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Arylations of Substituted Enamides by Aryl Iodides: Regio- and Stereoselective Synthesis of (*Z*)-*β*-Amido-*β*-Arylacrylates

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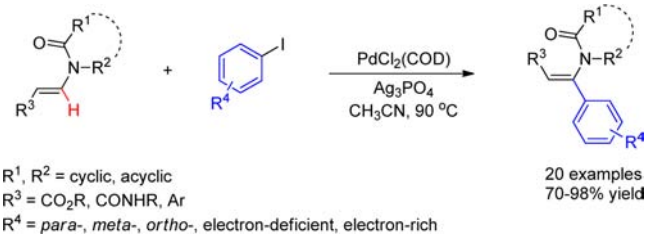
ABSTRACT



Arylations of substituted enamides by aryl iodides were achieved for the first time via an unusual $PdCl_2(COD)/Ag_3PO_4$ catalytic system. A broad range of (*Z*)-*β*-amido-*β*-arylacrylates were prepared regio- and stereoselectively in a highly efficient manner.

Palladium-catalyzed Heck arylation, one of the most useful reactions to construct carbon−carbon bonds, involves the coupling of aryl halides/pseudohalides with olefins.[1] Heck arylations were typically catalyzed by Pd(0) or Pd(II) with an added phosphine ligand and operating under a Pd(0)/Pd(II) catalytic cycle with the assistance of base to complete the cycle. In a program directed toward synthesis of enamides,[2] especially trisubstituted enamide *β*-amido-*β*-arylacrylates, substrate commonly used to prepare valuable chiral *β*-amino acid through asymmetric hydrogenation,[3] we noticed that classic methods of condensing *β*-ketoester with amino source to prepare this substrate suffer from low efficiency and poor stereocontrol of olefin geometry in general.[3d,f] Although progress has been made in palladium-catalyzed Heck arylation of enamide by using aryl triflates as arylation partner or through ionic liquid-promoted protocol as alternative approaches to address these problems, only unsubstituted

(1) (a) Mizoroki, T.; Mori, K.; Ozaki, A. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 581. (b) Heck, R. F.; Nolley, J. P., Jr. *J. Org. Chem.* **1972**, *37*, 2320. (c) Heck, R. F. *Acc. Chem. Res.* **1979**, *12*, 146. (d) Daves, G. D., Jr.; Hallberg, A. *Chem. Rev.* **1989**, *89*, 1433. (e) Whitcombe, N. J.; Hii, K. K.; Gibson, S. E. *Tetrahedron* **2001**, *57*, 7449. (f) Littke, A. F.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 6989. (g) Dounay, A. B.; Overman, L. E. *Chem. Rev.* **2003**, *103*, 2945. (h) Shibasaki, M.; Vogl, E. M.; Ohshima, T. *Adv. Synth. Catal.* **2004**, *346*, 1533. (i) Knowles, J. P.; Whiting, A. *Org. Biomol. Chem.* **2007**, *5*, 31. (j) Oestreich, M. *The Mizoroki-Heck Reaction*; Wiley: Chichester, U. K., 2009. (k) Larhed, M.; Hallberg, A. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E.-I., Ed.; Wiley Interscience: New York, 2002; Vol. 1, p 1133.

(2) (a) Matsubara, R.; Nakamura, Y.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2004**, *43*, 1679. (b) Terada, M.; Machioka, K.; Sorimachi, K. *Angew. Chem., Int. Ed.* **2006**, *45*, 2254. (c) Jia, Y.; Zhong, J.; Zhu, S.; Zhang, C.; Zhou, Q. *Angew. Chem., Int. Ed.* **2007**, *46*, 5565. (d) Berthiol, F.; Matsubara, R.; Kawai, N.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2007**, *46*, 7803. (e) Baudequin, C.; Zamfir, A.; Tsogoeva, S. B. *Chem. Commun.* **2008**, 4637. (f) Hayashi, Y.; Gotoh, H.; Masui, R.; Ishikawa, H. *Angew. Chem., Int. Ed.* **2008**, *47*, 4012. (g) Zu, L.; Xie, H.; Li, H.; Wang, J.; Yu, X.; Wang, W. *Chem.—Eur. J.* **2008**, *14*, 6333. (h) Guo, Q.; Peng, Y.; Zhang, J.; Song, L.; Feng, Z.; Gong, L. *Org. Lett.* **2009**, *11*, 4620. (i) Gourdet, B.; Rudkin, M. E.; Watts, C. A.; Lam, H. W. *J. Org. Chem.* **2009**, *74*, 7849. (j) Gourdet, B.; Lam, H. W. *J. Am. Chem. Soc.* **2009**, *131*, 3802. (k) Zheng, K.; Liu, X.; Zhao, J.; Yang, Y.; Lin, L.; Feng, X. *Chem. Commun.* **2010**, *46*, 3771. (l) Reeves, J. T.; Tan, Z.; Han, Z. S.; Li, G.; Zhang, Y.; Xu, Y.; Reeves, D. C.; Gonnella, N. C.; Ma, S.; Lee, H.; Lu, B. Z.; Senanayake, C. H. *Angew. Chem., Int. Ed.* **2012**, *51*, 1400.

(3) (a) Lubell, W. D.; Kitamura, M.; Noyori, R. *Tetrahedron: Asymmetry* **1991**, *2*, 543. (b) Zhu, G.; Chen, Z.; Zhang, X. *J. Org. Chem.* **1999**, *64*, 6907. (c) Xiao, D.; Zhang, Z.; Zhang, X. *Org. Lett.* **1999**, *1*, 1679. (d) Zhou, Y.; Tang, W.; Wang, W.; Li, W.; Zhang, X. *J. Am. Chem. Soc.* **2002**, *124*, 4952. (e) van den Berg, M.; Haak, R. M.; Minnaard, A. J.; de Vries, A. H. M.; de Vries, J. G.; Feringa, B. L. *Adv. Synth. Catal.* **2002**, *344*, 1003. (f) You, J.; Drexler, H.; Zhang, S.; Fischer, C.; Heller, D. *Angew. Chem., Int. Ed.* **2003**, *42*, 913. (g) Tang, W.; Wang, W.; Chi, Y.; Zhang, X. *Angew. Chem., Int. Ed.* **2003**, *42*, 3509. (h) Tang, W.; Zhang, X. *Chem. Rev.* **2003**, *103*, 3029. (i) Blaser, H. U.; Malan, C.; Pugin, B.; Spindler, F.; Steiner, H.; Studer, M. *Adv. Synth. Catal.* **2003**, *345*, 103. (j) Enthaler, S.; Erre, G.; Junge, K.; Addis, D.; Kadyrov, R.; Beller, M. *Chem. Asian J.* **2008**, *3*, 1104. (k) Chen, J.; Zhang, W.; Geng, H.; Li, W.; Hou, G.; Lei, A.; Zhang, X. *Angew. Chem., Int. Ed.* **2009**, *48*, 800. (l) Nugent, T. C.; El-Shazly, M. *Adv. Synth. Catal.* **2010**, *352*, 753. (m) Xie, J.; Zhu, S.; Zhou, Q. *Chem. Rev.* **2011**, *111*, 1713.

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enamide can be effectively arylated under these conditions.[4,5] Arylation of sterically hindered substituted enamide to build trisubstituted enamide, such as β-amido-β-arylacrylates, especially with regio- and stereocontrol, remains rare and underdeveloped, with only one example reported by Park using costly arylboronates through a Pd(0)/Pd(II) oxidative Heck manifold.[6] Cheaper aryl iodides are unprecedented for this transformation, until now, we disclose here that arylations of substituted enamides by aryl iodides can be achieved for the first time via an unusual catalytic system (Scheme 1). The reaction was promoted by $PdCl_2$(COD) and Ag_3PO_4, highly efficient to produce a broad range of (*Z*)-β-amido-β-arylacrylates exclusively in good to excellent yield with remarkable regio- and stereocontrol of olefin geometry.

In our efforts to optimize reaction conditions, we started with a model reaction in which methyl β-amido-acrylate (*E*)-**1a** was coupled with phenyl iodide **2a** (Table 1). The reaction could potentially yield β-arylated regioisomer **3aa** and/or the corresponding α-isomer **4aa**, with each isomer occurring as a mixture of *Z*/*E* olefins. With $Pd(TFA)_2$ as catalyst and CH_3CN as solvent at 90 °C, we screened a series of copper and silver salts and other organic/inorganic cocatalysts. Copper salts and other organic/inorganic cocatalysts were inefficient, basically affording no or trace amount of **3aa**. Silver salts were found to be the most efficient cocatalysts, yielding regioisomer **3aa** exclusively without formation of **4aa**. However, the yield and *Z*/*E* selectivity of **3aa** varied widely depending on the silver salt used.

We speculated that different Pd(II) catalysts could be used to fine-tune the reaction, due to the electronic and steric particularities of catalyst ligands. After further screening various Pd(II) catalysts in conjunction with silver salts, to our delight, we quickly identified $PdCl_2$-(COD)/Ag_3PO_4 as the best combination, which produced (*Z*)-**3aa** exclusively in 97% yield and *Z*:*E* > 20:1 (entry 1). Both $PdCl_2$(COD) and Ag_3PO_4 were indispensable to the reaction; removing either one led to no detectable product (entry 2−3). Further investigation showed that loading of $PdCl_2$(COD) and Ag_3PO_4 could be reduced to 15 mol % and 2 equiv, respectively, without affecting reaction efficiency (entry 4). Bases were detrimental to the reaction (entry 5−6), while AcOH affected the yield and selectivity only slightly (entry 7). The optimal reaction temperature was 90 °C. Acetonitrile remained the best solvent (see the Supporting Information for complete screenings of Pd(II), cocatalyst, solvent, and temperature conditions).

After optimizing the reaction conditions, we investigated the scope of the reaction. First, we examined the

Scheme 1. Arylations of Substituted Enamides by Aryl Iodides

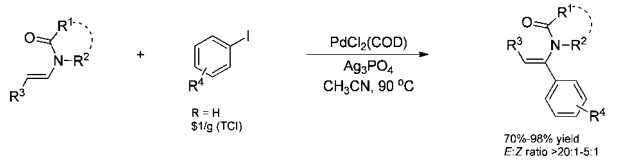
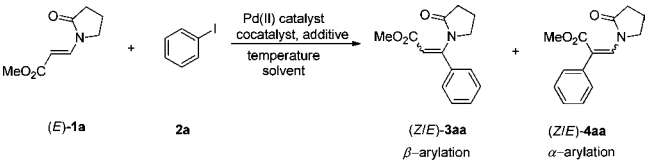


Table 1. Optimization of Reaction Conditions[a]



entry	Pd(II) (20 mol %)	cocatalyst (3 equiv)	yield of (*Z*)-**3aa**[b]	*Z*:*E* ratio of **3aa**[c]
1	$PdCl_2$(COD)	Ag_3PO_4	97%	>20:1
2	$PdCl_2$(COD)	—	0	NA[h]
3	—	Ag_3PO_4	0	NA[h]
4[d]	**$PdCl_2$(COD)**	**Ag_3PO_4**	**95%**	**>20:1**
5[e]	$PdCl_2$(COD)	Ag_3PO_4	48%	>20:1
6[f]	$PdCl_2$(COD)	Ag_3PO_4	0	NA[h]
7[g]	$PdCl_2$(COD)	Ag_3PO_4	93%	>20:1

[a] 0.18 mmol (*E*)-**1a**, 0.36 mmol **2a** used; 0.5 M concentration for 24−48 h with TLC control. [b] Determined by analysis of crude mixture by ^{1}H NMR with benzyl bromide as internal standard. [c] *E* isomer was prepared for analysis of crude mixture by 400 MHz ^{1}H NMR. [d] 15 mol % $PdCl_2$(COD), 2 equiv of Ag_3PO_4 used. [e] 2 equiv of K_2CO_3 added. [f] 2 equiv of pyridine added. [g] 2 equiv of AcOH added. [h] NA: not available.

ability of a variety of aryl iodides with electron-deficient or electron-rich substituents to arylate (*E*)-**1a** (Table 2). Most of these aryl iodides yielded the *Z*-products exclusively in good to excellent yield [entry 1−9, (*Z*)-**3aa-3ai**, 70−98%]. Aryl iodide with CN substituent was sluggish [entry 4, (*Z*)-**3ad**, 70%] compared to other electron-deficient iodides. Electron-rich aryl iodides were highly efficient in general [entry 6−7, (*Z*)-**3af-3ag**]. In addition, *ortho*-substituted aryl iodide **2i**, which contains a substitution pattern difficult to achieve in the arylboronate strategy,[6] arylated without problem [entry 9, (*Z*)-**3ai**, 95%].

Diverse functional groups were well tolerated in the reaction, including F, Cl, Br, CO_2Me, CN, OMe, and COMe, providing useful handles for downstream elaboration. Steric and electron influence from the R^3 substituent of (*E*)-**1** were minimum. Bulkier and electron-rich substrates all gave the corresponding *Z*-products exclusively in excellent yield [entry 10−14, (*Z*)-**3ba**−**3ea**, (*Z*)-**3fj**)]. It is worthy to note that substrate (*E*)-**1e** with an electron-donating aryl group, which exhibited moderate α/β regioselectivity in the arylboronate strategy,[6] was arylated with absolute regiocontrol in impressive yield and selectivity [entry 13, (*Z*)-**3ea**, 96%].

Finally, an acyclic amido substrate, methyl β-*N*-acetyl-acrylate (*E*)-**1g**, was arylated to yield a variety of methyl

(4) (a) Cabri, W.; Candiani, I.; Bedeschi, A. *J. Org. Chem.* **1993**, *58*, 7421. (b) Cabri, W.; Candiani, I. *Acc. Chem. Res.* **1995**, *28*, 2. (c) Vallin, K. S. A.; Zhang, Q.; Larhed, M.; Curran, D. P.; Hallberg, A. *J. Org. Chem.* **2003**, *68*, 6639. (d) Hansen, A. L.; Skrydstrup, T. *J. Org. Chem.* **2005**, *70*, 5997.

(5) (a) Mo, J.; Xu, L.; Xiao, J. *J. Am. Chem. Soc.* **2005**, *127*, 751. (b) Mo, J.; Liu, S.; Xiao, J. *Tetrahedron* **2005**, *61*, 9902. (c) Ruan, J.; Xiao, J. *Acc. Chem. Res.* **2011**, *44*, 614.

(6) Liu, Y.; Li, D.; Park, C.-M. *Angew. Chem., Int. Ed.* **2011**, *50*, 7333. Although 18 examples of this method were reported with yield range of 51−81%, *E*/*Z* ratios of the products were not provided.

(*Z*)-β-*N*-acetyl-β-arylacrylates efficiently [entry 15–20, (*Z*)-**3ga**–**3gm**], the most widely used substrate in asymmetric hydrogenation to prepare valuable chiral β-amino acid. Arylating this substrate with *para*- and *meta*-substituted aryl iodides led to greater *Z*-product selectivity than when the *ortho*-substituted analogue was used [entry 20, (*Z*)-**3gm**, 81%, *Z*:*E* = 5:1].

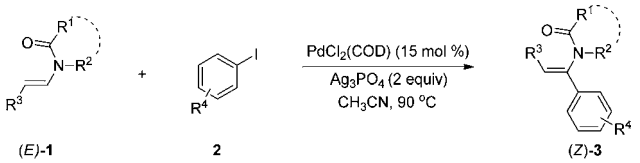
Overall, our method demonstrated broad substrate scope and general high efficiency for preparation of (*Z*)-β-amido-β-arylacrylates (70–98%, *Z*:*E* ratio > 20:1–5:1). It must be mentioned that *Z*-product was exclusively produced regardless to the geometry of **1**, presumably because the *Z*-isomer is thermodynamically more stable than the *E*-isomer.[7] However, our conditions did not support the arylation of (*E*)-**1a** by highly sterically hindered 2,4,6-trimethylphenyl iodide or strongly electron-deficient 4-trifluoromethylphenyl iodide. These reactants will require further optimization of reaction conditions.

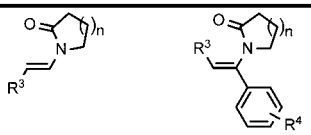
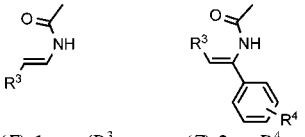
The utility of our method was demonstrated in the synthesis of 11-β-hydroxysteroid dehydrogenase inhibitor **5** from (*Z*)-**3ea** in a two-step transformation including hydrogenation and alkylation (Scheme 2).[8] In addition, asymmetric hydrogenation of (*Z*)-**3gb** could afford valuable chiral β-amino ester **6** according to literature procedure.[3d]

The mechanistic studies of the reaction merit discussion. When (*E*)-**1h**, which contains no amide carbonyl group, was mixed with **2a** under the standard condition for 48 h, no reaction occurred, and (*E*)-**1h** was left intact (Scheme 3A). This result suggests that the amide carbonyl group played an important role in the reaction. We also heated (*E*)-**1a** with 1 equiv of $PdCl_2$(COD) in CD_3CN in an NMR tube at 90 °C and performed ^{1}H NMR analysis at 2, 5, and 24 h. The analysis showed no change of either (*E*)-**1a** or $PdCl_2$(COD), with no new C–H activation intermediate detected. Thus, although the amide carbonyl has been used as a directing group when activating C–H bond,[9] the amide carbonyl of (*E*)-**1a** did not seem to function in this way under our reaction conditions.

To determine whether the first step in our arylation approach is oxidative insertion of a Pd(0) into aryl-I bond, we mixed (*E*)-**1a**, **2a** and Pd(0) under typical Heck conditions and observed no reaction (Scheme 3B). Although cationic Heck arylations starting with a Pd(II) catalyst were reported,[4a,10] these reactions were generally operated with an added phosphine ligand for the initial reduction of Pd(II) to Pd(0). Examples of Heck arylations without a phosphine ligand also appeared, but mechanism of this type of reaction was unknown.[11]

Table 2. Scope of Arylations of β-Amidoacrylates by Aryl Iodides[a]



entry	substrate (*E*)-**1**	product (*Z*)-**3**	yield of (*Z*)-**3**[b] (*Z*:*E* ratio)[c]
			
1	(*E*)-**1a** (R^3 = CO_2Me, n = 1)	(*Z*)-**3aa**, R^4 = *p*-H	95% (>20:1)
2	(*E*)-**1a**	(*Z*)-**3ab**, R^4 = *p*-F	94% (>20:1)
3	(*E*)-**1a**	(*Z*)-**3ac**, R^4 = *p*-Br	92% (>20:1)
4[d]	(*E*)-**1a**	(*Z*)-**3ad**, R^4 = *p*-CN	70% (>20:1)
5	(*E*)-**1a**	(*Z*)-**3ae**, R^4 = *p*-COMe	94% (>20:1)
6	(*E*)-**1a**	(*Z*)-**3af**, R^4 = *p*-OMe	90% (>20:1)
7	(*E*)-**1a**	(*Z*)-**3ag**, R^4 = *m*-Me	98% (>20:1)
8	(*E*)-**1a**	(*Z*)-**3ah**, R^4 = *m*-CO_2Me	93% (>20:1)
9	(*E*)-**1a**	(*Z*)-**3ai**, R^4 = *o*-OMe	95% (>20:1)
10	(*E*)-**1b** (R^3 = $CO_2{}^tBu$, n = 1)	(*Z*)-**3ba**, R^4 = *p*-H	95% (>20:1)
11	(*E*)-**1c** (R^3 = CO_2Bn, n = 1)	(*Z*)-**3ca**, R^4 = *p*-H	91% (>20:1)
12	(*E*)-**1d** (R^3 = CONHBn, n = 1)	(*Z*)-**3da**, R^4 = *p*-H	91% (17:1)
13	(*E*)-**1e** (R^3 = Ph, n = 1)	(*Z*)-**3ea**, R^4 = *p*-H	96% (>20:1)
14	(*E*)-**1f** (R^3 = CO_2Me, n = 2)	(*Z*)-**3fj**, R^4 = *m*-Br	95% (>20:1)
			
15	(*E*)-**1g** (R^3 = CO_2Me)	(*Z*)-**3ga**, R^4 = *p*-H	88% (17:1)
16	(*E*)-**1g**	(*Z*)-**3gb**, R^4 = *p*-F	90% (15:1)
17	(*E*)-**1g**	(*Z*)-**3gc**, R^4 = *p*-Br	81% (14:1)
18	(*E*)-**1g**	(*Z*)-**3gk**, R^4 = *p*-Me,	89% (17:1)
19	(*E*)-**1g**	(*Z*)-**3gl**, R^4 = *m*-OMe	80% (17:1)
20	(*E*)-**1g**	(*Z*)-**3gm**, R^4 = *o*-Cl	81% (5:1)

[a] 0.59 mmol **1**, 1.18 mmol **2** used; 0.5 M concentration for 24–48 h with TLC control. [b] Isolated yield. [c] Determined unambiguously by analysis of crude mixture by 400 MHz ^{1}H NMR with *E*-isomers prepared for selected examples. [d] 25% **1a** recovered.

(7) (*Z*)-**1g** also gave (*Z*)-**3ga** in 85% yield and *Z*:*E* = 18:1. The X-ray crystal structures of (*Z*)-and (*E*)-**3aa** and (*E*)-**3gb** were determined. CCDC-945636 and CCDC-945637 for (*E*)-**3aa** and (*E*)-**3gb**, respectively, contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

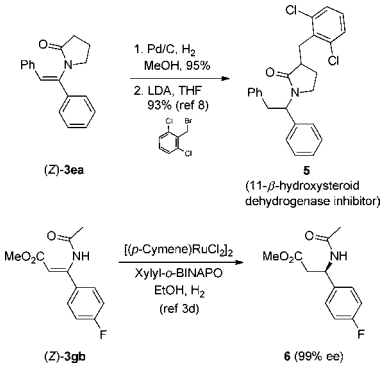
(8) Jaroskova, L.; Linders, J. T. M.; Buyck, C. F. R. N.; Van, D. V. L. J. E.; Dimitrov, V. D.; Nikiforov, T. T. WO 2005108360, 2005.

(9) (a) Tremont, S. J.; Rahman, H. U. *J. Am. Chem. Soc.* **1984**, *106*, 5759. (b) Boele, M. D. K.; van Strijdonck, G. P. F.; de Vries, A. H. M.; Kamer, P. C. J.; de Vries, J. G.; Leeuwen, P. W. N. M. *J. Am. Chem. Soc.* **2002**, *124*, 1586. (c) Zaitsev, V. G.; Daugulis, O. *J. Am. Chem. Soc.* **2005**, *127*, 4156. (d) Tsang, W. C. P.; Zheng, N.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 14560. (e) Daugulis, O.; Zaitsev, V. G. *Angew. Chem., Int. Ed.* **2005**, *44*, 4046. (f) Wan, X.; Ma, Z.; Li, B.; Zhang, K.; Cao, S.; Zhang, S.; Shi, Z. *J. Am. Chem. Soc.* **2006**, *128*, 7416. (g) Yang, S.; Li, B.; Wan, X.; Shi, Z. *J. Am. Chem. Soc.* **2007**, *129*, 6066.

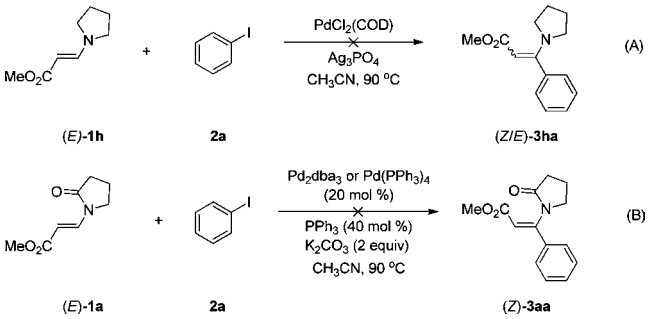
(10) (a) Karabelas, K.; Westerlund, C.; Hallberg, A. *J. Org. Chem.* **1985**, *50*, 3896. (b) Karabelas, K.; Hallberg, A. *J. Org. Chem.* **1986**, *51*, 5286. (c) Cabri, W.; Candiani, I.; Bedeschi, A.; Penco, S. *J. Org. Chem.* **1992**, *57*, 1481. (d) Cabri, W.; Candiani, I.; Bedeschi, A. *J. Org. Chem.* **1992**, *57*, 3558. (e) Ashimori, A.; Bachand, B.; Calter, M. A.; Govek, S. P.; Overman, L. E.; Poon, D. J. *J. Am. Chem. Soc.* **1998**, *120*, 6488. (f) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009.

(11) (a) Jafarpour, F.; Samaneh, Z.; Olia, M. B. A.; Jalalimanesh, N.; Rahiminejadan, S. *J. Org. Chem.* **2013**, *78*, 2957. (b) Zhou, W.; An, G.; Zhang, G.; Han, J.; Pan, Y. *Org. Biomol. Chem.* **2011**, *9*, 5833.

Scheme 2. Synthesis of 11-β-Hydroxysteroid Dehydrogenase Inhibitor and Asymmetric Hydrogenation



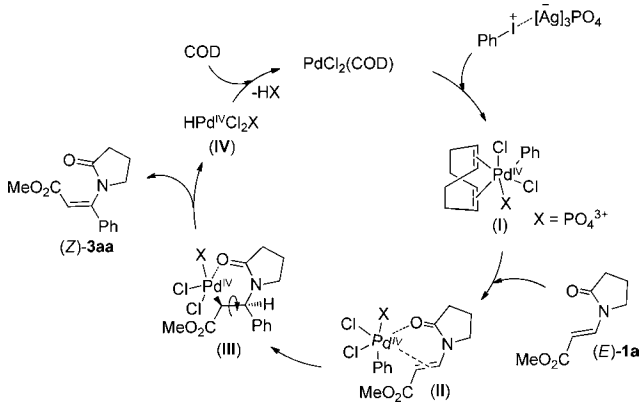
Scheme 3. Control Experiments



Although additional data were needed to establish the mechanism, the fact that no reaction occurred when Ag_3PO_4 was omitted suggested a critical role of the silver salt. This finding, combined with our other mechanistic studies, lead us to tentatively propose an unproven Pd(II)/Pd(IV) catalytic cycle (Scheme 4).[12] According to this proposal, oxidative insertion of the Pd(II) into the silver-polarized Ph-I bond produces a highly electrophilic cationic Pd(IV) species **I**, which would display lower electrophilicity under basic condition (bases were detrimental to the reaction). The amide carbonyl of substrate (*E*)-**1a** displaces 1,5-cyclooctadiene to form the intermediate **II**, in which the double bond of the substrate (*E*)-**1a** is brought close to Pd(IV) center in the proper orientation. Insertion of the double bond into Pd(IV)-Ph bond furnishes the intermediate **III**. Subsequent rotation of the C−C bond sets the stage for *syn*-elimination, yielding the thermodynamically stable isomer (*Z*)-**3aa**. The cycle is completed when HX is eliminated from **IV**, restoring the Pd(II) catalyst.

(12) Pd(II)/Pd(IV) catalysis in C-H activations: (a) Daugulis, O.; Zaitsev, V. G.; Shabashov, D.; Pham, Q.-N.; Lazarev, A. *Synlett* **2006**, *20*, 3382. (b) Deprez, N. R.; Kalyani, D.; Krause, A.; Sanford, M. S. *J. Am. Chem. Soc.* **2006**, *128*, 4972. (c) Hull, K. L.; Lanni, E. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2006**, *128*, 14047. (d) Kawai, H.; Kobayshi, Y.; Oi, S.; Inoue, Y. *Chem. Commun.* **2008**, 1464. (e) Sibbald, P. A.; Rosewall, C. F.; Swartz, R. D.; Michael, F. E. *J. Am. Chem. Soc.* **2009**, *131*, 15945. (f) Pilarski, L. T.; Selander, N.; Bose, D.; Szabo, K. *J. Org. Lett.* **2009**, *11*, 5518. (g) Racowski, J. M.; Ball, N. D.; Sanford, M. S. *J. Am. Chem. Soc.* **2011**, *133*, 18022. (h) Ano, Y.; Tobisu, M.; Chatani, N. *J. Am. Chem. Soc.* **2011**, *133*, 12984. (i) Wang, X.; Leow, D.; Yu, J.-Q. *J. Am. Chem. Soc.* **2011**, *133*, 13864.

Scheme 4. Proposed Catalytic Cycle



In summary, arylations of substituted enamides by aryl iodides were achieved for the first time via an unusual catalytic system under the assistance of a directing carbonyl group. $PdCl_2(COD)$ and Ag_3PO_4 were essential for the reaction to occur. Under the conditions, a broad range of (*Z*)-β-amido-β-arylacrylates were prepared regio- and stereoselectively in a highly efficient manner. A Pd(II)/Pd(IV) catalysis was tentatively proposed. Further studies are underway to establish the reaction mechanism and to expand the substrate scope to include the challenging alkyl iodides and highly electron-deficient and sterically hindered aryl iodides.

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

The authors declare no competing financial interest.