

Heterocycles

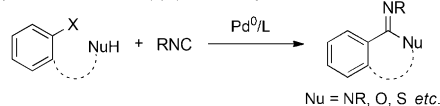
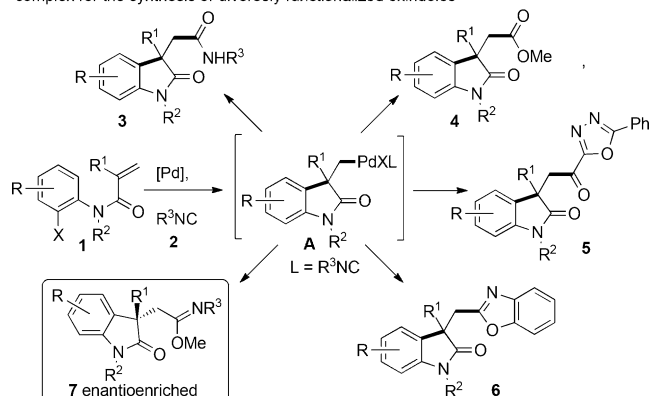
Deutsche Ausgabe: DOI: 10.1002/ange.201603950
Internationale Ausgabe: DOI: 10.1002/anie.201603950Synthesis of Diversely Functionalized Oxindoles Enabled by Migratory Insertion of Isocyanide to a Transient σ -Alkylpalladium(II) Complex

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Abstract: Palladium-catalyzed intramolecular carbopalladation of *N*-aryl acrylamides followed by migratory insertion of an isocyanide-coordinated $C(sp^3)$ -Pd intermediate afforded an alkylimidoyl-Pd^{II} complex, which can be intercepted by a nucleophile, including heteroarenes. In addition to amides, the alkylimidoyl-Pd^{II} complex was successfully converted into esters, ketones, and bis-heterocyclic compounds. An unprecedented palladium-catalyzed enantioselective domino process involving isocyanide was also documented.

The carbene-like reactivity of the isocyano group has been extensively exploited in the development of multicomponent reactions,^[1] insertion reactions,^[2] and polymerization processes.^[3] Being isoelectronic with carbon monoxide (CO),^[4] isocyanides have recently emerged as a valuable C_1 building block in palladium-catalyzed imidoylative/carbonylative coupling reactions.^[5] The added advantages of isocyanide relative to CO in such transformations reside on its easy handling, modular reactivity, and ability to bring molecular diversity by its organic residue. Until now, most of the reported imidoylative processes involved a $C(sp^2)$ -Pd^{II} intermediate generated in situ by oxidative addition of palladium to an aryl/vinyl halide (Scheme 1a). Reactions involving migratory insertion of isocyanide to $C(sp^3)$ -Pd^{II} complexes remain unexploited.^[6] In contrast, while the coordinating ability of isocyanide to transition metals has been well appreciated in organometallic chemistry,^[7] this property also renders the development of isocyanide-based enantioselective transformations difficult. To the best of our knowledge, only one single example has been reported from the group of Hayashi.^[8]

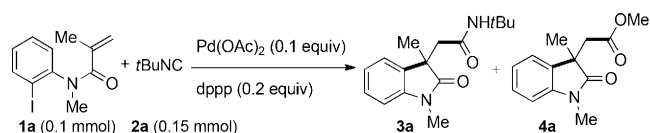
In connection with our interest in palladium-catalyzed domino processes^[9] and isocyanide chemistry,^[10] we envisaged that an intramolecular carbopalladation of alkenes followed by migratory insertion of the resulting isocyanide-coordinated $C(sp^3)$ -Pd^{II} complex **A** might be an attractive way to form an alkylimidoyl-Pd^{II} species which could be converted into a diversely functionalized oxindoles (Scheme 1b).^[11] We report herein that palladium-catalyzed reactions of *N*-aryl-acrylamides (**1**) with isocyanides (**2**) took place smoothly to afford a diverse set of 3,3-disubstituted oxindoles (**3–6**) incorporating an amide, an ester, a ketone, and a benzoxazole

a) Isocyanide insertion to $C(sp^2)$ -Pd^{II} complexb) This work: Domino carbopalladation and isocyanide insertion to $C(sp^3)$ -Pd^{II} complex for the synthesis of diversely functionalized oxindoles

Scheme 1. Palladium-catalyzed isocyanide insertion processes.

unit. We also document an unprecedented asymmetric carbopalladation/isocyanide insertion/methoxylation process for the synthesis of enantioenriched imidates (**7**).

The reaction between *N*-(2-iodophenyl)-*N*-methyl methacrylamide (**1a**) and *t*BuNC (**2a**) was examined in the presence of a catalytic amount of Pd(OAc)₂ and dppp (Scheme 2; see the Supporting Information for a survey of reaction conditions). When the reaction was performed in toluene/H₂O in the presence of Cs₂CO₃, the expected amide **3a** was formed in about 15 % yield.^[12] After having screened different bases and solvents, we were able to obtain the 3,3-disubstituted oxindole **3a** in 90 % yield upon isolation by performing the reaction in toluene/MeOH at 100 °C in the presence of KOH (2.0 equiv). Interestingly, by simply changing the solvent and the base [THF, NaOMe (3 equiv)], the same reaction afforded the ester **4a** in 72 % yield upon



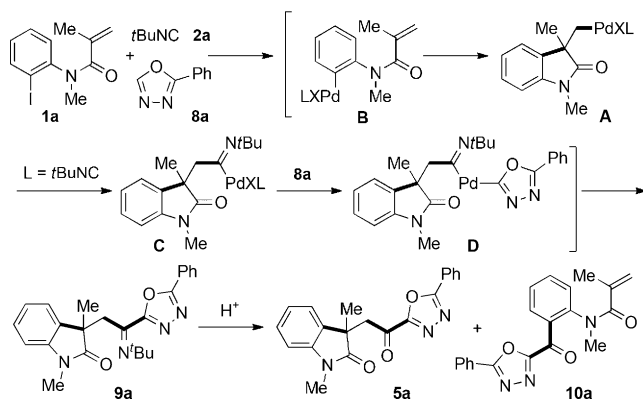
Scheme 2. Palladium-catalyzed reaction of the acetanilide **1a** with *t*BuNC (**2a**). Synthesis of the amide **3a** and ester **4a** by small changes in reaction conditions: KOH (2.0 equiv) in toluene/MeOH = 5:1 (2.0 mL) at 100 °C leads to **3a** in 90 % yield; and NaOMe (3.0 equiv) in THF (2.0 mL) at 100 °C leads to **4a** in 72 % yield. dppp = 1,3-bis(diphenylphosphanyl)propane.

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isolation. To the best of our knowledge, direct conversion of isocyanides into esters under imidoxylation conditions is unprecedented.

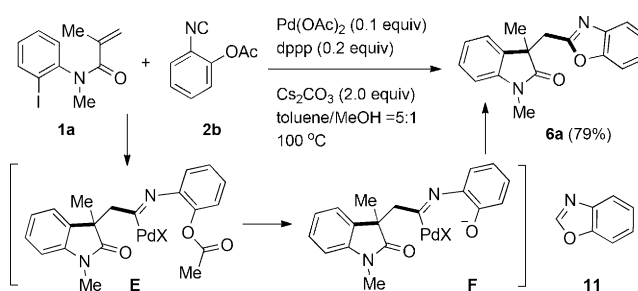
A three-component reaction of **1a**, **2a**, and 2-phenyl-1,3,4-oxadiazole (**8a**) was next investigated. The underlying principle is shown in Scheme 3. Oxidative addition of



Scheme 3. Three-component synthesis of ketone **5**. Optimized reaction conditions: **1a** (0.1 mmol), Pd(OAc)₂ (0.1 equiv), *t*BuDavePhos (0.2 equiv), 2-phenyl-1,3,4-oxadiazole (**8a**, 1.5 equiv), **2a** (2.0 equiv), Cs₂CO₃ (2.0 equiv), MeCN (2.0 mL), 110 °C; then HCl (1 N), RT, 2 h. *t*BuDavePhos = 2-Di-*tert*-butylphosphino-2'-(*N,N*-dimethylamino)-biphenyl.

isocyanide-ligated palladium(0) to aryl iodide would afford **B**, which upon intramolecular carbopalladation, would furnish the C(sp³)-Pd^{II} intermediate **A** (R = H, R¹ = R² = Me). Migratory insertion of isocyanide would provide the alkyl-imidoyl-Pd^{II} species **C** which was expected to activate, intermolecularly, the C–H bond of **8a** leading to **D**. Reductive elimination would afford **9a**,^[13] whose hydrolysis under acidic conditions would then furnish the ketone **5a**. Three C–C bonds would be created in this multicomponent reaction. After extensive screening of reaction conditions, the desired ketone **5a** was isolated in 72 % yield together with **10a** (12 %) by performing the reaction in MeCN in the presence of Pd(OAc)₂ (0.1 equiv), *t*Bu-Davephos (0.2 equiv), and Cs₂CO₃ (2.0 equiv) at 100 °C. The formation of **10a** could be accounted for by migratory insertion of isocyanide from **B** followed by direct imidoxylation of oxadiazole.^[14] It is interesting to note that the ligand plays a key role in the product distribution. Using dppp as ligand under otherwise identical reaction conditions, **5a** and **10a** were formed in a one to one ratio (for details, see Table S2 in the Supporting Information). The fact that direct arylation of the palladium(II) intermediates **A** (R = H, R¹ = R² = Me) and **B** by oxadiazole^[15,16] was not observed indicates that migratory insertion of isocyanide from these two complexes was a kinetically faster process. The high chemoselectivity observed is truly remarkable since neither the amide **3a** nor ester **4a** were isolated although methanol was used as a cosolvent.

Reaction of the functionalized isocyanide **2b** with **1a** afforded the bis(heterocyclic) compound **6a** in 79 % yield under optimized reaction conditions (Scheme 4; see Table S3).^[17] The domino process went presumably via the



Scheme 4. Synthesis of the oxindole-benzoxazole framework **6a**.

intermediate **E**, which, upon methanolysis, would afford the phenoxide **F**. Ligand exchange followed by reductive elimination would then provide the compound **6a** with concurrent regeneration of the palladium(0) catalyst. Alternatively, rapid hydrolysis of acetate followed by cyclization would convert **2b** into **11**, which can then be alkylated by **A** (R = H, R¹ = R² = Me) to give **6a**.^[18]

The scope and limitations of these new transformations were next examined and the results are shown in Table 1. Reaction of the *N*-benzyl acetanilide **1b** with *t*BuNC under four sets of reaction conditions afforded four different compounds, **3b**, **4b**, **5b**, and **6a** in good to excellent yields (entry 2). Since the *N*-benzyl group is readily removed, it constitutes a route to NH oxindoles. The introduction of an *n*-hexyl (**1c**), a methoxymethyl (**1d**), and a phenyl (**1e**) substituent at the C_α-position (R¹) of the acrylamide exerted only a minor effect on the reaction outcome (entries 3–5). Substrates bearing an electron-donating group (**1f–h**; entries 6–8) and an electron-withdrawing group (**1i**, **1j**; entries 9 and 10) on the aniline residue all underwent the domino process efficiently. Even the sterically encumbered C3-substituted aryl iodide **1h** participated in the reaction to provide the desired oxindoles in good yields (entry 8). *N*-(Naphthalen-2-yl)amide **1k** was converted to **3k**, **4k**, **5k** and **6k**, respectively, without event (entry 11). Finally, reaction of 1,1,3,3-tetramethylbutyl isocyanide with **1a** afforded **3l** and **4a** in yields of 85 and 62 %, respectively (for structure of **3l**, see the Supporting Information).

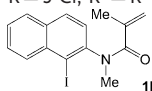
The development of a metal-catalyzed enantioselective isocyanide-based domino process remained exceptionally challenging. Indeed, coordination of isocyanide to the metal/chiral ligand complex could destroy or modify its chiral coordination sphere, hence the asymmetric induction. Our initial efforts on the enantioselective version of the aforementioned transformations using isocyanides **2a** and **2b** met with failure.^[19] Reasoning that bulky aryl isocyanides might diminish the adverse coordinative interaction of isocyanide with palladium, 2,6-dimethylphenyl isocyanide (**2c**) was chosen as a reaction partner (Scheme 5). Interestingly, the carboximidate **7ac** was isolated in 90 % yield under reaction conditions optimized for the formation of compound **6a** [**1a** (0.1 mmol), Pd(OAc)₂ (0.1 equiv), dppp (0.2 equiv), **2c** (2 equiv), Cs₂CO₃ (2 equiv), toluene/MeOH = 5:1 (2.0 mL), 100 °C].^[20] Furthermore, **7ac** was isolated in 58 % yield with an enantiomeric ratio (e.r.) of 62.5:37.5 when (*R*)-BINAP was used as a ligand (see Table S4–1).^[21] Addition of Ag₃PO₄ as

Table 1: Synthesis of diversely functionalized oxindoles.

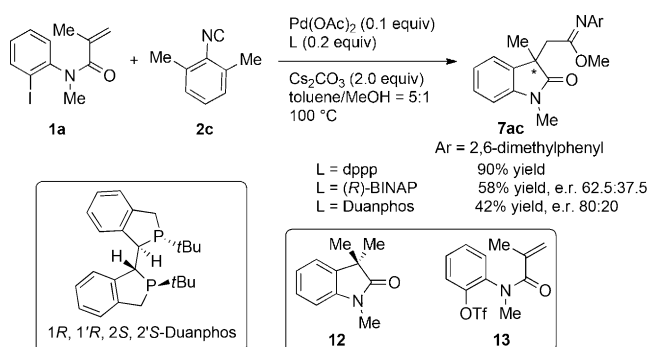
Reaction scheme showing the synthesis of oxindoles **3**, **4**, **5**, and **6** from starting material **1**.

Starting material **1** is a substituted oxindole derivative with substituents R , R^1 , and R^2 .

Path **a** leads to product **3** (NHtBu).
 Path **b** leads to product **4** (OMe).
 Path **c** leads to product **5** (N-phenyl oxadiazole).
 Path **d** leads to product **6** (N-phenyl oxadiazole).

Entry	1	Yield [%] ^[a]			
		3	4	5	6
1	R = H, R ¹ = R ² = Me (1a)	3a (90)	4a (71)	5a (72)	6a (79)
2	R = H, R ¹ = Me, R ² = Bn (1b)	3b (80)	4b (70)	5b (70)	6b (74)
3	R = H, R ¹ = <i>n</i> C ₆ H ₁₃ , R ² = Me (1c)	3c (71)	4c (78)	5c (64) ^[b]	6c (65)
4	R = H, R ¹ = CH ₂ OMe, R ² = Me (1d)	3d (51)	4d (60)	5d (68)	6d (64)
5	R = H, R ¹ = Ph, R ² = Me (1e)	3e (72)	4e (70)	5e (< 5)	6e (70)
6	R = 4- <i>t</i> Bu, R ¹ = R ² = Me (1f)	3f (83)	4f (66)	5f (62)	6f (78)
7	R = 4-OMe, R ¹ = R ² = Me (1g)	3g (72)	4g (70)	5g (74)	6g (78)
8	R = 3-Me, R ¹ = R ² = Me (1h)	3h (75)	4h (66)	5h (66)	6h (76)
9	R = 4-F, R ¹ = R ² = Me (1i)	3i (74)	4i (61)	5i (60)	6i (73)
10	R = 5-Cl, R ¹ = R ² = Me (1j)	3j (68)	4j (55)	5j (68)	6j (70)
11		3k (74)	4k (68)	5k (67)	6k (76)

Reaction conditions: a) **1** (0.1 mmol), Pd(OAc)₂ (0.1 equiv), dppp (0.2 equiv), **2a** (1.5 equiv), KOH (2.0 equiv), toluene/MeOH = 5:1 (1.8 mL), 100 °C. b) **1** (0.1 mmol), Pd(OAc)₂ (0.1 equiv), dppp (0.2 equiv), **2a** (1.5 equiv), NaOMe (5.4 mmol) in MeOH, 0.05 mL, THF (2.0 mL), 100 °C. c) **1** (0.1 mmol), Pd(OAc)₂ (0.1 equiv), *t*BuDavePhos (0.2 equiv), 2-phenyl-1,3,4-oxadiazole (**8a**, 1.5 equiv), **2a** (2.0 equiv), Cs₂CO₃ (2.0 equiv), MeCN (2.0 mL), 110 °C; then HCl (1 N), RT, 2 h. d) **1** (0.1 mmol), Pd(OAc)₂ (0.1 equiv), dppp (0.2 equiv), **2b** (2.0 equiv), Cs₂CO₃ (2.0 equiv), toluene/MeOH = 5:1 (1.8 mL), 100 °C. [a] Yield is that of the isolated product. [b] 2-(4-(trifluoromethoxy)phenyl)-1,3,4-oxadiazole was used instead of **8a**.

**Scheme 5.** Enantioselective domino process between **1a** and **2c**. BINAP = 2,2'-bis(diphenylphosphanyl)-1,1'-binaphthyl, Tf = trifluoromethanesulfonyl.

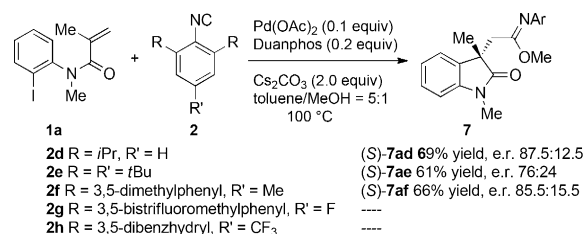
a halide scavenger provided 1,3,3-trimethylindolin-2-one (**12**) as a major product in 50 % yield. In line with this result, the aryl triflate **13** failed to afford the desired product.

Encouraged by this preliminary result, a wide range of chiral ligands was screened (Scheme 5; see Table S4–2). An electron-rich and conformationally rigid *P*-stereogenic bis(phospholane) ligand (1*R*,1'*R*,2*S*,2'*S*-Duanphos)^[22] proved to be the most effective in terms of enantioselectivity, thus

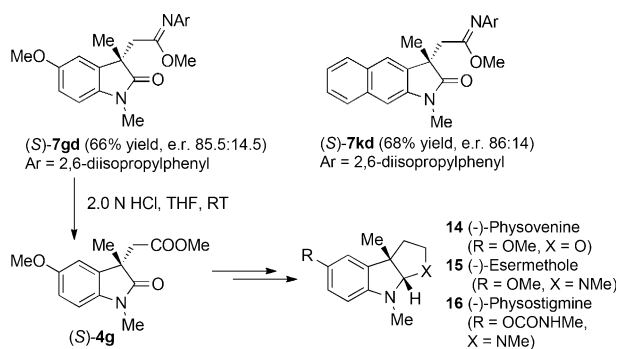
providing **7ac** with a promising e.r. value of 80:20. Aiming at further increasing the enantioselectivity of the process, the structure of the aryl isocyanides was next examined (Scheme 6). Gratefully, using the sterically more demanding 2,6-diisopropylphenyl isocyanide (**2d**), the desired product **7ad** was isolated in 69 % yield with an e.r. value of 87.5:12.5. A similar result was obtained with 2,6-di(3,5-dimethylphenyl)-6-methylphenyl isocyanide (**2f**). However, enantioselectivity was reduced with the bulkier isocyanide **2e**. By using electron-deficient isocyanides **2g** (R' = F) and **2h** (R' = CF₃), only the reduced product **12** was isolated in yields of 50 and 52 %, respectively.

Applying this enantioselective domino imido-ylative Heck reaction to **1g** and **1k** led to the formation of the corresponding oxindoles (*S*)-**7gd** and (*S*)-**7kd** with e.r. values of 85.5:14.5 and 86:14, respectively (Scheme 7). Hydrolysis of (*S*)-**7gd** under acidic conditions (2.0 N HCl, THF, RT) afforded the ester **4g** whose absolute configuration was determined to be *S* by comparison of its optical rotation value with that reported in the literature.^[23] (*S*)-**4g** is a known precursor of (–)-physovenine (**14**), (–)-esermethole (**15**), and (–)-physostigmine (**16**).^[23] We note that previous efforts on the palladium-catalyzed carbonylative Heck reaction of **1a** with CO afforded **4** with an e.r. value of 64:36.^[24]

In conclusion, we have developed a series of palladium-catalyzed domino processes involving migratory insertion of isocyanide to the C(sp³)–

**Scheme 6.** Effect of isocyanide structure on the enantioselectivity of the domino process.

Pd^{II} complex generated by an intramolecular carbopalladation reaction. Depending on the reaction conditions, the reaction can be tuned to generate either the amides **3** or esters **4**.^[25] In addition, a three-component reaction involving a key intermolecular direct arylation of an alkylimido-yl-Pd^{II} complex was documented for the first time^[26] and a cyclizative heterocoupling reaction^[27] leading to the indolinone-benzoxazole framework was achieved using a functionalized isocyanide (**2b**). An enantioselective domino carbopalladation/isocyanide insertion/methoxylation has been developed. Efforts are ongoing to decipher factors controlling the enantioselectivity of transition metal catalyzed processes involving isocyanide as a substrate, a still unsolved problem in asymmetric catalysis.



Scheme 7. Application of enantioselective imidoxylation Heck process. THF = tetrahydrofuran.

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Keywords: asymmetric synthesis · heterocycles · multicomponent reactions · palladium · synthetic methods

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- [1] *Multicomponent Reactions in Organic Synthesis* (Eds.: J. Zhu, Q. Wang, M.-X. Wang), Wiley-VCH, Weinheim, **2015**.
- [2] For reviews, see: a) A. V. Lygin, A. de Meijere, *Angew. Chem. Int. Ed.* **2010**, *49*, 9094; *Angew. Chem.* **2010**, *122*, 9280; b) M. Tobisu, N. Chatani, *Chem. Lett.* **2011**, *40*, 330.
- [3] M. Sugimoto, Y. Ito, *Adv. Polym. Sci.* **2004**, *171*, 77.
- [4] A. Brennfürer, H. Neumann, M. Beller, *Angew. Chem. Int. Ed.* **2009**, *48*, 4114; *Angew. Chem.* **2009**, *121*, 4176.
- [5] a) T. Vlaar, E. Ruijter, B. W. Maes, R. V. A. Orru, *Angew. Chem. Int. Ed.* **2013**, *52*, 7084; *Angew. Chem.* **2013**, *125*, 7222; b) S. Lang, *Chem. Soc. Rev.* **2013**, *42*, 4867; c) G. Qiu, Q. Ding, J. Wu, *Chem. Soc. Rev.* **2013**, *42*, 5257.
- [6] a) H. Jiang, H. Gao, B. Liu, W. Wu, *Chem. Commun.* **2014**, *50*, 15348; b) J. Wang, S. Luo, J. Huang, T. Mao, Q. Zhu, *Chem. Eur. J.* **2014**, *20*, 11220.
- [7] R. A. Michelin, A. J. L. Pombeiro, M. F. C. Guedes da Silva, *Coord. Chem. Rev.* **2001**, *218*, 75.
- [8] S. Park, R. Shintani, T. Hayashi, *Chem. Lett.* **2009**, *38*, 204.
- [9] a) T. Piou, L. Neuville, J. Zhu, *Angew. Chem. Int. Ed.* **2012**, *51*, 11561; *Angew. Chem.* **2012**, *124*, 11729; b) T. Piou, A. Bunescu, Q. Wang, L. Neuville, J. Zhu, *Angew. Chem. Int. Ed.* **2013**, *52*, 12385–12389; *Angew. Chem.* **2013**, *125*, 12611–12615.
- [10] a) Y. Odabachian, Q. Wang, J. Zhu, *Chem. Eur. J.* **2013**, *19*, 12229; b) Y. Odabachian, S. Tong, Q. Wang, M.-X. Wang, J. Zhu, *Angew. Chem. Int. Ed.* **2013**, *52*, 10878; *Angew. Chem.* **2013**, *125*, 11078; c) T. Buyck, Q. Wang, J. Zhu, *Angew. Chem. Int. Ed.* **2013**, *52*, 12714; *Angew. Chem.* **2013**, *125*, 12946; d) T. Buyck, Q. Wang, J. Zhu, *J. Am. Chem. Soc.* **2014**, *136*, 11524; e) S. Tong, Q. Wang, M.-X. Wang, J. Zhu, *Angew. Chem. Int. Ed.* **2015**, *54*, 1293; *Angew. Chem.* **2015**, *127*, 1309; f) For an account of our earlier work, see: J. Zhu, *Eur. J. Org. Chem.* **2003**, 1133.
- [11] For selected examples of oxindole synthesis, see: a) R. Grigg, I. Köppen, M. Rasparini, V. Sridharan, *Chem. Commun.* **2001**, 964; b) R. Yanada, S. Obika, T. Inokuma, K. Yanada, M. Yamashita, S. Ohta, Y. Takemoto, *J. Org. Chem.* **2005**, *70*, 6972; c) O. René, D. Lapointe, K. Fagnou, *Org. Lett.* **2009**, *11*, 4560; d) M. Bararjanian, S. Balalaie, F. Rominger, B. Movassagh, H. R. Bijanzadeh, *J. Org. Chem.* **2010**, *75*, 2806; e) S. Jaegli, J. Dufour, H. Wei, T. Piou, X. Duan, J. P. Vors, L. Neuville, J. Zhu, *Org. Lett.* **2010**, *12*, 4498; f) S. Jaegli, W. Erb, P. Retailleau, J. P. Vors, L. Neuville, J. Zhu, *Chem. Eur. J.* **2010**, *16*, 5863; g) S. Jaegli, J. P. Vors, L. Neuville, J. Zhu, *Tetrahedron* **2010**, *66*, 8911; h) G. R. Dong, S. Park, D. Lee, K. J. Shin, J. H. Seo, *Synlett* **2013**, 1993; i) X. Liu, X. Ma, Y. Huang, Z. Gu, *Org. Lett.* **2013**, *15*, 4814; j) J. Fan, W. Wei, M. Zhou, R. Song, J.-H. Li, *Angew. Chem. Int. Ed.* **2014**, *53*, 6650; *Angew. Chem.* **2014**, *126*, 6768; k) M.-B. Zhou, X.-C. Huang, Y.-Y. Liu, R.-J. Song, J.-H. Li, *Chem. Eur. J.* **2014**, *20*, 1843; l) D. D. Vachhani, H. H. Butani, N. Sharma, U. C. Bhoja, A. K. Shah, E. V. Van der Eycken, *Chem. Commun.* **2015**, *51*, 14862; For recent reviews, see: m) J. E. M. N. Klein, R. J. K. Taylor, *Eur. J. Org. Chem.* **2011**, 6821; n) “C-H Activations in Domino Processes”: G. C. Tsui, M. Lautens in *Domino Reactions* (Ed.: L. F. Tietze), Wiley-VCH, Weinheim, **2014**, p. 67; o) R.-J. Song, Y. Liu, Y.-X. Xie, J.-H. Li, *Synthesis* **2015**, *47*, 1195.
- [12] Imidoxylation of C(sp²)–Pd^{II} complexes leading to amides, see: a) H. Jiang, B. Liu, Y. Li, A. Wang, H. Huang, *Org. Lett.* **2001**, *3*, 1028; b) J. Peng, L. Liu, Z. Hu, J. Huang, Q. Zhu, *Chem. Commun.* **2012**, *48*, 3772; c) G. Qiu, C. Chen, L. Yao, J. Wu, *Adv. Synth. Catal.* **2013**, *355*, 1579; d) Z. Hu, D. Liang, J. Zhao, J. Huang, Q. Zhu, *Chem. Commun.* **2012**, *48*, 7371; e) G. Qiu, X. Qiu, J. Liu, J. Wu, *Adv. Synth. Catal.* **2013**, *355*, 2441; f) U. M. V. Basavanag, A. D. Santos, L. E. Kaim, R. Gámez-Montaño, L. Grimaud, *Angew. Chem. Int. Ed.* **2013**, *52*, 7194; *Angew. Chem.* **2013**, *125*, 7335; g) Z. Xia, Q. Zhu, *Org. Lett.* **2013**, *15*, 4110; h) N. Thirupathi, M. H. Babu, V. Dwivedi, R. Kant, M. S. Reddy, *Org. Lett.* **2014**, *16*, 2908.
- [13] a) M. Tobisu, S. Imoto, S. Ito, N. Chatani, *J. Org. Chem.* **2010**, *75*, 4835; b) Y.-J. Liu, H. Xu, W.-J. Kong, M. Shang, H.-X. Dai, J.-Q. Yu, *Nature* **2014**, *515*, 389; c) K. Takamatsu, K. Hirano, M. Miura, *Org. Lett.* **2015**, *17*, 4066; d) W.-J. Kong, Y.-J. Liu, H. Xu, Y.-Q. Chen, H.-X. Dai, J.-Q. Yu, *J. Am. Chem. Soc.* **2016**, *138*, 2146; See also: e) J. Zhao, D. Yue, M. A. Campo, R. C. Larock, *J. Am. Chem. Soc.* **2007**, *129*, 5288.
- [14] U. K. Sharma, N. Sharma, J. Xu, G. Song, E. V. Van der Eycken, *Chem. Eur. J.* **2015**, *21*, 4908.
- [15] W. Kong, Q. Wang, J. Zhu, *J. Am. Chem. Soc.* **2015**, *137*, 16028.
- [16] U. K. Sharma, N. Sharma, Y. Kumar, B. C. Singh, E. V. Van der Eycken, *Chem. Eur. J.* **2016**, *22*, 481.
- [17] For related examples, see: a) P. J. Boissarie, Z. E. Hamilton, S. Lang, J. A. Murphy, C. J. Suckling, *Org. Lett.* **2011**, *13*, 6256; b) J. V. Geden, A. K. Pancholi, M. Shipman, *J. Org. Chem.* **2013**, *78*, 4158.
- [18] We thank referee for this suggestion. The following control experiments have been performed: a) treatment of **2b** under our reaction conditions for 2 h afforded the corresponding benzoxazole **11** in 88 % yield; b) reaction of **1a** with **11** under standard conditions provided **6a**, albeit in only 30 % yield; c) reaction of **1a** with **11** using *t*BuOLi as a base under otherwise identical conditions furnished **6a** in 86 % yield. Therefore, we assumed that both pathways might be operational. For details, see the Supporting Information.
- [19] Enantioselective domino processes involving carbopalladation followed by intermolecular nucleophilic trapping of the resulting C(sp³)–Pd complex remain rare. See: a) P. Diaz, F. Gendreau, L. Stella, B. Charpentier, *Tetrahedron* **1998**, *54*, 4579; b) A. Minatti, X. Zheng, S. L. Buchwald, *J. Org. Chem.* **2007**, *72*, 9253; c) A. Pinto, Y. Jia, L. Neuville, J. Zhu, *Chem. Eur. J.* **2007**, *13*, 961; d) Y. Yasui, H. Kamisaki, Y. Takemoto, *Org. Lett.* **2008**, *10*, 3303; e) G. Yue, K. Lei, H. Hirao, J. Zhou, *Angew. Chem. Int. Ed.* **2015**, *54*, 6531; *Angew. Chem.* **2015**, *127*, 6631; f) C. Shen, R. Liu, R. Fan, Y. Li, T. Xu, J. Gao, Y. Jia, *J. Am. Chem. Soc.* **2015**, *137*, 4936, and ref. 15.

- [20] Imidate formation from aryl/vinyl halides: a) M. Kosugi, T. Ogata, H. Tamura, H. Sano, T. Migita, *Chem. Lett.* **1986**, 1197; b) C. G. Saluste, R. J. Whitby, M. Furber, *Tetrahedron Lett.* **2001**, 42, 6191; c) K. K. R. Tetala, R. J. Whitby, M. E. Light, M. B. Hurtshouse, *Tetrahedron Lett.* **2004**, 45, 6991; d) C. G. Saluste, S. Crumpler, M. Furber, R. J. Whitby, *Tetrahedron Lett.* **2004**, 45, 6995; e) X. Fei, Z. Ge, T. Tang, Y. Zhu, S. Ji, *J. Org. Chem.* **2012**, 77, 10321.
- [21] a) A. Steven, L. E. Overman, *Angew. Chem. Int. Ed.* **2007**, 46, 5488; *Angew. Chem.* **2007**, 119, 5584; b) M. A. Schmidt, M. Movassaghi, *Synlett* **2008**, 313; c) A. B. Dounay, L. E. Overman, *Chem. Rev.* **2003**, 103, 2945; d) M. Shibasaki, E. M. Vogl, T. Ohshima, *Adv. Synth. Catal.* **2004**, 346, 1533; e) D. M. Cartney, P. Guiry, *Chem. Soc. Rev.* **2011**, 40, 5122.
- [22] D. Liu, X. Zhang, *Eur. J. Org. Chem.* **2005**, 646.
- [23] Q. Yu, W. Luo, Y. Li, A. Brossi, *Heterocycles* **1993**, 36, 1279.
- [24] T. Matsuura, L. E. Overman, D. J. Poon, *J. Am. Chem. Soc.* **1998**, 120, 6500. See the note (as ref. [27]) and SI of this article.
- [25] Using CO as a C1 building block for the synthesis of related esters and amides have been reported with similar catalyst loading. See for example: a) R. Grigg, V. Sridharan, *Tetrahedron Lett.* **1993**, 34, 7471; b) P. Evans, R. Grigg, M. I. Ramzan, V. Sridharan, M. York, *Tetrahedron Lett.* **1999**, 40, 3021; To the best of our knowledge, only tertiary amides were accessible by this method. Therefore, our imidoylative approach leading to secondary amides is complementary to the known protocols in this regard.
- [26] The same reaction using CO as a C₁ synthon is, to the best of our knowledge, unknown. The compound **5** was not formed when the reaction was performed using CO (1 atm) instead of *t*BuNC under otherwise identical reaction conditions. The direct C-arylation product was isolated instead. For details, see the Supporting Information. We thank referee for suggesting this experiment.
- [27] a) B. Yao, Q. Wang, J. Zhu, *Angew. Chem. Int. Ed.* **2013**, 52, 12992; *Angew. Chem.* **2013**, 125, 13230; b) B. Yao, Q. Wang, J. Zhu, *Chem. Eur. J.* **2015**, 21, 7413.

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