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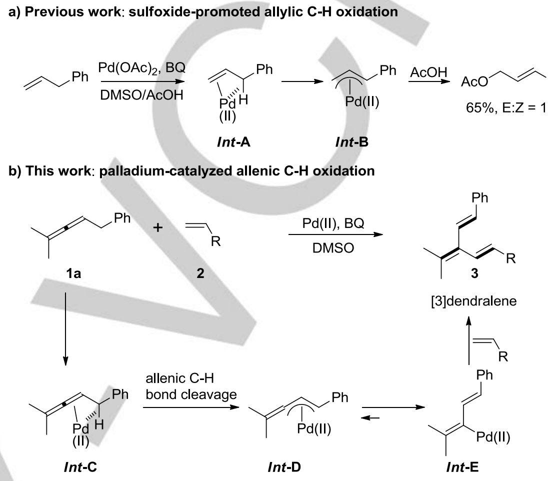
Highly Selective Palladium-Catalyzed Allenic C–H Bond Oxidation for Synthesis of [3]Dendralenes

Youai Qiu[+],* Daniels Posevins[+], and Jan-E. Bäckvall*

Abstract: A highly selective palladium-catalyzed allenic C–H bond oxidation was developed, which provides a novel and straightforward synthesis of [3]dendralene derivatives. A variety of [3]dendralenes with diverse substitution patterns are accessible with good efficiency and high stereoselectivity. The reaction tolerates a broad substrate scope containing various functional groups on the allene moiety, including ketone, aldehyde, ester and phenyl groups. Also, a wide range of olefins with both electron-donating and electron-withdrawing aryls, acrylate, sulfone and phosphonate groups are tolerated.

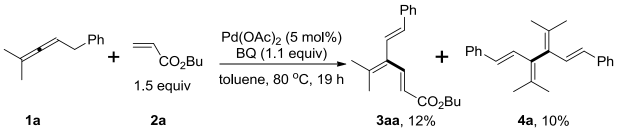
Palladium-catalyzed direct C–H functionalization with various directing groups has provided a straightforward approach for selective formation of carbon-carbon and carbon-heteroatom bonds in recent years.[1] Compared to the widely developed transition-metal catalyzed C–H functionalization with the assistance of specialized directing groups, in the absence of assisting/directing groups, the reaction outcome is mainly determined by intrinsic reactivity of the substrate. In the palladium-catalyzed allylic C–H acetoxylation reaction, early studies on cyclic alkenes by Åkermark[2] and our group[3] showed that the reaction proceeds via an π-allylpalladium(II) intermediate generated through allylic C–H bond cleavage. White *et al*. has more recently reported on Pd(II)-catalyzed allylic C–H oxidation of acyclic olefins.[4] The addition of sulfoxide ligands promoted the allylic C–H acetoxylation via the π-allylpalladium(II) intermediate ***Int*-B** (Scheme 1a).

On the basis of these observations and our group's long-term interest in palladium-catalyzed oxidation of allenes bearing assisting π-bond moieties[5-8] to construct carbocyclic skeletons,[9,10] we were particularly interested in palladium-catalyzed selective allenic C–H oxidation of allene **1a** in the absence of conventional directing groups (Scheme 1b). We envisioned that π-allylpalladium(II) intermediate ***Int*-D** may be generated through selective allenic C–H bond cleavage, followed by rearrangement to vinylpalladium intermediate ***Int*-E** that would undergo subsequent intermolecular olefin insertion[11] to afford [3]dendralene derivatives **3**.[12] The challenge would be the control of the involved regio- and stereoselectivity in the absence of directing groups. [3]Dendralenes or cross-conjugated trienes have attracted the attention of organic chemists, due to their unique role in polymer and synthetic chemistry, as well as their occurrence in various natural products.[12,13] A noticeable breakthrough in practical synthesis of dendranlenes was reported by the Sherburn group in 2009.[14]. After that, a handful of elegant procedures available for the synthesis of dendralenes were developed by their group and other groups.[15,16]



Scheme 1. Palladium-catalyzed selective allylic and allenic C–H oxidation.

Our study began with the palladium-catalyzed reaction of readily accessible allene **1a**[17] with butyl acrylate **2a** using BQ (*p*-benzoquinone) as the oxidant in toluene at 80 °C for 19 h (Scheme 2). To our delight, [3]dendralene (2*E*,5*E*)-**3aa** was obtained in 12% yield with high regio- and stereoselectivity along with dimer **4a** in 10% yield. To the best of our knowledge, to date there have been no reports on efficient synthesis of functionalized [3]dendralenes that would involve palladium-catalyzed allenic C–H bond oxidation.



Scheme 2. Initial attempt for formation of [3]dendralene **3aa**.

With these inspiring results in hand, we set out to optimize the reaction conditions for the selective formation of **3aa** (Table 1). Catalyst screening showed that Pd(OAc)$_2$ was still the best catalyst for this transformation (Table 1, entries 1-5). Solvent screening revealed that the yield of **3aa** could be increased to 23% by the use of CH$_3$CN as solvent (Table 1, entries 6-9). The favored formation of **3aa** in CH$_3$CN is probably due to

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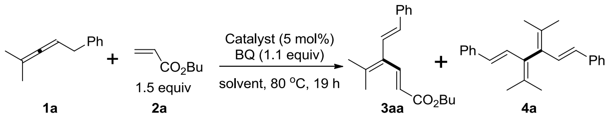
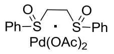
coordination of CH_3CN to palladium, which could stabilize the key vinylpalladium intermediate. Based on this observation, we envisioned that a more strongly coordinating solvent might favor the formation of product **3aa**. The yield of **3aa** was improved to 40% by using DMSO as solvent (Table 1, entry 10). The yield was further increased to 45%, when the reaction was conducted at room temperature (Table 1, entry 11). The oxidant also plays a crucial role in the selective Pd-catalyzed olefination (Table 1, entries 12-15). The use of 2,6-dimethyl-BQ enhanced the formation of product **3aa** (78% yield) and inhibited the formation of the dimeric byproduct **4a** (Table 1, entry 14).

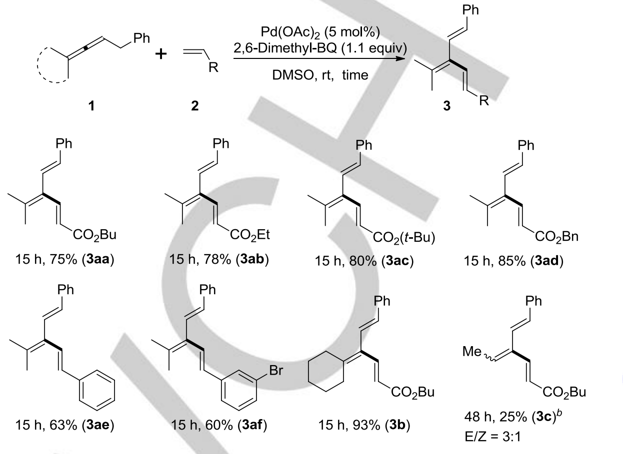
Table 1. Optimization of the reaction conditions.[a]



Entry	Catalyst	Solvent	Yield of **3aa** (%)[b]	Yield of **4a** (%)[b]	Recovery of **1a** (%)[b]
1	$Pd(OAc)_2$	toluene	12	10	5
2	$Pd(TFA)_2$	toluene	11	10	-
3	$Pd(OPiv)_2$	toluene	10	16	-
4		toluene	15	15	-
5	$PdCl_2$	toluene	-	-	78
6	$Pd(OAc)_2$	DCE	8	15	18
7	$Pd(OAc)_2$	*i*-PrOH	8	10	10
8	$Pd(OAc)_2$	dioxane	7	11	30
9	$Pd(OAc)_2$	MeCN	23	25	17
10	$Pd(OAc)_2$	DMSO	40	3	10
11[c]	$Pd(OAc)_2$	DMSO	45	3	35
12[c,d]	$Pd(OAc)_2$	DMSO	-	-	81
13[c,e]	$Pd(OAc)_2$	DMSO	16	-	70
14[c,f]	**$Pd(OAc)_2$**	**DMSO**	**78**	**2**	**-**
15[c,g]	$Pd(OAc)_2$	DMSO	71	3	5

[a] The reaction was conducted in the indicated solvent (1 mL) at 80 °C using **1a** (0.2 mmol), **2a** (1.5 equiv), BQ (1.1 equiv) in the presence of palladium catalyst (5 mol%). [b] Determined by NMR using anisole as the internal standard. [c] The reaction was conducted at room temperature. [d] F_4-BQ was used instead of BQ. [e] 2,6-Dimethoxy-BQ was used instead of BQ. [f] 2,6-Dimethyl-BQ was used instead of BQ. [g] 2,5-Dimethyl-BQ was used instead of BQ.

Under the optimal reaction conditions, we first studied the reaction of substrates **1** with different alkene coupling partners (Scheme 3). Aliphatic acrylate derivatives afforded the corresponding [3]dendralenes in good yields. In addition to two methyl substituents on the allene moiety, cyclohexylidene allene also afforded the corresponding product **3b**. Monomethyl-substituted allene also underwent the olefination and afforded product **3c** in moderate yield with an *E*/*Z* value of 3/1. However, the corresponding [3]dendralenes **3d** could not be obtained using terminal hydrogen-substituted allene (for details, see the Supporting Information) as a substrate under the standard conditions, which shows that electron-donating groups on the allene moiety are crucial for selective allenic C–H bond oxidation.



Scheme 3. Scope for formation of **3**. [a] The reaction was conducted in DMSO at room temperature using **1** (0.2 mmol), **2** (1.5 equiv), 2,6-dimethyl-BQ (1.1 equiv) in the presence of $Pd(OAc)_2$ (5 mol%).[b] all of the starting material was consumed.

We next turned our attention to other substituted substrates (Scheme 4), it is worth noting that the reactions involving substrates bearing ketone or aldehyde functionalities all proceeded well and gave the corresponding [3]dendralenes **6** in good yields. We were delighted to find that the reaction conditions were also suitable for the olefination reactions of a readily accessible 3,4-dienoates **5**.[18] Aliphatic acrylate derivatives, *n*-butyl, methyl, ethyl, and benzyl, furnished the corresponding products **7aa**-**7ad** in good yields. Useful olefin coupling partners, such as the phenyl vinyl sulfone and vinyl phosphonate also were found to react smoothly to afford the products **7ae** and **7af**. Styrenes with both electron-donating and electron-withdrawing groups on the phenyl ring reacted smoothly We also examined the aliphatic olefin, such as 1-octene, which afforded product **7am** in 52% yield. Selective C–C bond formation in the internal position[19] was also observed with allylbenzene, ethyl vinyl ether, and 2,3-dihydrofuran which afforded **7an**, **7ao**, and **7ap**, respectively, in good yields.

The reactivity of substrates with different substituents on the allene moiety was next investigated (Scheme 5). In addition to two methyl substituents on the allene moiety, two ethyl, and cyclohexylidene allenes (**5b** and **5d**) also afforded the corresponding products (**7b** and **7da**) in good yields. It is noteworthy that the reaction of cyclopentylidene allene **5c** afforded the **7c** and **7c'** in 80% and 10% yields, respectively.[20] **7c'** was successfully converted to **7c** using copper(II) catalysis to afford the desired [3]dendralene product **7c** in 85% combined yield (for details, see the Supporting Information). Trisubstituted allene **5e** also underwent the olefination and afforded product **7e** in moderate yield with E/Z value 3/1. The reaction of the unsymmetrical allene **5f**, bearing methyl and phenyl groups, and **5g**, bearing methyl and *i*-Pr groups, afforded **7fa** in 82%, **7fb** in 80%, and **7g** in 91% yield, respectively. To our delight, using tetrasubstituted allene **5h**, the corresponding [3]dendralene derivative **7h** can also be obtained in moderate yield. Styrene,

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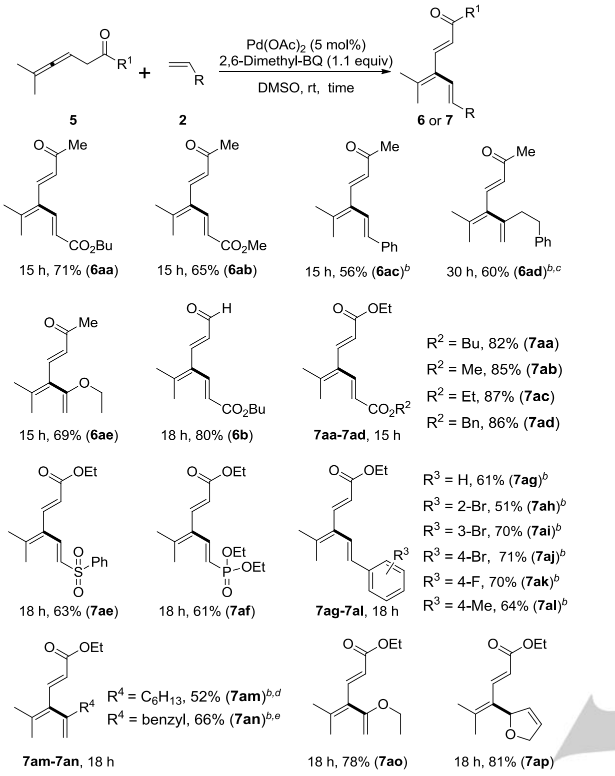
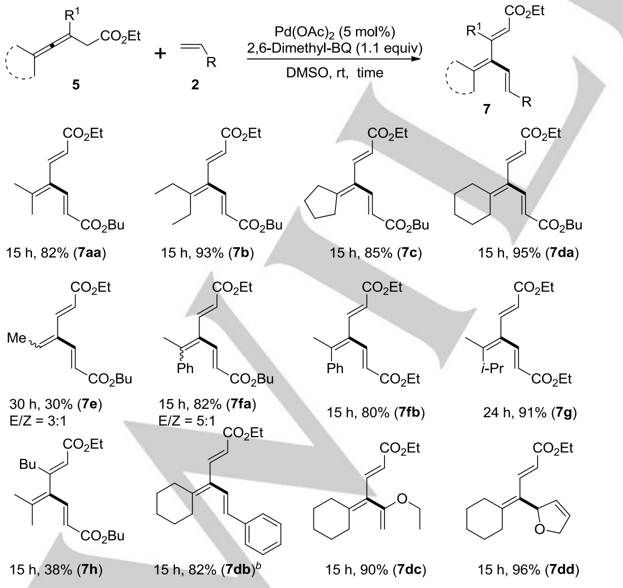
ethyl vinyl ether, and 2,3-dihydrofuran all reacted smoothly and afforded **7db**, **7dc**, and **7dd** in good to excellent yields.

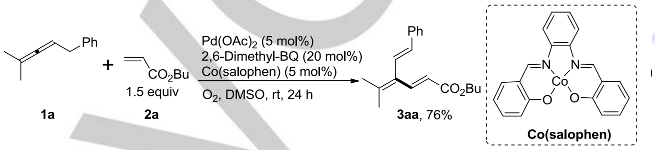


Scheme 4. Scope for formation of **6** or **7**. [a] The reaction was conducted in DMSO at room temperature using **5** (0.2 mmol), **2** (3.0 equiv), 2,6-dimethyl-BQ (1.1 equiv) in the presence of Pd(OAc)$_2$ (5 mol%). [b] 5.0 equivalents of **2** was used. [c] Selectivity of Heck reaction is 30:1 (ratio refers to the amount of the desired isomer versus all other isomers). [d] Selectivity of Heck reaction is 10:1. [e] Selectivity of Heck reaction is 5:1.

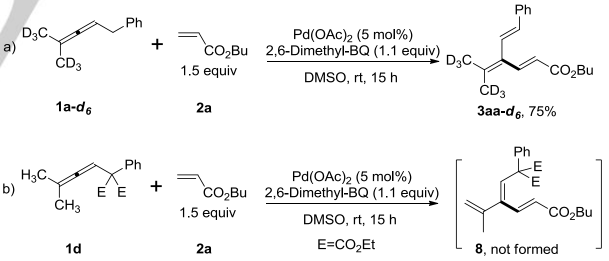


Scheme 5. Scope of allenes for formation of **7**. [a] The reaction was conducted in DMSO at room temperature using **5** (0.2 mmol), **2** (3.0 equiv), 2,6-dimethyl-BQ (1.1 equiv) in the presence of Pd(OAc)$_2$ (5 mol%). [b] 5.0 equivalents of **2** was used.

A biomimetic oxidation approach with the use of electron-transfer mediators (ETMs) could decrease the kinetic barrier for the reoxidation of Pd(0) by O$_2$.[3c,21] Catalytic amounts of oxidant (2,6-dimethyl-BQ) would be sufficient to realize the desired transformation. When the reaction of **1a** was treated with butyl acrylate **2a** (1.5 equiv), 2,6-dimethyl-BQ (20 mol%), Pd(OAc)$_2$ (5 mol%), and cobalt(salophen) (5 mol%) under an atmosphere of O$_2$ (balloon), the desired product **3aa** was obtained in 76% yield (eq 1).



In order to understand the mechanism of this transformation, we performed the reaction with the deuterium-labeled substrate **1a-*d*$_6$**. The expected [3]dendralene product **3aa-*d*$_6$** was obtained in 75% yield (Scheme 6a). We also performed the same reaction in the presence of acetic acid (1.0 equivalent) as an additive (for details, see the Supporting Information). The product **3aa-*d*$_6$** was obtained in 65% yield without any scrambling of the deuterium content. We also examined the reaction of a malonate-tethered substrate **1d**, but formation of the envisioned product **8** was not observed (Scheme 6b).These comparative experiments indicate that the C–H bond cleavage selectively occurs at the benzylic position.



Scheme 6. Comparative experiments.

The observation that there is no deuterium loss in the CD$_3$ groups in the transformation of **1a-*d*$_6$** to **3aa-*d*$_6$** rules out a reaction mechanism that involves allenic C–H bond cleavage of a methyl group to form a vinyl-Pd intermediate followed by C–C coupling and rearrangement to give [3]dendralene **3aa**. The ruling out of the latter mechanism was also supported by deuterium kinetic isotope effect studies.[22] An intermolecular competition experiment was conducted at room temperature using a 1:1 mixture of **1a** and **1a-*d*$_6$**, which afforded a competitive KIE of k_H/k_D = 1.02. Furthermore, parallel kinetic experiments using **1a** and **1a-*d*$_6$**, gave a KIE (k_H/k_D from initial rate) value of k_H/k_D = 1.02.

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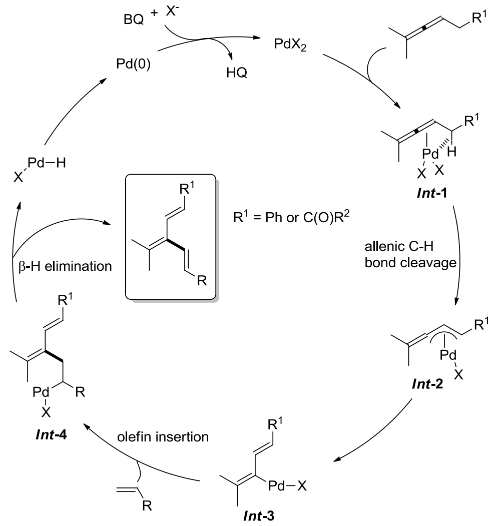
Based on the reaction outcome, a possible mechanism for the palladium-catalyzed oxidative allenic C–H bond oxidation to afford [3]dendralenes is proposed in Scheme 7. The reaction of $Pd(OAc)_2$ with allene could give intermediate ***Int*-1**. Then π-allylpalladium(II) intermediate ***Int*-2** may be generated through selective allenic C–H bond cleavage. Intermediate ***Int*-2** may transfer to vinylpalladium intermediate ***Int*-3**, which could undergo an intermolecular olefin insertion to form the intermediate ***Int*-4**. Subsequent β-H elimination would produce the [3]dendralene derivatives.



Scheme 7. Proposed mechanism.

In conclusion, we have described a highly selective approach for formation of [3]dendralene derivatives via palladium-catalyzed allenic C–H bond oxidation, that involves an intermolecular C–C bond formation. The reaction is proven to be highly regio- and stereoselective and proceeds under very mild conditions tolerating various functional groups. Another attractive feature of this study is the diverse functionality of obtained [3]dendralene derivatives, that offer new opportunities in organic synthesis and materials science. Further studies on the scope and synthetic application of this newly developed reaction are currently carried out in our laboratory.

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Keywords: allenic C–H oxidation • [3]dendralene • palladium • olefination • regio- and stereoselectivity

[1] Selected recent reviews of Pd-catalyzed C−H functionalization: a) C. Jia, T. Kitamura, Y. Fujiwara, *Acc. Chem. Res.* **2001**, *34*, 633; b) I. V. Seregin, V. Gevorgyan, *Chem. Soc. Rev.* **2007**, *36*, 1173; c) D. Alberico, M. E. Scott, M. Lautens, *Chem. Rev.* **2007**, *107*, 174; d) X. Chen, K. M. Engle, D.-H. Wang, J.-Q. Yu, *Angew. Chem., Int. Ed.* **2009**, *48*, 5094; *Angew. Chem*. **2009**, *121*, 5196; e) O. Daugulis, H.-Q. Do, D. Shabashov, *Acc. Chem. Res.* **2009**, *42*, 1074; f) T. W. Lyons, M. S. Sanford, *Chem. Rev.* **2010**, *110*, 1147; g) J. Wencel-Delord, T. Droge, F. Liu, F. Glorius, *Chem. Soc. Rev.* **2011**, *40*, 4740; h) L. Ackermann, *Chem. Rev.* **2011**, *111*, 1315; i) C. S. Yeung, V. M. Dong, *Chem. Rev.* **2011**, *111*, 1215; j) G. Rouquet, N. Chatani, *Angew. Chem., Int. Ed.* **2013**, *52*, 11726; *Angew. Chem*. **2013**, *125*, 11942; k) K. M. Engle, T.-S. Mei, M. Wasa, J.-Q. Yu, *Acc. Chem. Res.* **2012**, *45*, 788.

[2] a) S. Hansson, A. Heumann, T. Rein, B. Åkermark, *J. Org. Chem.* **1990**, *55*, 975; b) A. Heumann, B. Åkermark, *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 453; *Angew. Chem.* **1984**, *96*, 443.

[3] a) H. Grennberg, V. Simon, J.-E. Bäckvall, *J. Chem. Soc. Chem. Commun.* **1994**, 265; b) H. Grennberg, J.-E. Bäckvall, *Chem. Eur. J.* **1998**, *4*, 1083. c) J.-E. Bäckvall, R. B. Hopkins, H. Grennberg, M. Mader, A. K. Awasthi, *J. Am. Chem. Soc.* **1990**, *112*, 5160;

[4] a) M. S. Chen, M. C. White, *J. Am. Chem. Soc.* **2004**, *126*, 1346; b) M. S. Chen, N. Prabagaran, N. A. Labenz, M. C. White, *J. Am. Chem. Soc.* **2005**, *127*, 6970; c) K. J. Fraunhoffer, N. Prabagaran, L. E. Sirois, M. C. White, *J. Am. Chem. Soc.* **2006**, *128*, 9032; d) S. Lin, C. Song, G. Cai, W. Wang, Z. Shi, *J. Am. Chem. Soc.* **2008**, *130*, 12901; for mechansitic studies, see: e) C. Engelin, T. Jensen, S. Rodriguez-Rodriguez, P. Fristrup, *ACS. Catal.* **2013**, *3*, 294.

[5] For recent reviews of transition-metal-catalyzed π-bond-assisted C-H bond activation, see: a) P. Gandeepan, C.-H. Cheng, *Chem. Asian J.* **2015**, *10*, 824; b) Y. Minami, T. Hiyama, *Acc. Chem. Res.* **2016**, *49*, 67.

[6] For selected examples involving palladium-catalyzed oxidative carbocyclizations of enallenes, see: a) A. K. Å. Persson, J.-E. Bäckvall, *Angew. Chem. Int. Ed.* **2010**, *49*, 4624; *Angew. Chem*. **2010**, *122*, 4728; b) A. K. Å. Persson, T. Jiang, M. Johnson, J.-E. Bäckvall, *Angew. Chem. Int. Ed.* **2011**, *50*, 6155; *Angew. Chem*. **2011**, *123*, 6279; c) a) T. Jiang, T. Bartholomeyzik, J. Mazuela, J. Willersinn, J.-E. Bäckvall, *Angew. Chem. Int. Ed*. **2015**, *54*, 6024; *Angew. Chem*. **2015**, *127*, 6122; d) Y. Qiu, B. Yang, C. Zhu, J.-E. Bäckvall, *Angew. Chem. Int. Ed.* **2016**, *55*, 6520; *Angew. Chem*. **2016**, *128*, 6630. e) Y. Qiu, B. Yang, C. Zhu, Bäckvall, J.-E. *J. Am. Chem. Soc.* **2016**, *138*, 13846; f) Y. Qiu, B. Yang, T. Jiang, C. Zhu, J.-E. Bäckvall, *Angew. Chem. Int. Ed.* **2017**, *56*, 3221; *Angew. Chem*. **2017**, *129*, 3269; g) Y. Qiu, B. Yang, C. Zhu, Bäckvall, J.-E. *Chem. Sci.* **2017**, *8*, 616.

[7] For selected examples involving palladium-catalyzed oxidative carbocyclizations of allenynes, see: a) Y. Deng, T. Bartholomeyzik, A. K. Å. Persson, J. Sun, J.-E. Bäckvall, *Angew. Chem. Int. Ed*. **2012**, *51*, 2703; *Angew. Chem*. **2012**, *124*, 2757; b) T. Bartholomeyzik, J. Mazuela, R. Pendrill, Y. Deng, J.-E. Bäckvall, *Angew. Chem. Int. Ed.* **2014**, *53*, 8696; *Angew. Chem*. **2014**, *126*, 8840.

[8] For selected examples involving palladium-catalyzed oxidative carbocyclizations of bisallenes, see: a) M. R. Volla, J.-E. Bäckvall, *ACS Catal.,* **2016**, *6*, 6398; b) C. Zhu, B. Yang, Y. Qiu, J.-E. Bäckvall, J.-E. *Angew. Chem. Int. Ed.* **2016**, *55*, 14405; *Angew. Chem*. **2016**, *128*, 14617; c) V. R. Naidu, D. Posevins, C. M. R. Volla, J. E. Bäckvall, *Angew. Chem. Int. Ed.* **2017**, *56*, 1590; *Angew. Chem*. **2017**, *129*, 1612.

[9] For selected reviews involving palladium oxidative carbocyclization, see: a) E. M. Beccalli, G. Broggini, M. Martinelli, S. Sottocornola, *Chem. Rev.* **2007**, *107*, 5318; b) F. Dénès, A. Pérez-Luna, F. Chemla, *Chem. Rev.* **2010**, *110*, 2366; c) C. S. Yeung, V. M. Dong, *Chem. Rev.* **2011**, *111*, 1215; d) Y. Deng, A. K. Å. Persson, J.-E. Bäckvall, *Chem. Eur. J.* **2012**, *18*, 11498.

[10] For selected examples involving palladium-catalyzed oxidative carbocyclizations, see: a) T. Wu, X. Xu, G. Liu, *Angew. Chem. Int. Ed*. **2011**, *50*, 12578; *Angew. Chem*. **2011**, *123*, 12786; b) X. Xu, T. Wu, H. Wang, Y. Guo, G. Liu, *J. Am. Chem. Soc.* **2012**, *134*, 878; c) R. Zhu, S. L. Buchwald, *Angew. Chem. Int. Ed*. **2012**, *51*, 1926; *Angew. Chem*. **2012**, *124*, 1962; d) S. Jaegli, J. Dufour, H. Wei, T. Piou, X. Duan, J. Vors, L.

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Neuville, J. Zhu, *Org. Lett.* **2010**, *12*, 4498; e) Y. Wei, I. Deb, N. Yoshikai, *J. Am. Chem. Soc.* **2012**, *134*, 9098.

[11] For selected reviews, see: a) R. F. Heck, *Acc. Chem. Res*. **1979**, *12*, 146; b) I. P. Beletskaya, A. V. Cheprakov, *Chem. Rev.* **2000**, *100*, 3009; c) G. Zeni, R. C. Larock, *Chem. Rev.* **2006**, *106*, 4644.

[12] H. Hopf, M. S. Sherburn, *Angew. Chem. Int. Ed.* **2012**, *51*, 2298; *Angew. Chem*. **2012**, *124*, 2346;

[13] a) H. Hopf, *Angew. Chem. Int. Ed.* **2001**, *40*, 705; *Angew. Chem*. **2001**, *113*, 727; b) K. Takenaka, S. Amamoto, H. Takeshta, M. Miya, T. Shiomi, *Macromolecules* **2013**, *46*, 7282; c) H. Hopf, *Nature* **2009**, *460*, 183; d) C. D. Diakoumakos, *J. A.* Mikroyannidis, *J. Appl. Polym. Sci.* **1994**, *53*, 201; e) C. J; Rieder, K. J. Winberg, F. G. West, *J. Am. Chem. Soc.* **2009**, *131*, 7504; f) N. J. Green, A. L. Lawrence, G. Bojase, A. C. Willis, M. N. Paddon-Row, M. S. Sheburn, *Angew. Chem. Int. Ed.* **2013**, *52*, 8333; *Angew. Chem*. **2013**, *125*, 8491; g) A. Arnone, R. Cardillo, V. Dimodugno, G. Nasini, *J. Chem. Soc. Perkin Trans. 1* **1989**, 1995; h) A. D. Payne, A. C. Willis, M. S. Sherburn, *J. Am. Chem. Soc.* **2005**, *127*, 12188.

[14] A. D. Payne, G. Bojase, M. N. Paddon-Row, M. S. Sherburn, *Angew. Chem. Int. Ed.* **2009**, *48*, 4836; *Angew. Chem*. **2009**, *121*, 4930.

[15] For palladium catalysis, see:a) S. Fielder, D. D. Rowan, M. S. Sherburn, *Angew. Chem. Int. Ed.* **2000**, *39*, 4331; *Angew. Chem*. **2000**, *112*, 4501; b) M. S. Sherburn, *Acc. Chem. Res.* **2015**, *48*, 1961; for rhodium catalysis, see: c) H. Wang, B. Beiring, D. Yu, K. D. Collins, F. Glorius, *Angew. Chem. Int. Ed.* **2013**, *52*, 12430; *Angew. Chem*. **2013**, *125*, 12657; d) K. Sakashita, Y. Shibata, K. Tanaka, *Angew. Chem. Int. Ed.* **2016**, *55*, 6753; *Angew. Chem*. **2016**, *128*, 6865; for ruthenium, see: e) N. Thies, E. Haak, *Angew. Chem. Int. Ed.* **2015**, *54*, 4097; *Angew. Chem*. **2015**, *127*, 4170.

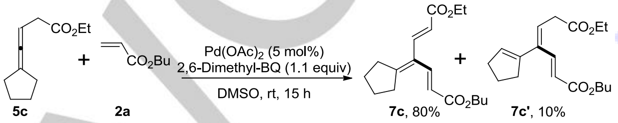
[16] For synthesis of dendralene from allene bearing a leaving group, see: a) D. J. Lippincott, R. T. H. Linstadt, M. R. Maser, B. H. Lipshutz, *Angew. Chem. Int. Ed.* **2017**, *56*, 847; *Angew. Chem*. **2017**, *129*, 865; b) M. Mao, L. Zhang, Y. Chen, J. Zhu, L. Wu, *ACS Catal.* **2017**, *7*, 181.

[17] S. N. Kessler, J.-E. Bäckvall, *Angew. Chem. Int. Ed*. **2016**, *55*, 3734; *Angew. Chem*. **2016**, *128*, 3798.

[18] C. Fu, S. Ma, *Org. Lett.* **2005**, *7*, 1707.

[19] a) H. A. Dieck, R. F. Heck, *J. Am. Chem. Soc.* **1974**, *96*, 1133; b) A. C. Albéni z, P. Espinet, B. Martín-Ruiz, D. Milstein, *J. Am. Chem. Soc.* **2001**, *123*, 11504; c) V. Calò, A. Nacci, A. Monopoli, P. Cotugno, *Angew. Chem. Int. Ed*. **2009**, *48*, 6101; *Angew. Chem*. **2009**, *121*, 6217; d) E. W. Werner, M. S. Sigman, *J. Am. Chem. Soc.* **2011**, *133*, 9692; e) L. Qin, H. Hajime, J. Zhou, *Chem. Commun.* **2013**, *49,* 10236.

[20] The reaction of cyclopentylidene allene **5c** with butyl acrylate **2a** afforded the **7c** and **7c’** in 80% and 10% yields, respectively (for details, see the Supporting Information).



[21] a) J. Piera, J.-E. Bäckvall, *Angew. Chem. Int. Ed.* **2008**, *47*, 3506; *Angew. Chem*. **2008**, *120*, 3558; b) C. M. R. Volla, J.-E. Bäckvall, *Angew. Chem. Int. Ed.* **2013**, *52*, 14209; *Angew. Chem*. **2013**, *125*, 14459. c) N. Gigant, J. E. Bäckvall, *Org. Lett.* **2014**, *16*, 1664; d) J. L. Henry, D. Posevins, B. Yang, Y. Qiu, J.-E. Bäckvall, *Chem. Eur. J*, **2017**, *23*, 7896.

[22] For details of kinetic isotope effect study, see the Supporting Information.

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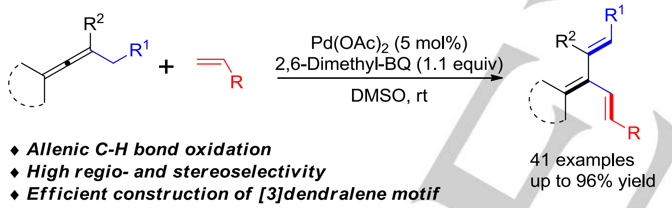

- ***Allenic C-H bond oxidation***
- ***High regio- and stereoselectivity***
- ***Efficient construction of [3]dendralene motif***
- ***Broad substrate scope and diverse functional group tolerance***

A highly selective and straightforward formation of [3]dendralene derivatives via palladium-catalyzed allenic C–H bond oxidation was developed. The reaction is highly stereoselective and compatible with numerous functional groups on the allene substrate and the olefin.

Youai Qiu, Daniels, Posevins, and Jan-E. Bäckvall**

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Highly Selective Palladium-Catalyzed Allenic C–H Bond Oxidation for Synthesis of [3]Dendralenes

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