ORGANIC LETTERS

2013
Vol. 15, No. 11
2574–2577

Pd-Catalyzed C−H Lactonization for Expedient Synthesis of Biaryl Lactones and Total Synthesis of Cannabinol

Yan Li, Yan-Jun Ding, Jian-Yong Wang, Yi-Ming Su, and Xi-Sheng Wang*

Department of Chemistry, University of Science and Technology of China, 96 Jinzhai Road, Hefei, Anhui 230026, China

xswang77@ustc.edu.cn

Received January 11, 2013

ABSTRACT

A practical Pd(II)/Pd(IV)-catalyzed carboxyl-directed C−H activation/C−O cyclization to construct biaryl lactones has been developed. The synthetic utility of this new reaction was demonstrated in an atom-economical and operationally convenient total synthesis of the natural product cannabinol from commercially available starting materials, with the newly developed method used for two key steps.

Palladium-catalyzed C−H functionalization[1] has recently emerged as a powerful synthetic strategy, offering new retrosynthetic disconnections for the total synthesis of complex natural products and drug molecules.[2] Although a diverse collection of direct C−H functionalization methods with broadly useful substrate classes has recently been developed with Pd catalysts, there are still relatively few examples of applications of these catalytic reactions in total synthesis.[3] The development of a novel site-selective Pd-catalyzed C−H functionalization methodology that operates under mild reaction conditions for use in total synthesis remains a major challenge.

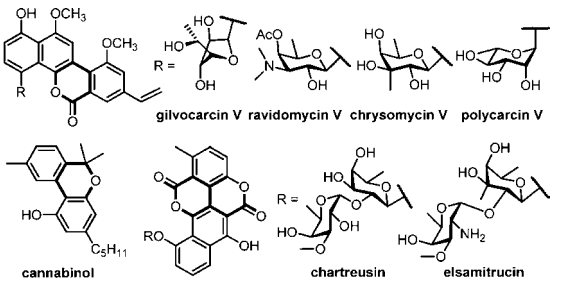


Figure 1. Natural products and pharmaceuticals that contain biaryl lactones or their derivatives.

Biaryl lactones and their derivatives are key structural motifs found in many natural products and pharmaceuticals (Figure 1) and widely used as intermediates in the total synthesis of axially chiral natural products.[4] While a number of methods, such as cyclization of the hydroxyl carboxylic

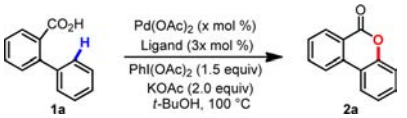
(1) For selected reviews, see: (a) Daugulis, O.; Do, H.-Q.; Shabashov, D. *Acc. Chem. Res.* **2009**, *42*, 1074. (b) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094. (c) Xu, L.-M.; Li, B.-J.; Yang, Z.; Shi, Z.-J. *Chem. Soc. Rev.* **2010**, *39*, 712. (d) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147. (e) Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, *111*, 1215. (f) Wencel-Delord, J.; Dröge, T.; Liu, F.; Glorius., F. *Chem. Soc. Rev.* **2011**, *40*, 4740–4761.

(2) For selected reviews of C−H functionalization in total synthesis, see: (a) Taber, D. F.; Stiriba, S.-E. *Chem.—Eur. J.* **1998**, *4*, 990. (b) Godula, K.; Sames, D. *Science* **2006**, *312*, 67. (c) Davies, H. M. L.; Manning, J. R. *Nature* **2008**, *451*, 417. (d) Ishihara, Y.; Baran, P. S. *Synlett* **2010**, 1733. (e) Gutekunst, W. R.; Baran, P. S. *Chem. Soc. Rev.* **2011**, *40*, 1976. (f) McMurray, L.; O'Hara, F.; Gaunt, M. J. *Chem. Soc. Rev.* **2011**, *40*, 1885. (g) Brückl, T.; Baxter, R. D.; Ishihara, Y.; Baran, P. S. *Acc. Chem. Res.* **2012**, *45*, 826. (h) Yamaguchi, J.; Yamaguchi, A. D.; Itami, K. *Angew. Chem., Int. Ed.* **2012**, *51*, 8960.

(3) For selected examples of Pd-catalyzed C−H functionalization in the total synthesis of natural products, see: (a) Bringmann, G.; Jansen, J. R.; Rink, H.-P. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 913. (b) Hosoya, T.; Takashiro, E.; Matsumoto, T.; Suzuki, K. *J. Am. Chem. Soc.* **1994**, *116*, 1004. (c) Ohmori, K.; Tamiya, M.; Kitamura, M.; Kato, H.; Oorui, M.; Suzuki, K. *Angew. Chem., Int. Ed.* **2005**, *44*, 3871. (d) Beck, E. M.; Hatley, R.; Gaunt, M. J. *Angew. Chem., Int. Ed.* **2008**, *47*, 3004. (e) Stang, E. M.; White, M. C. *Nat. Chem.* **2009**, *1*, 547. (f) Feng, Y.; Chen, G. *Angew. Chem., Int. Ed.* **2010**, *49*, 958. (g) Wang, D.-H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2011**, *133*, 5767. (h) Butler, J. R.; Wang, C.; Bian, J.; Ready, J. M. *J. Am. Chem. Soc.* **2011**, *133*, 9956. (i) Gutekunst, W. R.; Baran, P. S. *J. Am. Chem. Soc.* **2011**, *133*, 19076. (j) Mandal, D.; Yamaguchi, A. D.; Yamaguchi, J.; Itami, K. *J. Am. Chem. Soc.* **2011**, *133*, 19660. (k) Gutekunst, W. R.; Gianatassio, R.; Baran, P. S. *Angew. Chem., Int. Ed.* **2012**, *51*, 7507.

10.1021/ol400877q
Published on Web 05/10/2013

Table 1. Pd(II)-Catalyzed C−H Activation/C−O Cyclization of Biphenyl Carboxylic Acid: Survey of Ligands[a,b]



entry	$Pd(OAc)_2$ [mol %]	ligand	time [h]	yield [%][b]	entry	$Pd(OAc)_2$ [mol %]	ligand	time [h]	yield [%][b]
1	10	–	24	18	11	10	Ac-Gly-OH	24	70
2	10	IMes	24	14	12	10	Ac-Ile−OH	24	58
3	10	IPr	24	21	13	10	Ac-Leu-OH	24	67
4	10	HOAc	24	26	14	10	Ac-Val-OH	24	49
5	10	PivOH	24	28	15[c]	10	Ac-Leu-OH	24	80
6	10	1-AdCO_2H	24	25	16[c,d]	10	Ac-Leu-OH	24	90
7	10	Ac-Ala-OH	24	66	17[c,d]	5	Ac-Leu-OH	24	84
8	10	Boc-Ala-OH	24	26	18[c,d,e]	5	Ac-Leu-OH	24	88
9	10	Cbz-Ala-OH	24	34	19[c,d,e]	5	Ac-Leu-OH	12	91
10	10	Piv-Ala-OH	24	13	20[c,d,e]	5	Ac-Gly-OH	12	93, 91[f]

[a] Unless otherwise noted, the reaction conditions were as follows: **1a** (0.2 mmol, 1 equiv), $Pd(OAc)_2$ (10 mol %), ligand (30 mol %), KOAc (0.4 mmol, 2.0 equiv), $PhI(OAc)_2$ (0.3 mmol, 1.5 equiv) in *t*-BuOH (2 mL) at 100 °C for 24 h. [b] Isolated yield. [c] 80 °C. [d] *t*-BuOH (4 mL) was used. [e] $PhI(OAc)_2$ (2.0 equiv) was used. [f] $Pd(OAc)_2$ (3 mol %) was used.

acids,[5] radical C−O coupling of 2-phenyl carboxylic acids,[6] and C−O cyclization of 2-halo-biphenyl acids,[7] have been used to construct such motifs, the C−C cyclization of 2-halo-biphenyl esters[8] proved to be the most accessible pathway, even for bulky structures, and demonstrated broad applicability in the total synthesis of natural biaryl products.[4f] Unfortunately, these methods are still hampered by some limitations such as the requirement for prefunctionalization and low substrate availability. Herein we report a new biaryl lactone forming process *via* carboxyl-directed C−H activation[9]/C−O bond formation,[10,11] in which a carboxyl directing group is strategically integrated into the desired product structure. The synthetic potential of this method has also been illustrated by application in the total synthesis of the natural product cannabinol[12] from commercially available starting materials in an atom-economical and operationally convenient manner.

We commenced our study by examining the C−H activation/C−O cyclization of 2-phenylbenzoic acid (**1a**)[13] in the presence of $Pd(OAc)_2$ (10 mol %) and $KHCO_3$ (2 equiv) at 100 °C. A wide range of oxidants were tested, in an effort to induce C−O reductive elimination from putative Pd(II), Pd(III),[14] or Pd(IV)[15] intermediates

(4) (a) Gaoni, Y.; Mechoulam, R. *J. Am. Chem. Soc.* **1964**, *86*, 1646. (b) Zhang, Y.-J.; Abe, T.; Tanaka, T.; Yang, C.-R.; Kouno, I. *J. Nat. Prod.* **2001**, *64*, 1527. (c) Orabi, M. A. A.; Taniguchi, S.; Yoshimura, M.; Yoshida, T.; Kishino, K.; Sakagami, H.; Hatano, T. *J. Nat. Prod.* **2010**, *73*, 870. (d) Pfundstein, B.; El Desouky, S. K.; Hull, W. E.; Haubner, R.; Erben, G.; Owen, R. W. *Phytochemistry* **2010**, *71*, 1132. (e) Disadee, W.; Mahidol, C.; Sahakitpichan, P.; Sitthimonchai, S.; Ruchirawat, S.; Kanchanapoom, T. *Phytochemistry* **2012**, *74*, 115. For reviews of the total synthesis of axially chiral natural products via biaryl lactones, see: (f) Bringmann, G.; Menche, D. *Acc. Chem. Res.* **2001**, *34*, 615. (g) Bringmann, G.; Gulder, T.; Gulder, T. A. M.; Breuning, M. *Chem. Rev.* **2011**, *111*, 563.

(5) (a) Glover, S. A.; Golding, S. L.; Goosen, A.; McCleland, C. W. *J. Chem. Soc., Perkin Trans. 1* **1981**, 842. (b) Hager, A.; Mazunin, D.; Mayer, P.; Trauner, D. *Org. Lett.* **2011**, *13*, 1386.

(6) (a) Balanikas, G.; Hussain, N.; Amin, S.; Hecht, S. S. *J. Org. Chem.* **1988**, *53*, 1007. (b) Togo, H.; Muraki, T.; Yokoyama, M. *Tetrahedron Lett.* **1995**, *36*, 7089. (c) Furuyama, S.; Togo, H. *Synlett* **2010**, 2325.

(7) (a) Thasana, N.; Worayuthakarn, R.; Kradanrat, P.; Hohn, E.; Young, L.; Ruchirawat, S. *J. Org. Chem.* **2007**, *72*, 9379. (b) Ceylan, S.; Klande, T.; Vogt, C.; Friese, C.; Kirschning, A. *Synlett* **2010**, 2009.

(8) (a) Bringmann, G.; Jansen, J. R.; Rink, H.-P. *Angew. Chem., Int. Ed.* **1986**, *25*, 913. (b) Harayama, T.; Yasuda, H. *Heterocycles* **1997**, *46*, 61. (c) Bringmann, G.; Pabst, T.; Henschel, P.; Kraus, J.; Peters, K.; Peters, E.-M.; Rycroft, D. S.; Connolly, J. D. *J. Am. Chem. Soc.* **2000**, *122*, 9127. (d) Bringmann, G.; Menche, D. *Angew. Chem., Int. Ed.* **2001**, *40*, 1687. (e) Harrowven, D. C.; Woodcock, T.; Howes, P. D. *Angew. Chem., Int. Ed.* **2005**, *44*, 3899. (f) Taylor, S. R.; Ung, A. T.; Pyne, S. G. *Tetrahedron* **2007**, *63*, 10889. (g) Sun, C.-L.; Liu, J.; Wang, Y.; Zhou, X.; Li, B.-J.; Shi, Z.-J. *Synlett* **2011**, 883.

(9) Pd-catalyzed carboxyl-directed C−H activation; for a review, see: (a) Engle, K. M.; Mei, T.-S.; Wasa, M.; Yu, J.-Q. *Acc. Chem. Res.* **2012**, *45*, 788. For selected examples, see: (b) Miura, M.; Tsuda, T.; Satoh, T.; Pivsa-Art, S.; Nomura, M. *J. Org. Chem.* **1998**, *63*, 5211. (c) Giri, R.; Maugel, N. L.; Li, J.-J.; Wang, D.-H.; Breazzano, S. P.; Saunders, L. B.; Yu, J.-Q. *J. Am. Chem. Soc.* **2007**, *129*, 3510. (d) Wang, D.-H.; Mei, T.-S.; Yu, J.-Q. *J. Am. Chem. Soc.* **2008**, *130*, 17676.

(10) For Pd-catalyzed carboxyl-directed allylic and benzylic $C(sp^3)$−H activation/C−O bond formation to synthesis lactones, see: (a) Covell, D. J.; White, M. C. *Angew. Chem., Int. Ed.* **2008**, *47*, 6448. (b) Novák, P.; Correa, A.; Gallardo-Donaire, J.; Martin, R. *Angew. Chem., Int. Ed.* **2011**, *50*, 12236. For Pd-catalyzed carboxyl-directed enantioselective C−H activation/C−O bond formation to synthesize chiral benzofuranones, see: (c) Cheng, X.-F.; Li, Y.; Su, Y.-M.; Yin, F.; Wang, J.-Y.; Sheng, J.; Vora, H. U.; Wang, X.-S.; Yu, J.-Q. *J. Am. Chem. Soc.* **2013**, *135*, 1236.

(11) For Pd-catalyzed hydroxyl-directed C−H activation/C−O bond formation, see: (a) Wang, X.; Lu, Y.; Dai, H.-X.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 12203. (b) Xiao, B.; Gong, T.-J.; Liu, Z.-J.; Liu, J.-H.; Luo, D.-F.; Xu, J.; Liu, L. *J. Am. Chem. Soc.* **2011**, *133*, 9250. (c) Wei, Y.; Yoshikai, N. *Org. Lett.* **2011**, *13*, 5504.

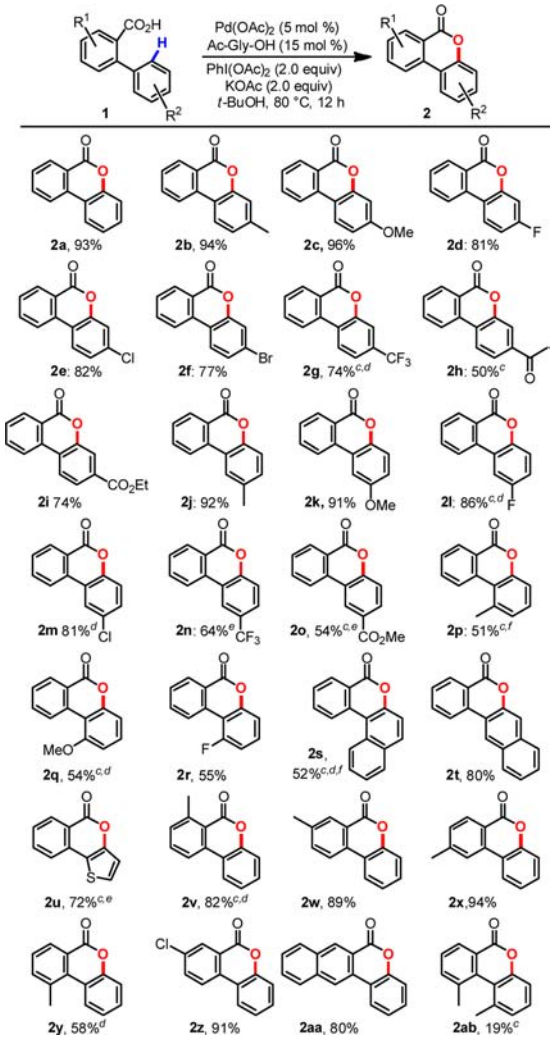
(12) (a) Meltzer, P. C.; Dalzell, H. C.; Razdan, R. K. *Synthesis* **1981**, 985. (b) Hattori, T.; Suzuki, T.; Hayashizaka, N.; Koike, N.; Miyano, S. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 3034. (c) Teske, J. A.; Deiters, A. *Org. Lett.* **2008**, *10*, 2195. (d) Nandaluru, P. R.; Bodwell, G. J. *Org. Lett.* **2012**, *14*, 310.

(13) (a) Voutchkova, A.; Coplin, A.; Leadheater, N. E.; Crabtree, R. H. *Chem. Commun.* **2008**, 6312. (b) Wang, C.; Piel, I.; Glorius, F. *J. Am. Chem. Soc.* **2009**, *131*, 4194.

(14) (a) Powers, D. C.; Ritter, T. *Nat. Chem.* **2009**, *1*, 302. (b) Deprez, N. R.; Sanford, M. S. *J. Am. Chem. Soc.* **2009**, *131*, 11234.

(15) (a) Muñiz, K. *Angew. Chem., Int. Ed.* **2009**, *48*, 9412. (b) Hickman, A. J.; Sanford, M. S. *Nature* **2012**, *484*, 177.

Table 2. Scope of 2-Aryl Carboxylic Acid Substrates[a,b]



[a] Unless otherwise noted, the reaction conditions were as follows: **1** (0.2 mmol, 1.0 equiv), $Pd(OAc)_2$ (5 mol %), Ac-Gly-OH (15 mol %), $PhI(OAc)_2$ (0.4 mmol, 2.0 equiv), KOAc (0.4 mmol, 2.0 equiv), *t*-BuOH (4 mL), 80 °C, 24 h. [b] Isolated yield. [c] 100 °C. [d] $Pd(OAc)_2$ (8 mol %) and Ac-Gly-OH (24 mol %) were used. [e] $Pd(OAc)_2$ (10 mol %) and Ac-Gly-OH (30 mol %) were used. [f] CsOAc was used as the base.

(see Supporting Information (SI)). First, Ag(I) and Cu(II) salts were examined, but these gave no desired product, suggesting that the C−O bond-forming reductive elimination step from the putative Pd(II) intermediate was challenging in this case (Table 2 in the SI). Considering reductive elimination of carbon−heteroatom bonds is known to be more facile from Pd(IV) species,[1d,e,15] a series of well-established oxidants for converting Pd(II) to Pd(IV) were tested. Although a wide range of these oxidants failed to give the desired biaryl lactone product, we found that **2a** was obtained in 23% yield with $PhI(OAc)_2$, a generally effective oxidant in Pd(II)/Pd(IV) catalytic cycles (entry 1, Table 3 in the SI).[11a,16]

Next, we examined different ligands in an effort to improve the catalytic efficiency, such as IMes, IPr, and a variety of organic acids, but these gave no improvement (entries 2−6, Table 1). Fortunately, we eventually found that commercially available monoprotected amino acid derivatives, which had recently been developed as powerful ligands in Pd(II)-catalyzed direct C−H functionalizations by Yu et al.,[17] significantly improved the yield after careful reinvestigation of the base and solvent (Tables 5−7 in the SI). We further optimized the reaction conditions and discovered that acetyl-protected glycine (Ac-Gly-OH), the only achiral proteinogenic amino acid, provided the best performance along with KOAc and *t*-BuOH, giving 93% isolated yield (entry 20, Table 1). Importantly, when the Pd(II) catalyst was reduced to 3 mol %, approximately the same yield could be obtained.

With the optimized reaction conditions in hand, we next investigated the substrate scope of this C−H activation/C−O cyclization process. A variety of 2-aryl carboxylic acids were cyclized to give the corresponding biaryl lactones in modest to excellent yields (up to 96%) (Table 2). Both electron-donating groups, such as OMe and Me, and electron-withdrawing groups, such as CF_3, F, Cl, Br, CO_2Et, and Ac, were tolerated on the aryl rings. The presence of halogen atoms (Br, Cl, and F) in the products of Table 2 offers the potential for further synthetic elaboration by well-established transition-metal-catalyzed cross-coupling reactions. When *meta*-substituted (R^2) biaryl acids were used, activation of the sterically less hindered C−H bond was observed, and the other regioisomer was not observed. Interesingly, cyclization of *ortho*-substituted (R^1 or R^2) substrates, **1p**−**s** and **1y**, gave the desired products in only moderate yields (**2p**−**s** and **2y**) with >30% starting materials recoverd, presumably because the added steric hindrance increases the activation energy of the C−H cleavage step.[11b,c,18]

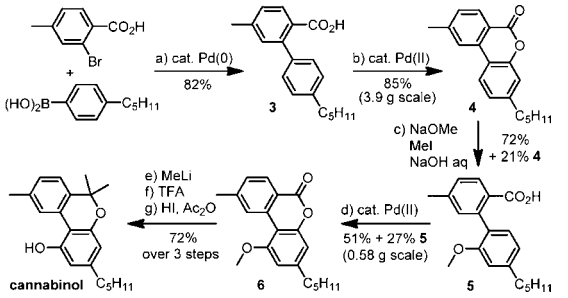
To demonstrate the potential of this new methodology, we next attempted to carry out a concise total synthesis of the natural product cannabinol using our C−H activation/C−O cyclization reaction for two key steps. Whereas previous total syntheses of cannabinol employed complex starting materials, prepared through several steps,[12] our synthetic strategy is comparatively straightforward (Scheme 1). With Pd(0) as the catalyst, commercially available 2-bromo-4-methyl benzoic acid and 4-pentylphenyl boronic acid were coupled smoothly, giving the biaryl acid **3** in 82% yield (4.6 g scale). The cyclization of **3** under our optimized conditions [$Pd(OAc)_2$ (5 mol %)] gave the biaryl lactone **4** in 85% yield (3.9 g scale). Subsequently,

(16) (a) Yoneyama, T.; Crabtree, R. H. *J. Mol. Catal. A: Chem.* **1996**, *108*, 35. (b) Dick, A. R.; Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2004**, *126*, 2300. (c) Jordan-Hore, J. A.; Johansson, C. C. C.; Gulias, M.; Beck, E. M.; Gaunt, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 16184. (d) Zhang, S.-Y.; He, G.; Zhao, Y.; Wright, K.; Nack, W. A.; Chen, G. *J. Am. Chem. Soc.* **2012**, *134*, 7313.

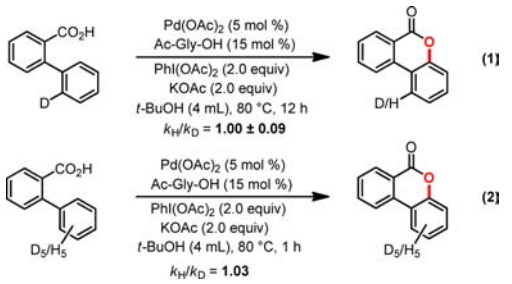
(17) (a) Wang, D.-H.; Engle, K. M.; Shi, B.-F.; Yu, J.-Q. *Science* **2010**, *327*, 315. (b) Lu, Y.; Wang, D.-H.; Engle, K. M.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 5916. (c) Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 14137. (d) Lu, Y.; Leow, D.; Wang, X.; Engle, K. M.; Yu, J.-Q. *Chem. Sci.* **2011**, *2*, 967. (e) Engle, K. M.; Thuy-Boun, P. S.; Dang, M.; Yu, J.-Q. *J. Am. Chem. Soc.* **2011**, *133*, 18183. (f) Leow, D.; Li, G.; Mei, T.-S.; Yu, J.-Q. *Nature* **2012**, *486*, 518.

(18) Zhao, J.; Wang, Y.; He, Y.; Liu, L.; Zhu, Q. *Org. Lett.* **2012**, *14*, 1078.

Scheme 1. Total Synthesis of Cannabinol



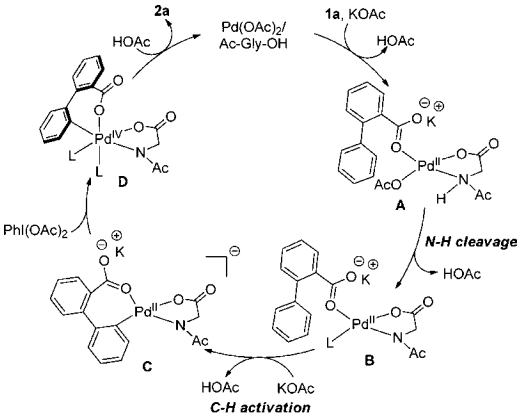
Scheme 2. Kinetic Isotope Effect (KIE)



lactone **4** was opened by nucleophilic attack of NaOMe, quenched by MeI, and then fully hydrolyzed through the addition of aqueous sodium hydroxide to give the corresponding acid **5**. To finish the assembly of the core structure we again turned to our biaryl lactone-forming reaction, which gave the biphenyl lactone **6** in 51% yield with 27% of **5** recovered (0.58 g scale). The synthesis was completed following a reported synthetic route:[12c] treatment of biaryl lactone **6** with MeLi, cyclization with TFA, and finally demethylation to reveal the free phenol. This sequence gave cannabinol in 72% yield (356 mg) over the three steps.

To understand the mechanism of this transformation, we carried out a series of experiments. First, we attempted to perform the reaction using a stoichiometric amount of $Pd(OAc)_2$ in the absence of $PhI(OAc)_2$, and we observed no desired product, consistent with the hypothesis that C−O reductive elimination from Pd(II) was unfavorable. Isotope labeling experiments were next undertaken. We probed the nature of the aromatic C−H bond activation step by performing an intramolecular competition experiment using monodeuterated carboxylic acid **1a**-*d*, which exhibited no significant kinetic isotope effect (k_H/k_D = 1.00) (eq 1, Scheme 2). Similarly, an intermolecular competition experiment between 2-phenyl carboxylic

Scheme 3. Possible Mechanism for the Synthesis of Biaryl Lactones



acid **1a** and its pentadeuterated analogue **1a**-d_5 exhibited a KIE of 1.03 (eq 2, Scheme 2). Both observations are consistent with a catalytic cycle in which the C−H activation step is not rate-determining. At this stage, we hypothesize that the C−O reductive elimination step is the rate-determining step.

On the basis of these observations, a mechanism involving a plausible Pd(II)/Pd(IV) catalytic cycle is depicted in Scheme 3. The powerful ligand Ac-Gly-OH accelerates C−H bond cleavage, presumably through the N−H activation pathway suggested by the computational studies of Musaev et al.,[19,20] which gives the cyclopalladated complex **C**. Subsequently, oxidation of the Pd(II) complex to a high-valent Pd(IV) species **D** takes place, followed by C−O reductive elimination to afford the biphenyl lactone **2a**.

In summary, we have developed a practical carboxyl-directed C−H activation/C−O cyclization to construct biaryl lactones via a Pd(II)/Pd(IV) catalytic cycle. The synthetic utility of this new transformation was demonstrated in a concise total synthesis of the natural product cannabinol from commercially available starting materials. Additional work to elucidate more clearly the mechanistic details of this reaction and to apply it in the total synthesis of more complex natural products is currently underway in our laboratory.

Acknowledgment. We gratefully acknowledge the Chinese Academy of Sciences, the Ministry of Education (SRFDP 20123402110040), the National Science Foundation of China (No. 21102138), and University of Science and Technology of China (USTC) for financial support. We thank Mr. Keary M. Engle (The Scripps Research Institute, USA) and Prof. Yang-Hui Zhang (Tongji University, China) for helpful discussions.

Supporting Information Available. Experimental procedure and characterization of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

(19) (a) Musaev, D. G.; Kaledin, A. L.; Shi, B.-F.; Yu, J.-Q. *J. Am. Chem. Soc.* **2012**, *134*, 1690. (b) Baxter, R. D.; Sale, D.; Engle, K. M.; Yu, J.-Q.; Blackmond, D. G. *J. Am. Chem. Soc.* **2012**, *134*, 4600.

(20) At this stage, a stepwise route involving C−H bond acetoxylation/lactonization cannot be excluded. For related studies, see: (a) Huang, C.; Ghavtadze, N.; Chattopadhyay, B.; Gevorgyan, V. *J. Am. Chem. Soc.* **2011**, *133*, 17630. (b) Huang, C.; Ghavtadze, N.; Godoi, B.; Gevorgyan, V. *Chem.—Eur. J.* **2012**, *18*, 9789.

The authors declare no competing financial interest.