams by Palladium-Catalyzed Intramolecular Hydroaminocarbonylation of Aminoalkynes. *Org. Lett.* **2017**, *19*, 5070. (d) Gao, B.; Huang, H. Palladium-Catalyzed Hydroaminocarbonylation of Alkynes with Tertiary Amines via C−N Bond Cleavage. *Org. Lett.* **2017**, *19*, 6260. (e) Zhu, J.; Gao, B.; Huang, H. Palladium-Catalyzed Highly Regioselective Hydroaminocarbonylation of Aromatic Alkenes to Branched Amides. *Org. Biomol. Chem.* **2017**, *15*, 2910. (f) Gao, B.; Zhang, G.; Zhou, X.; Huang, H. Palladium-Catalyzed Regiodivergent Hydroaminocarbonylation of Alkenes to Primary Amides with Ammonium Chloride. *Chem. Sci.* **2018**, *9*, 380. (g) Zhou, X.; Zhang, G.; Gao, B.; Huang, H. Palladium-Catalyzed Hydrocarbonylative C−N Coupling of Alkenes with Amides. *Org. Lett.* **2018**, *20*, 2208.

(11) (a) Seayad, A.; Ahmed, M.; Klein, H.; Jackstell, R.; Gross, T.; Beller, M. Internal Olefins to Linear Amines. *Science* **2002**, *297*, 1676. (b) Jimenez Rodriguez, C.; Foster, D. F.; Eastham, G. R.; Cole-Hamilton, D. J. Highly Selective Formation of Linear Esters from Terminal and Internal Alkenes Catalysed by Palladium Complexes of bis-(*di-tert*-butylphosphinomethyl)benzene. *Chem. Commun.* **2004**, *15*, 1720. (c) Roesle, P.; Caporaso, L.; Schnitte, M.; Goldbach, V.; Cavallo, L.; Mecking, S. A Comprehensive Mechanistic Picture of the Isomerizing Alkoxycarbonylation of Plant Oils. *J. Am. Chem. Soc.* **2014**, *136*, 16871. (d) Busch, H.; Stempfle, F.; Hess, S.; Grau, E.; Mecking, S. Selective Isomerization−Carbonylation of A Terpene Trisubstituted Double Bond. *Green Chem.* **2014**, *16*, 4541. (e) Li, H.; Dong, K.; Jiao, H.; Neumann, H.; Jackstell, R.; Beller, M. The Scope and Mechanism of Palladium-Catalysed Markovnikov Alkoxycarbonylation of Alkenes. *Nat. Chem.* **2016**, *8*, 1159. (f) Sang, R.; Kucmierczyk, P.; Dong, K. W.; Franke, R.; Neumann, H.; Jackstell, R.; Beller, M. Palladium-Catalyzed Selective Generation of CO from Formic Acid for Carbonylation of Alkenes. *J. Am. Chem. Soc.* **2018**, *140*, 5217.

DOI: 10.1021/acs.orglett.9b02230
Org. Lett. XXXX, XXX, XXX−XXX