Organic LETTERS

Palladium-Catalyzed Difunctionalization of Internal Alkynes via Highly Regioselective 6-*Endo* Cyclization and Alkenylation of Enynoates: Synthesis of Multisubstituted Pyrones

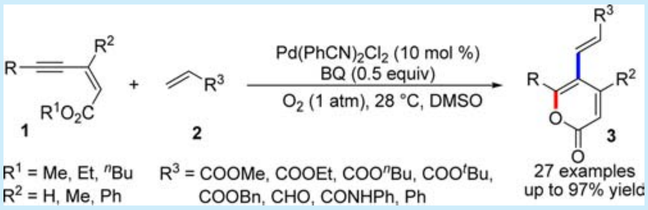
Pan-Pan Tian,[†] Sai-Hu Cai,[†] Qiu-Ju Liang, Xing-Yi Zhou,[†] Yun-He Xu,*[,†] and Teck-Peng Loh*[,†,‡]

[†]Hefei National Laboratory for Physical Sciences at the Microscale and Department of Chemistry, University of Science and Technology of China, 96 Jinzhai Road, Hefei, Anhui 230026, China

[‡]Division of Chemistry and Biological Chemistry, School of Physical and Mathematical Sciences, Nanyang Technological University, Singapore 637371, Singapore

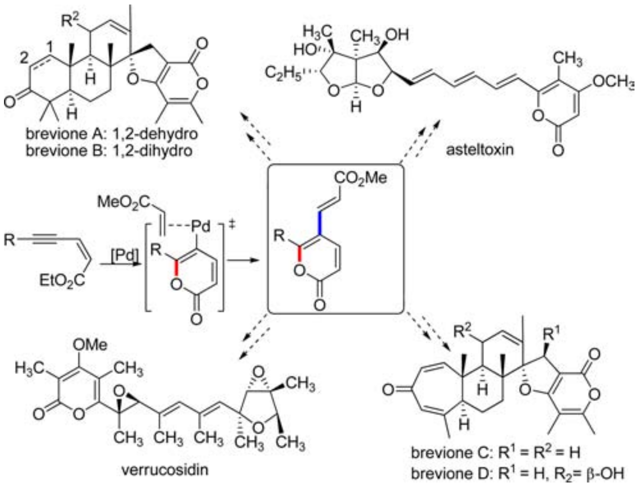
S *Supporting Information*

ABSTRACT: An efficient Pd(II)-catalyzed difunctionalization reaction of internal alkynes is reported. In this reaction, various enynoates and electron-deficient alkenes were used for the syntheses of useful highly substituted pyrone derivatives via a 6-*endo* cyclization and subsequent alkenylation pathway. The corresponding products could be obtained in moderate to good yields under very mild reaction conditions. The high regioselectivity and wide compatibility with different functional groups found in the desired products demonstrate this method to be a general and useful tool for the synthesis of highly substituted pyrone derivatives.



Pyrone structural subunits are widely observed in many natural products and pharmaceutical molecules (Scheme 1).[1] Pyrones are also useful building blocks for the synthesis of a variety of heterocyclic compounds.[2] Consequently, the construction of this class of compounds has attracted much attention. Traditional approaches and organometallic methods to access this class of compounds have been well studied.[3] However, limited substrate scope and/or harsh reaction conditions restrict the wide application of these methods. Therefore, more efficient and general methods to access functional pyrones deserve to be developed. Recently, methods developed using different electrophiles such as I_2, ICl, NIS, PhSeCl mediated cyclization reactions of enynoates have been reported by Larock,[4] Rossi,[5] Burton[6] et al. as useful supplements for the synthesis of heteroatom substituted pyrone compounds. To achieve the multicarbon-substituted pyrone fragments, these obtained products need to be further functionalized in subsequent steps.[7] Simultaneously, transition-metal-catalyzed cyclization reactions of enynes to prepare the pyrone derivatives have been studied which would be more efficient and convenient methods for the synthesis of this type of products.[8] However, the high control of high 5-*exo* or 6-*endo* regioselectivity of the products and suppression of protonation side reaction are difficult.[9] To the best of our knowledge, few examples of palladium-catalyzed difunctionalization of conjugated enynes via 6-*endo* cyclization have been achieved.[10] Inspired by the fruitful research results of the application of vinylpalladium species generated *in situ* in coupling reactions to synthesize complex molecules,[11−13] as well as our continuous interest in developing cross-coupling reactions between alkenes,[14] we embarked on the study of a palladium-catalyzed difunctionalization reaction of internal alkynes[15] via highly selective 6-*endo* cyclization and alkenylation using easily available enynoates[16] and electron-deficient alkenes (Scheme 1).

Scheme 1. Palladium-Catalyzed Cyclization of Enynoates for Synthesis of Highly Substituted Pyrones

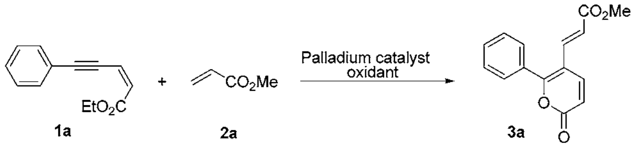


Initially, the optimization of reaction conditions was carried out using *Z*-enynoate **1a** and methyl acrylate **2a**; the summarized results are shown in Scheme 2. After numerous attempts, it was

Received: January 28, 2015
Published: March 19, 2015

DOI: 10.1021/acs.orglett.5b00272
Org. Lett. 2015, 17, 1636−1639

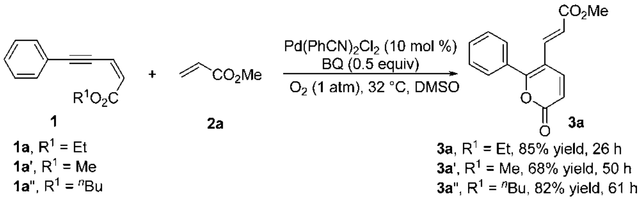
Scheme 2. Optimization of Reaction Conditions for the Cyclization and Alkenylation of Enynoate **1a** with Methyl Acrylate **2a**[a,b]



entry	catalyst (10 mol %)	oxidant (equiv)	solvent	temp (°C)	time (h)	yield (%)
1	$Pd(OAc)_2$	BQ (1) + O_2 (1 atm)	DMSO	32	18	52
2	$Pd(OAc)_2$	BQ (1) + O_2 (1 atm)	DMA	32	48	< 5
3	$Pd(OAc)_2$	BQ (1) + O_2 (1 atm)	DMF	32	48	< 5
4	$Pd(OAc)_2$	BQ (1) + O_2 (1 atm)	1,4-Dioxane	32	48	< 5
5	$Pd(OAc)_2$	BQ (1) + Air (1 atm)	DCE	32	48	< 5
6	$Pd(OAc)_2$	O_2 (1 atm)	DMSO	32	30	28
7	$Pd(OAc)_2$	Ag_2O (1) + O_2 (1atm)	DMSO	32	24	49
8	$Pd(OAc)_2$	AgOAc (1) + O_2 (1 atm)	DMSO	32	32	52
9	$Pd(OAc)_2$	$Cu(OAc)_2$ (1) + O_2 (1 atm)	DMSO	32	70	7
10	$Pd(OAc)_2$	$K_2S_2O_8$ (1) + Air (1 atm)	DMSO	32	24	22
11	$Pd(OAc)_2$	^{t}BuOOH (1) + Air (1 atm)	DMSO	32	24	63
12	$Pd(OAc)_2$	H_2O_2 (1) + Air (1 atm)	DMSO	32	29	9
13	$Pd(MeCN)_2Cl_2$	^{t}BuOOH (1) + Air (1 atm)	DMSO	32	43	67
14	$Pd(MeCN)_4(BF_4)_2$	^{t}BuOOH (1) + Air (1 atm)	DMSO	32	67	45
15	$PdCl_2$	^{t}BuOOH (1) + Air (1 atm)	DMSO	32	67	72
16	$Pd(PPh_3)Cl_2$	^{t}BuOOH (1) + Air (1 atm)	DMSO	32	69	< 5
17	$Pd(PhCN)_2Cl_2$	^{t}BuOOH (1) + Air (1 atm)	DMSO	32	59	84
18	$Pd(PhCN)_2Cl_2$	^{t}BuOOH (1) + Air (1 atm)	DMSO	50	26	74
19	**$Pd(PhCN)_2Cl_2$**	**BQ (0.5) + O_2 (1 atm)**	**DMSO**	**32**	**26**	**85**
20	$Pd(PhCN)_2Cl_2$	BQ (1) + O_2 (1 atm)	DMSO	32	29	79
21[c]	$Pd(PhCN)_2Cl_2$	BQ (0.5) + O_2 (1 atm)	DMSO	32	51	62

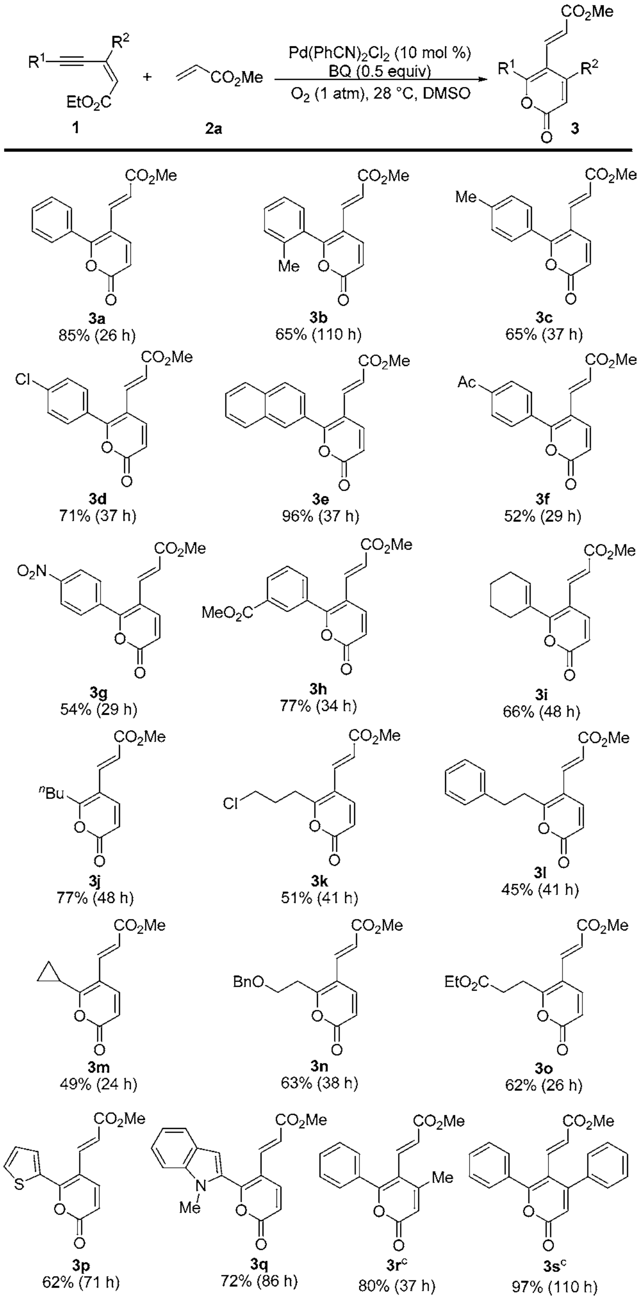
[a] Reaction conditions: The mixture of **1a** (0.3 mmol), **2a** (0.6 mmol), oxidant in indicated solvent (1.0 mL) was stirred for corresponding hours. [b] Isolated yields. [c] 5 mol % $Pd(PhCN)_2Cl_2$ was used as catalyst.

Scheme 3. Different Enynoates were Tested for Palladium-Catalyzed Cyclization and Alkenylation Reactions



found that the system of the Pd(II) catalyst with an oxidant could favor the product's formation. The use of dimethyl sulfoxide (DMSO) as solvent in the reaction could greatly improve the product's yield as compared to other tested solvents. Moreover, the combined oxidant systems such as BQ with oxygen, silver salt with oxygen, or *tert*-butylhydroperoxide in air could afford the desired product in reasonable yield, while the use of only oxygen, copper(II) acetate with oxygen, or hydrogen peroxide in air were found to be completely inefficient. Next, various Pd(II) catalysts were screened; except for $Pd(PPh_3)_2Cl_2$, other Pd(II) species could all afford the desired product in acceptable yields. Especially, a high yield of product could be obtained when $Pd(PhCN)_2Cl_2$ was applied in this reaction. Further detailed studies using $Pd(PhCN)_2Cl_2$ as the catalyst showed that elevating the temperature to 50 °C would shorten the reaction time significantly with a slightly decreased product yield. Furthermore, it was observed that replacing the oxidant system with BQ and an oxygen atmosphere would favor the product's formation, while a high loading of BQ or low loading of the palladium catalyst would diminish the yield of product **3a** (Scheme 2, entries 20 and 21 respectively).

Scheme 4. Pd(II)-Catalyzed 6-*Endo* Cyclization and Alkenylation of **1** with Methyl Acrylate[a,b]

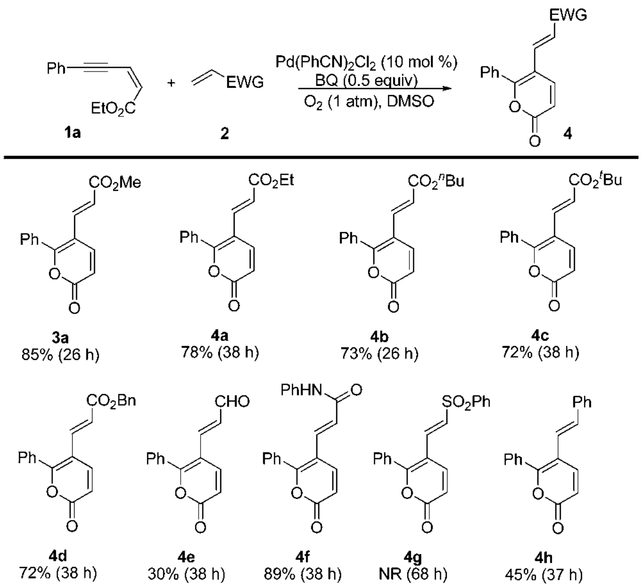


[a] Reaction conditions: The reactions were carried out under the standard reaction conditions: **1** (0.3 mmol), **2a** (0.6 mmol, 2 equiv), $Pd(PhCN)_2Cl_2$ (0.03 mmol, 0.1 equiv), BQ (0.5 equiv), and O_2 (1 atm) in 1.0 mL of DMSO were stirred at 32 °C for corresponding hours shown in parentheses. [b] Isolated yields. [c] The reactions were carried out at 60 °C.

Furthermore, enynes with different ester groups were investigated to react with methyl acrylate respectively under the optimized reaction conditions. It was noticed that the ethyl-group-substituted compound **1a** is the best choice in terms of yield and reaction duration (Scheme 3).

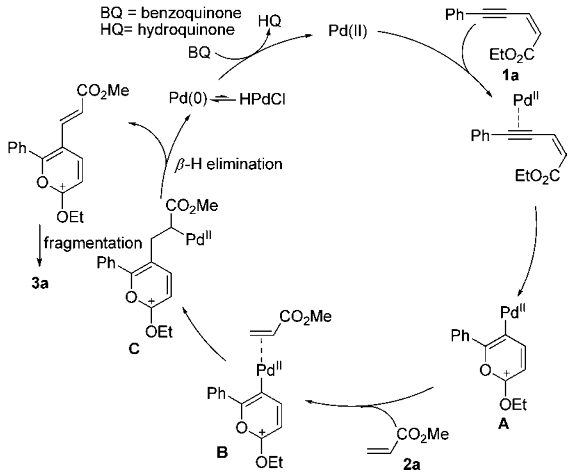
Therefore, the generality of the cascade reactions between ethyl-group-substituted enynoates and methyl acrylate was

Scheme 5. Pd(II)-Catalyzed Cyclization and Alkenylation of 1a with Different Electron-Deficient Alkenes 2[a,b]



[a]Reaction conditions: The reactions were conducted under the standard reaction conditions: **1a** (0.3 mmol), **2** (0.6 mmol, 2 equiv), $Pd(PhCN)_2Cl_2$ (0.03 mmol, 0.1 equiv), BQ (0.5 equiv) in 1.0 mL of DMSO under an oxygen atmosphere (1 atm) were stirred at 32 °C for 24 h. [b]Isolated yields.

Scheme 6. Proposed Possible Mechanism for the Pd(II)-Catalyzed 6-*Endo* Cyclization and Olefination Reactions of Enynoates



evaluated (Scheme 4). The substrates with electron-donating or -withdrawing group on the phenyl ring all could afford the desired products in moderate to excellent yields. However, the presence of a methyl substituent at the *ortho*-position of the phenyl ring will prolong the reaction time greatly due to possible steric hindrance. Additionally, the cyclohexenyl as well as the aliphatic group substituted enynoates could also be employed in the cascade reactions. The tolerance of various functional groups such as halide, ether, and ester in products allows them to be further functionalized in subsequent steps. When thioenyl- or indole-substitued enynoate was used to react with methyl acrylate, the desired products **3p** and **3q** could be generated in 62% and 72% yields respectively by prolonging the reaction duration. Finally, excellent yields could also be obtained for the substrates with a *β*-substituent (Scheme 4, **3r** and **3s**).

Next, various electron-deficient alkenes were tested as the coupling partners (Scheme 5). The corresponding products could be smoothly obtained in high yields when different acrylates (Scheme 4, **3a**, **4a–4d**) as well as the acrylamide (Scheme 5, **4f**) were used in the reaction. However, only low yields of the products **4e** and **4h** were found when acrolein and styrene were used as the coupling partners, respectively.

A plausible reaction pathway for the Pd(II)-catalyzed 6-*endo* cyclization and alkenylation reactions of enynoates was proposed as shown in Scheme 6.[17] First, a 6-*endo* cyclization of the enynoate will occur which was activated by the alkyne Pd(II) ion. Therefore, an active vinylpalladium species **B** will be generated to react with methyl acrylate and afford the intermediate **C** via migratory insertion. The desired product **3a** could be formed after reductive elimination and followed by the reoxidation of Pd(0) species into the next catalytic cycle by benzoquinone (BQ).

In conclusion, Pd(II)-catalyzed highly regioselective 6-*endo* cyclization and alkenylation reactions have been developed. Various multifunctionalized pyrones could be obtained in good yields under mild reaction conditions in a one-pot manner. Further studies on the application of this method for the synthesis of natural products are in progress.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental details and spectroscopic data for all products. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: xyh0709@ustc.edu.cn.
*E-mail: teckpeng@ntu.edu.sg.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We gratefully acknowledge the funding support of the National Natural Science Foundation of China (21372210), the State Key Program of National Natural Science Foundation of China (21432009), Natural Science Foundation of Anhui Province (1308085QB37), and the National Science Foundation for Postdoctoral Scientists of China (2012M521231). The authors also thank Nanyang Technology University for financial support of this research. The authors are grateful to Mr. Koh Peng Fei Jackson (Nanyang Technological University, Singapore) for his careful proofreading of the final manuscript.

■ REFERENCES

(1) (a) Chen, K. K.; Kovarikova, A. J. *J. Pharm. Sci.* **1967**, *56*, 1535. (b) Venkataraman, H.; Cha, J. K. *Tetrahedron Lett.* **1987**, *28*, 2455. (c) Abraham, W. R.; Arfmann, H. *Phytochemistry* **1988**, *27*, 3310. (d) Posner, G. H.; Nelson, T. D.; Kinter, C. M.; Johnson, N. *J. Org. Chem.* **1992**, *57*, 4083. (e) Vara Prasad, J. V. N.; Para, K. S.; Lunney, E. A.; Ortwine, D. F.; Dunbar, J. B., Jr.; Ferguson, D.; Tummino, P. J.; Hupe, D.; Tait, B. D.; Domagala, J. M.; Humblet, C.; Bhat, T. N.; Liu, B.; Guerin, D. M. A.; Baldwin, E. T.; Erickson, J. W.; Sawyer, T. K. *J. Am. Chem. Soc.* **1994**, *116*, 6989. (f) Schlingmann, G.; Milne, L.; Carter, G. T. *Tetrahedron* **1998**, *54*, 13013. (g) Yokoe, H.; Mitsuhashi, C.; Matsuoka,

Y.; Yoshimura, T.; Yoshida, M.; Shishido, K. *J. Am. Chem. Soc.* **2011**, *133*, 8854.

(2) (a) Kozytska, M. V.; Dudley, G. B. *Tetrahedron Lett.* **2008**, *49*, 2899. (b) Larsson, R.; Sterner, O.; Johansson, M. *Org. Lett.* **2009**, *11*, 657. (c) Nelson, H. M.; Gordon, J. R.; Virgil, S. C.; Stoltz, B. M. *Angew. Chem., Int. Ed.* **2013**, *52*, 6699.

(3) (a) Komiyama, T.; Takaguchi, Y.; Tsuboi, S. *Tetrahedron Lett.* **2004**, *45*, 6299. (b) Sheibani, H.; Islami, M. R.; Khabazzadeh, H.; Saidi, K. *Tetrahedron* **2004**, *60*, 5931. (c) Ma, S.; Yu, S.; Yin, S. *J. Org. Chem.* **2003**, *68*, 8996. (d) Biagetti, M.; Bellina, F.; Carpita, A.; Rossi, R. *Tetrahedron Lett.* **2003**, *44*, 607. (e) Anastasia, L.; Xu, C.; Negishi, E. *Tetrahedron Lett.* **2002**, *43*, 5673. (f) Fringuelli, F.; Piermatt, O.; Pizzo, F. *Heterocycles* **1999**, *50*, 611. (g) Tidwell, T. T.; Sammtleben, F.; Christl, M. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2031. (h) Cerezo, S.; Moreno-Mañas, M.; Pleixats, R. *Tetrahedron Lett.* **1998**, *54*, 7813. (i) Dubuffet, T.; Cimetiere, B.; Lavielle, G. *Synth. Commun.* **1997**, *27*, 1123. (j) Liebeskind, L. S.; Wang, J. *Tetrahedron* **1993**, *49*, 5461. (k) West, F. G.; Hartke-Karger, C.; Koch, D. J.; Kuehn, C. E.; Arif, A. M. *J. Org. Chem.* **1993**, *58*, 6795. (l) Tsuda, T.; Morikawa, S.; Saegusa, T. *J. Chem. Soc., Chem. Commun.* **1989**, 9. (m) Dieter, R. K.; Fishpaugh, J. R. *J. Org. Chem.* **1988**, *53*, 2031. (n) Henry, W.; Hughes, R. P. *J. Am. Chem. Soc.* **1986**, *108*, 7862. (o) Pavlik, J. W.; Patten, A. D.; Bolin, D. R.; Bradford, K. C.; Clennan, E. L. *J. Org. Chem.* **1984**, *49*, 4523. (p) Ishibe, N.; Sunami, M.; Odani, M. *J. Am. Chem. Soc.* **1973**, *95*, 463. (q) Ishibe, N.; Yutaka, S. *J. Org. Chem.* **1978**, *43*, 2138. (r) Hayasi, Y.; Nozaki, H. *Tetrahedron* **1971**, *27*, 3085.

(4) (a) Yao, T.; Larock, R. C. *Tetrahdron Lett.* **2002**, *43*, 7401. (b) Yao, T.; Larock, R. C. *J. Org. Chem.* **2003**, *68*, 5936.

(5) (a) Bellina, F.; Biagetti, M.; Carpita, A.; Rossi, R. *Tetrahedron* **2001**, *57*, 2857. (b) Biagetti, M.; Bellina, F.; Carpita, A.; Viel, S.; Mannina, L.; Rossi, R. *Eur. J. Org. Chem.* **2002**, 1063.

(6) Wang, Y.; J. Burton, D. *J. Org. Chem.* **2006**, *71*, 3859.

(7) Frébault, F.; Oliveira, M. T.; Wöstefeld, E.; Maulide, N. *J. Org. Chem.* **2010**, *75*, 762 and ref 5.

(8) (a) For a Ag(I)-catalyzed cyclization of enyne carboxylic acids, please see: Yoshikawa, T.; Shindo, M. *Org. Lett.* **2009**, *11*, 5378. (b) For Cu-catalyzed cyclization and bromination examples, see: Liang, Y.; Xie, Y.-X.; Li, J.-H. *Synthesis* **2007**, 400. (c) Please see the example of a Pd-catalyzed 6-*endo* cyclization and arylation reaction: Rossi, R.; Bellina, F.; Biagetti, M.; Catanese, A.; Mannina, L. *Tetrahedron Lett.* **2000**, *41*, 5281. (d) Two examples of a Pd-catalyzed tandem annulation of enyne with methyl vinyl ketone: Wang, H.; Han, X.; Lu, X. *Tetrahedron* **2013**, *69*, 8626.

(9) (a) Arai, S.; Nishida, A. *Synlett* **2012**, *23*, 2880 and references cited therein. (b) Xia, Y.; Qu, S.; Xiao, Q.; Wang, Z.-X.; Qu, P.; Chen, L.; Liu, Z.; Tian, L.; Huang, Z.; Zhang, Y.; Wang, J. *J. Am. Chem. Soc.* **2013**, *135*, 13502. (c) Hu, F.; Xia, Y.; Ma, C.; Zhang, Y.; Wang, J. *Org. Lett.* **2014**, *16*, 4082. Also please see ref 5a.

(10) Negish, E.; Kotora, M. *Tetrahedron* **1997**, *53*, 6707. Also please see refs 8c and 8d.

(11) (a) Examples of vinylpalladium species generated from alkenyl halides: (a) Heck, R. F.; Nolley, J. P. *J. Org. Chem.* **1972**, *37*, 2320. (b) Mizoroki, T.; Mori, K.; Ozaki, A. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 581. (c) de Meijere, A.; Meyer, F. E. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2379. (d) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009. (e) Dounay, A. B.; Overman, L. E. *Chem. Rev.* **2003**, *103*, 2945. (f) Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem., Int. Ed.* **2005**, *44*, 4442. Examples of vinylpalladium species generated from alkenyl organometallic compounds: (g) Negish, E.; King, A. O.; Okukado, N. *J. Org. Chem.* **1977**, *42*, 1821. (h) Miyaura, N.; Yamada, K.; Suzuki, A. *Tetrahedron Lett.* **1979**, *20*, 3437. (i) Hallberg, A.; Westerlund, C. *Chem. Lett.* **1982**, 1993. (j) Still, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508.

(12) Examples of vinylpalladium species generated *via* transition-metal catalyzed alkenyl C−H bond palladation: (a) Hatamoto, Y.; Sakaguchi, S.; Ishii, Y. *Org. Lett.* **2004**, *6*, 4623. (b) Giri, R.; Yu, J.-Q. *J. Am. Chem. Soc.* **2008**, *130*, 14082. (c) Ge, H.; Niphakis, X.; Georg, M. J. G. I. *J. Am. Chem. Soc.* **2008**, *130*, 3708. (d) Han, X.; Lu. *Org. Lett.* **2009**, *11*, 2381. (e) Mochida, S.; Hirano, K.; Satoh; Miura, M. *J. Org. Chem.* **2009**, *74*, 6295. (f) Ho, C.-Y.; He, L. *Angew. Chem., Int. Ed.* **2010**, *49*, 9182. (g) Yu, H.; Jin, W.; Sun, C.; Chen, J.; Du, W.; He, S.; Yu, Z. *Angew. Chem., Int. Ed.* **2010**, *49*, 5792. (h) Hu, P.; Huang, S.; Xu, J.; Shi, Z.-J.; Su, W. *Angew. Chem., Int. Ed.* **2011**, *50*, 9926. (i) Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, *111*, 1215. (j) Besset, T.; Kuhl, N.; Paturean, F. W.; Glorious, F. *Chem.—Eur. J.* **2011**, *17*, 7167. (k) Li, C.; Zhang, Y.; Li, P.; Wang, L. *J. Org. Chem.* **2011**, *76*, 4692. (l) Bai, Y.; Zeng, J.; Cai, S.; Liu, X.-W. *Org. Lett.* **2011**, *13*, 4394. (m) Bi, L.; Georg, G. I. *Org. Lett.* **2011**, *13*, 5413. (n) Yu, Y.-Y.; Niphakis, M. J.; Georg, G. I. *Org. Lett.* **2011**, *13*, 5932. (o) Shi, Z.; Zhang, C.; Tang, C.; Jiao, N. *Chem. Soc. Rev.* **2011**, *41*, 3381. (p) Liwosz, T. W.; Chemler, S. R. *J. Am. Chem. Soc.* **2012**, *134*, 2020. (q) Yuan, F.-Q.; Han, F.-S. *Org. Lett.* **2012**, *14*, 1218. (r) Zhang, Y.; Cui, Z.; Li, Z.; Liu, Z.-Q. *Org. Lett.* **2012**, *14*, 1838. (s) Dong, J.; Huan g, Y.; Qiu, X.; Cheng, Y.; Hao, J.; Wan, D.; Li, W.; Liu, X.; You, J. *Chem.—Eur. J.* **2012**, *18*, 6158. (t) Wencel-Delord, J.; Nimphius, C.; Patureau, F. W.; Glorius, F. *Chem.—Asian. J.* **2012**, *7*, 1208. (u) Giant, N.; Giuaizeau, I. *Org. Lett.* **2012**, *14*, 3304. (v) Yu, W.; Chen, J.; Gao, K.; Liu, Z.; Zhang, Y. *Org. Lett.* **2014**, *16*, 4870 and ref 12.

(13) Examples of vinylpalladium species generated via nucleophilic addition of alkynes: (a) Ma, S.; Lu, X. *J. Org. Chem.* **1993**, *58*, 1245. (b) Zhang, Q.; Lu, X. *J. Am. Chem. Soc.* **2000**, *122*, 7604. (c) Lei, A.; Lu, X. *Org. Lett.* **2000**, *2*, 2699. (d) Zhao, L.; Lu, X. *Org. Lett.* **2002**, *4*, 3903. (e) Song, J.; Shen, Q.; Xu, F.; Lu, X. *Org. Lett.* **2007**, *9*, 2947. (f) Shen, K.; Han, X.; Lu, X. *Org. Lett.* **2012**, *14*, 1756. (g) Liu, H.; EI-Salfiti, M.; Chai, D. I.; Auffret, J.; Lautens, M. *Org. Lett.* **2012**, *14*, 3648. (h) Keilitz, J.; Newman, S. G.; Lautens, M. *Org. Lett.* **2013**, *15*, 1148. (i) Chinchilla, R.; Nájera, C. *Chem. Rev.* **2014**, *114*, 1783 and references cited therein.

(14) (a) Zhou, H.; Chung, W.-J.; Xu, Y.-H.; Loh, T.-P. *Chem. Commun.* **2009**, *45*, 3472. (b) Zhou, H.; Xu, Y.-H.; Chang, W.-J.; Loh, T.-P. *Angew. Chem., Int. Ed.* **2009**, *48*, 5355. (c) Xu, Y.-H.; Chok, Y.-K.; Loh, T.-P. *Chem. Sci.* **2011**, *2*, 1822. (d) Pankajakshan, S.; Xu, Y.-H.; Cheng, J.-K.; Low, M.-T.; Loh, T. P. *Angew. Chem., Int. Ed.* **2012**, *51*, 5701. (e) Feng, C.; Loh, T.-P. *Chem. Sci.* **2012**, *3*, 3458. (e) Zhang, X.; Wang, M.; Xu, Y.-H.; Loh, T.-P. *Org. Lett.* **2013**, *15*, 5531. (g) Xu, Y.-H.; He, T.; Zhang, Q.-C.; Loh, T.-P. *Chem. Commun.* **2014**, *50*, 2784.

(15) Examples: (a) Ma, S.; Lu, X. *J. Org. Chem.* **1991**, *56*, 5120. (b) Zhou, C.; Emich, D. E.; Larock, R. C. *Org. Lett.* **2003**, *5*, 1579. (c) Patel, S. J.; Jamison, T. F. *Angew. Chem., Int. Ed.* **2003**, *42*, 1364. (d) Nakao, Y.; Oda, S.; Hayama, T. *J. Am. Chem. Soc.* **2004**, *126*, 13904. (e) Zhou, C.; Larock, R. C. *J. Org. Chem.* **2006**, *71*, 3184. (f) Nakao, Y.; Yada, A.; Hayama, T. *J. Am. Chem. Soc.* **2010**, *132*, 10024. (g) Suárez, L. L.; Greaney, M. F. *Chem. Commun.* **2011**, 7992. (h) Minami, Y.; Yoshiyasu, H.; Nakao, Y.; Hiyama, T. *Angew. Chem., Int. Ed.* **2013**, *52*, 883. (i) Walkinshaw, A. J.; Xu, W.; Suero, M. G.; Gaunt, M. J. *J. Am. Chem. Soc.* **2013**, *135*, 12532.

(16) (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, *16*, 4467. (b) Andrus, M. B.; Lepore, S. D.; Turner, T. M. *J. Am. Chem. Soc.* **1997**, *119*, 12159. (c) Paterson, I.; Paquet, T. *Org. Lett.* **2010**, *12*, 2158.

(17) (a) Huang, Q.; Larock, R. C. *J. Org. Chem.* **2003**, *68*, 980. (b) Zhao, P.; Chen, D.; Song, G.; Han, K.; Li, X. *J. Org. Chem.* **2012**, *77*, 1579.

DOI: 10.1021/acs.orglett.5b00272
Org. Lett. 2015, 17, 1636−1639