A Pd-Catalyzed Cascade Protocol towards 2-Alkyl-4-aryl-4*H*-benz[1,4]oxazin-3-ones from Aryl Amines and 2-(2-Halophenoxy)alkanoates

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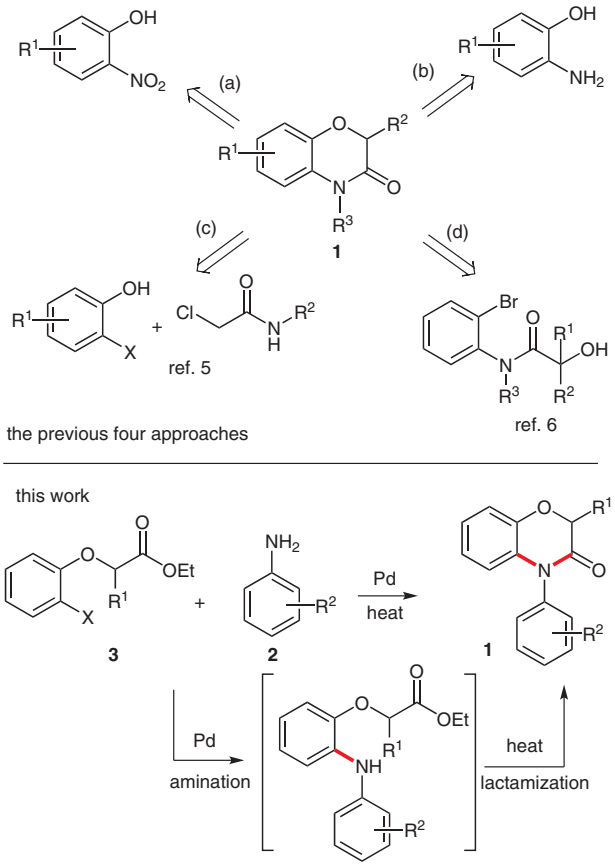
Abstract: A cascade process, consisting of Pd-catalyzed intermolecular amination and subsequent thermal intramolecular amidation, has been established for efficient one-pot synthesis of 4*H*-benz[1,4]oxazin-3-ones from anilines and 2-(2-halophenoxy)alkanoates. Use of Cs_2CO_3 as the base was found to be determinant for the process and alkyl groups attached to the α position of alkanoates are beneficial for achieving good yields. Various substrates were compatible to afford the desired products in good to excellent yields. It is an attractive process for synthesizing a library of 4*H*-benz[1,4]oxazin-3-ones.

Key words: cascade reaction, palladium catalysis, amination, 4*H*-benz[1,4]oxazin-3-ones, lactamization

A great deal of naturally occurring and synthetic derivates of 4*H*-benz[1,4]oxazin-3-one **1** exhibit potent biological and medicinal activities,[1] thus its synthesis has attracted the attention of synthetic chemists.[2] So far, four novel strategies have been developed for their preparation[2–6] (Scheme 1): (a) O-alkylation of 2-nitrophenols, followed by nitro group reduction and spontaneous annulation;[3] (b) regioselective N-acylation of 2-aminophenols with 2-haloalkanoyl chlorides or bromides, followed by intramolecular O-alkylation;[4] (c) intermolecular O-alkylation and Cu-catalyzed intramolecular amidation sequence from 2-halophenols and 2-halo amides;[5] and (d) a simple Pd-catalyzed intramolecular O-arylation of the corresponding precursor.[6] From the synthetic points of view, these methods are inconvenient for the synthesis of 4*H*-benz[1,4]-oxazin-3-ones, as stepwise synthetic sequences were adopted. Therefore, the development of an alternative or an improved procedure towards this heterocycle is still in demand.

Palladium catalysis plays an important role in organic synthesis. A variety of fundamental transformations, such as hydrogenation of multiple bonds,[7] cross-coupling reactions,[8] heteroatoms (N, O, S) arylations,[9] C–H bond functionalizations[10] and so on,[11] rely heavily on palladium species. Recently, much attention has been paid to the palladium-catalyzed cascade process for efficient synthesis of heterocycles.[12]

The development of cascade process for efficient synthesis of biologically active heterocycles via Pd-catalysis is our ongoing interest. We envisaged that 4*H*-benz[1,4]oxazin-3-one scaffold might be efficiently constructed from 2-(2-halophenoxy)alkanoates **3** and anilines **2** in the presence of Pd catalyst through a sequence of intermolecular amination and spontaneous lactamization under heating (Scheme 1). Although the tandem process seems feasible, there are two unique challenges: (1) the oxidative addition in the amination step may be difficult due to alkoxy group at the *ortho* position of the aryl bromide; and (2) the lactamization of the *N*-arylaniline product may be hampered when R^2 is an electron-withdrawing group, which can reduce the nucleophilicity of nitrogen atom. Herein, we report our original investigations on the Pd-catalyzed cascade process, consisting of intermolecular amination and spontaneous lactamization, for efficient synthesis of 2-alkyl-4-aryl-4*H*-benz[1,4]oxazin-3-ones.



Scheme 1 Strategies for synthesis of 4*H*-benz[1,4]oxazin-3-ones

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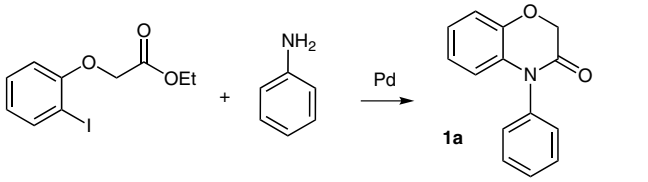
Ethyl 2-(2-iodophenoxy)acetate and aniline were used as the model substrates to optimize the reaction conditions in terms of catalyst,[13] ligand, base, temperature, and catalyst loading under N_2 atmosphere. Ethyl 2-(2-iodophenoxy)acetate was prepared in 95% yield by treating 2-iodophenol with ethyl 2-bromoacetate in the presence of K_2CO_3 at room temperature for three hours.[14,15] The results are summarized in Table 1. We used toluene as the solvent as it is less toxic and commonly employed in Pd-catalyzed N-arylation reactions. Also, the reaction temperature and time were set at 90 °C and 24 hours, respectively. Initially, the combination of $Pd(OAc)_2$ (10 mol%), BINAP (10 mol%), and K_2CO_3 (2.0 equiv) was tried, but no expected product was observed after heating the reaction mixture at 90 °C for 24 hours (entry 1). When *t*-BuONa was used as the base, the desired product was isolated in 28% yield, along with 68% conversion of the starting ethyl 2-(2-iodophenoxy)acetate (entry 2). Gratifyingly, the yield of 4-phenyl-4*H*-benz[1,4]oxazin-3-one (**1a**) was increased up to 96% and the starting ethyl 2-(2-iodophenoxy)acetate was consumed completely by employing Cs_2CO_3 as the base (entry 3). The above results indicate that the nature of base has great impact on the cascade process. Therefore, Cs_2CO_3 was selected as the base in the following optimizations. In an effort to find other efficient phosphine ligand for the present transformation, dppf, $P(Ph)_3$, XPhos, and Xantphos were screened (entries 4–7) and it was found that XPhos was as efficient as BINAP (95% vs. 96%). Subsequently, the effect of palladium source was investigated. It was found that $Pd_2(dba)_3$ was not a good choice of catalyst for this process, as only 40% yield and 77% conversion were observed (entry 8). On the other hand, $PdCl_2$ was found to be an effective precatalyst, which provided the desired product in 92% yield (entry 9). Finally, an effort for reducing the catalyst loading was attempted. However, when the loading of catalyst and ligand was reduced from 10 mol% to 5 mol%, the yield and conversion were decreased to 50% and 51%, respectively (entry 10). Meanwhile, we found that the yield could be increased to 78% by simply raising the reaction temperature to 110 °C (entry 11). Further enhancing the reaction temperature to 120 °C afforded the product in slightly higher yield (82% vs. 78%, entry 12).

With the optimized conditions in hand, the generality of the process was then investigated. Firstly, the reaction of ethyl 2-(2-iodophenoxy)acetate with various anilines was studied. As shown in Table 2, most of aryl amines examined provided the desired products in good to excellent yields. Anilines possessing methyl group at *ortho*, *meta*, or *para* positions provided the corresponding products in excellent yields. In particular, the highly bulky 2,6-dimethylaniline also afforded the expected product in 61% yield under the same conditions. Moreover, the reaction was compatible with anilines bearing both electron-donating and electron-withdrawing groups. For example, *para*- and *meta*-methoxyanlines exhibited high reactivity, furnishing **1f** and **1g** in 80% and 72% yields, respectively. Meanwhile, anilines bearing Cl, Br, CF_3, and COOEt groups also provided the products **1h–l** in good yields. In addition, the reaction of 4-trifluoromethoxyaniline and 1-naphthylamine with ethyl 2-(2-iodophenoxy)acetate provided the corresponding products in 88% and 68% yields, respectively. On comparing the yield of **1b** with **1c**, or **1i** with **1j**, it is obvious that *ortho*-substituted anilines show some steric effect, resulting in ca. 10% lower yield than their *para* counterpart.

Subsequently, we investigated the reaction of ethyl 2-(2-bromophenoxy)acetate with aromatic amines under the same conditions. According to the data in Table 2, we can conclude that the yields obtained from the bromides were much lower than those of the iodides (**1b**, **1d**, and **1m**), except for one case that produced 4-phenyl-4*H*-benz[1,4]oxazin-3-one (**1a**) in the comparable yield of 91%. These results indicate that bromides exhibited lower reactivity, which was consistent with the reported reactivity order. It is noteworthy that when the more challenging 2-(2-chlorophenoxy)acetate was employed, 4-phenyl-4*H*-benz-

Table 1 Optimization for the Synthesis of 4-Phenyl-4*H*-benz[1,4]oxazin-3-ones[a]

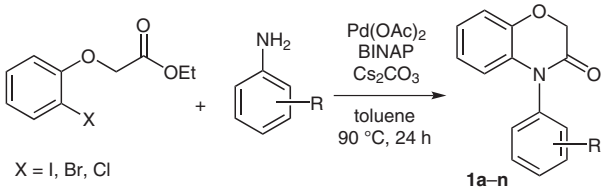


Entry	Catalyst, ligand,[c] base	Temp (°C)	Conv. (%)[d]	Yield (%)[e]
1	$Pd(OAc)_2$, BINAP, K_2CO_3	90	–	0
2	$Pd(OAc)_2$, BINAP, *t*-BuONa	90	68	28
3	$Pd(OAc)_2$, BINAP, Cs_2CO_3	90	100	96
4	$Pd(OAc)_2$, dppf, Cs_2CO_3	90	48	46
5	$Pd(OAc)_2$, Ph_3P, Cs_2CO_3	90	–	trace
6	$Pd(OAc)_2$, Xphos, Cs_2CO_3	90	100	95
7	$Pd(OAc)_2$, Xantphos, Cs_2CO_3	90	85	73
8	$Pd_2(dba)_3$, BINAP, Cs_2CO_3	90	77	40
9	$PdCl_2$, BINAP, Cs_2CO_3	90	100	92
10[b]	$Pd(OAc)_2$, BINAP, Cs_2CO_3	90	51	50
11[b]	$Pd(OAc)_2$, BINAP, Cs_2CO_3	110	–	78
12[b]	$Pd(OAc)_2$, BINAP, Cs_2CO_3	120	90	82

[a] Reaction conditions: ethyl 2-(2-iodophenoxy)acetate (1.0 equiv), catalyst (10 mol%), ligand (10 mol%), base (2.0 equiv), aniline (1.5 equiv), toluene (0.1 M), 90 °C, 24 h. All reactions were carried out in a sealed vial.
[b] The loadings of $Pd(OAc)_2$ and BINAP were 5 mol% and 5 mol%, respectively. The reaction time was 24 h.
[c] Racemic BINAP was used.
[d] The conversion was calculated based on the recovered ethyl 2-(2-iodophenoxy)acetate.
[e] Isolated yield.

[1,4]oxazin-3-one (**1a**) could be obtained in 45% yield due to the incompletion of the reaction.

Table 2 Synthesis of 4-Aryl-4*H*-benz[1,4]oxazin-3-ones from 2-(2-Halophenoxy)acetates and Aryl Amines via Pd-Catalyzed Cascade Process[a]



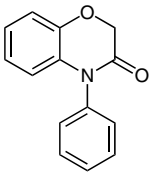
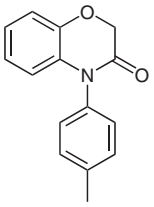
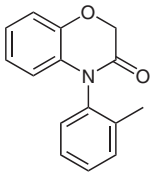
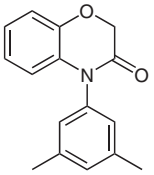
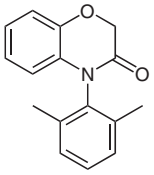
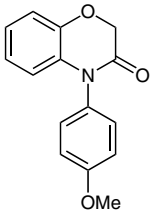
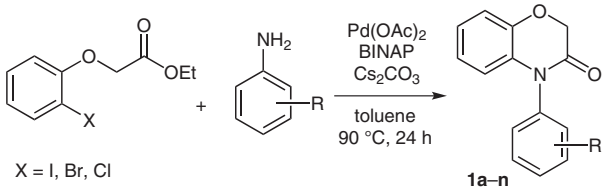
Entry	Product	Yield
1	 **1a**	X = I (96%) X = Br (91%) X = Cl (45%)
2	 **1b**	X = I (94%) X = Br (63%)
3	 **1c**	X = I (84%)
4	 **1d**	X = I (93%) X = Br (58%)
5	 **1e**	X = I (61%)
6	 **1f**	X = I (80%)

Table 2 Synthesis of 4-Aryl-4*H*-benz[1,4]oxazin-3-ones from 2-(2-Halophenoxy)acetates and Aryl Amines via Pd-Catalyzed Cascade Process[a] (continued)



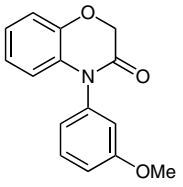
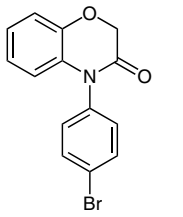
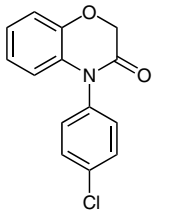
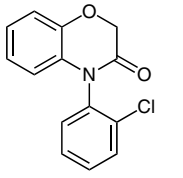
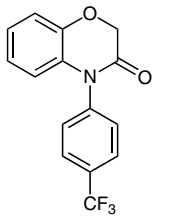
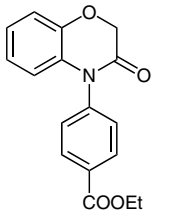
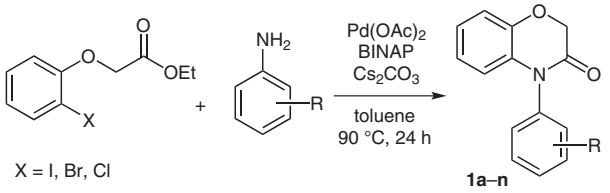
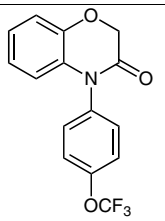
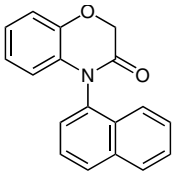
Entry	Product	Yield
7	 **1g**	X = I (72%)
8	 **1h**	X = I (68%)
9	 **1i**	X = I (75%)
10	 **1j**	X = I (63%)
11	 **1k**	X = I (85%)
12	 **1l**	X = I (79%)

Table 2 Synthesis of 4-Aryl-4*H*-benz[1,4]oxazin-3-ones from 2-(2-Halophenoxy)acetates and Aryl Amines via Pd-Catalyzed Cascade Process[a] (continued)



Entry	Product	Yield
13	 **1m**	X = I (88%) X = Br (75%)
14	 **1n**	X = I (68%)

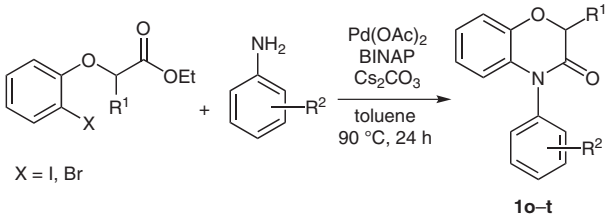
[a] Reaction conditions: ethyl 2-(2-halophenoxy)acetate (1.0 equiv), $Pd(OAc)_2$ (10 mol%), (±)BINAP (10 mol%), Cs_2CO_3 (2.0 equiv), amine (1.5 equiv), toluene (0.1 M), 90 °C, 24 h. All reactions were carried out in a sealed vial.

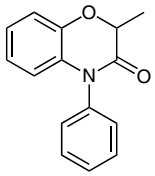
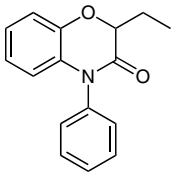
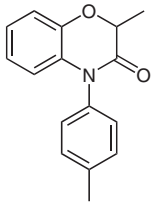
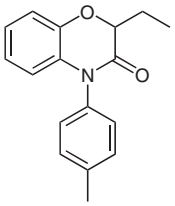
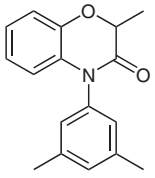
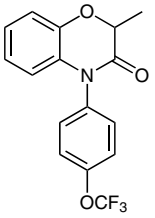
Finally, the influence of substitutions at the α position of 2-(2-halophenoxy)alkanoates was evaluated and the results are listed in Table 3. Gratifyingly, it was found that alkyl groups (R^1 = Et and Me) were beneficial for the process, affording the products in excellent yields; even less reactive 2-(2-bromophenoxy)alkanoates could be employed. Interestingly, with these alkyl groups in substrates, the yields of 2-(2-bromophenoxy)alkanoates were comparable with those of the corresponding aryl iodides.

In summary, we have established a novel cascade protocol,[16] consisting of Pd-catalyzed intermolecular amination and spontaneous cyclization, for efficient synthesis of 4*H*-benz[1,4]oxazin-3-ones from readily available starting materials. It was found that Cs_2CO_3 used as the base is crucial for the transformation and alkyl groups at α-position of ethyl 2-(2-halophenoxy)alkanoates is beneficial for achieving high yields. The process developed shows good generality, thus it is quite attractive for efficient synthesis of a library of 4*H*-benz[1,4]oxazin-3-ones. It should be useful in pharmaceutical and biochemical field.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synlett.

Table 3 Synthesis of 2-Alkyl-4-aryl-4*H*-benz[1,4]oxazin-3-ones via Pd-Catalyzed Cascade Process[a]



Entry	Product	Yield
1	 **1o**	X = I (90%) X = Br (96%)
2	 **1p**	X = I (84%) X = Br (83%)
3	 **1q**	X = Br (72%)
4	 **1r**	X = Br (96%)
5	 **1s**	X = Br (92%)
6	 **1t**	X = Br (90%)

[a] Reaction conditions: ethyl 2-(2-halophenoxy)acetate (1.0 equiv), $Pd(OAc)_2$ (10 mol%), (±)BINAP (10 mol%), Cs_2CO_3 (2.0 equiv), amine (1.5 equiv), toluene (0.1 M), 90 °C, 24 h. All reactions were carried out in a sealed vial.

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References and Notes

(1) For selected examples, see: (a) Minami, Y.; Yoshida, K.; Azuma, R.; Saeki, M.; Otani, T. *Tetrahedron Lett.* **1993**, *34*, 2633. (b) Dudley, D. A.; Bunker, A. M.; Chi, L.; Cody, W. L.; Holland, D. R.; Ignasiak, D. P.; Janiczek-Dolphin, N.; McClanahan, T. B.; Mertz, T. E.; Narasimhan, L. S.; Rapundalo, S. T.; Trautschold, J. A.; Van Huis, C. A.; Edmunds, J. J. *J. Med. Chem.* **2000**, *43*, 4063. (c) Caliendo, G.; Perissutti, E.; Santagada, V.; Fiorino, F.; Severino, B.; d'Emmanuele di Villa Bianca, R.; Lippolis, L.; Pinto, A.; Sorrentino, R. *Bioorg. Med. Chem.* **2002**, *10*, 2663. (d) Rybczynski, P. J.; Zeck, R. E.; Dudash, J.; Comb, D. W.; Burris, T. P.; Yang, M.; Osborne, M. C.; Chen, X.; Demarest, K. T. *J. Med. Chem.* **2004**, *47*, 196. (e) Matsuoka, H.; Ohi, N.; Mihara, M.; Suzuki, H.; Miyamoto, K.; Maruyama, N.; Tsuji, K.; Kato, N.; Akimoto, T.; Takeda, Y.; Yano, K.; Kuroki, T. *J. Med. Chem.* **1997**, *40*, 105 . For recent reviews, see: (f) Sebille, S.; de Tullio, P.; Boverie, S.; Antoine, M. H.; Lebrun, P.; Pirotte, B. *Curr. Med. Chem.* **2004**, *11*, 1213. (g) Macias, F. A.; Marin, D.; Oliveros-Bastidas, A.; Molinillo, J. M. G. *Nat. Prod. Rep.* **2009**, *26*, 478.

(2) For recent reviews, see: (a) Ilaš, J.; Anderluh, P. S.; Dolenc, M. S.; Kikelj, D. *Tetrahedron* **2005**, *61*, 7325. (b) Achari, B.; Mandal, S. B.; Dutta, P. K.; Chowdhury, K. *Synlett* **2004**, 2449 . For selected examples, see: (c) Feng, G.; Wu, J.; Dai, W.-M. *Tetrahedron* **2006**, *62*, 4635. (d) Hashimoto, Y.; Ishizaki, T.; Shudo, K. *Tetrahedron* **1991**, *47*, 1837. (e) Wu, J.; Nie, L.; Luo, J.; Dai, W.-M. *Synlett* **2007**, 2728. (f) Xing, X.; Wu, J.; Feng, G.; Dai, W.-M. *Tetrahedron* **2006**, *62*, 6774. (g) Dai, W.-M.; Wang, X.; Ma, C. *Tetrahedron* **2005**, *61*, 6879. (h) Feng, G.; Wu, J.; Dai, W.-M. *Tetrahedron Lett.* **2007**, *48*, 401. (i) Yuan, Y.; Liu, G.; Li, L.; Wang, Z.; Wang, L. *J. Comb. Chem.* **2007**, *9*, 158. (j) Rybczynski, P. J.; Zeck, R. E.; Combs, D. W.; Turchi, I.; Burris, T. P.; Xu, J. Z.; Yang, M.; Demarest, K. T. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 235. (k) Matsumoto, Y.; Uchida, A.; Nakahara, H.; Yanagisawa, I.; Shibanuma, T.; Nohira, H. *Chem. Pharm. Bull.* **2000**, *48*, 428. (l) Banfi, L.; Basso, A.; Giardini, L.; Riva, R.; Rocca, V.; Guanti, G. *Eur. J. Org. Chem.* **2011**, 100. (m) Zuo, H.; Meng, L.; Ghate, M.; Hwang, K.-H.; Cho, Y. K.; Chandrasekhar, S.; Reddy, C. R.; Shi, D.-S. *Tetrahedron Lett.* **2008**, *49*, 3827.

(3) (a) Touzeau, F.; Arrault, A.; Guillaumet, G.; Scalbert, E.; Pfeiffer, B.; Rettori, M.; Renard, P.; Mérour, J.-Y. *J. Med. Chem.* **2003**, *46*, 1962. (b) Arrault, A.; Touzeau, F.; Guillaumet, G.; Léger, J.-M.; Jarry, C.; Mérour, J.-Y. *Tetrahedron* **2002**, *58*, 8145. (c) Ramesh, C.; Raju, B. R.; Kavala, V.; Kuo, C.-W.; Yao, C.-F. *Tetrahedron* **2011**, *67*, 1187. (d) For a solid-phase synthesis, see: Lee, C. L.; Chan, K. P.; Lam, Y.; Lee, S. Y. *Tetrahedron Lett.* **2001**, *42*, 1167.

(4) Caliendo, G.; Perissutti, E.; Santagada, V.; Fiorino, F.; Severino, B.; Cirillo, D.; d'Emmanuele di Villa Bianca, R.; Lippolis, L.; Pinto, A.; Sorrentino, R. *Eur. J. Med. Chem.* **2004**, *39*, 815.

(5) (a) Feng, E.; Huang, H.; Zhou, Y.; Ye, D.; Jiang, H.; Liu, H. *J. Org. Chem.* **2009**, *74*, 2846. (b) Chen, D.; Shen, G.; Bao, W. *Org. Biomol. Chem.* **2009**, *7*, 4067.

(6) Ylijoki, K. E. O.; Kundig, E. P. *Chem. Commun.* **2011**, *47*, 10608.

(7) For selected examples, see: (a) Okamoto, K.; Akiyama, R.; Kobayashi, S. *J. Org. Chem.* **2004**, *69*, 2871. (b) Wang, Y.-Q.; Lu, S.-M.; Zhou, Y.-G. *Org. Lett.* **2005**, *7*, 3235.

(8) For a recent example, see: Cheng, K.; Wang, C.; Ding, Y.; Song, Q.; Qi, C.; Zhang, X.-M. *J. Org. Chem.* **2011**, *76*, 9261.

(9) For recent examples, see: (a) Salvi, L.; Davis, N. R.; Ali, S. Z.; Buchwald, S. L. *Org. Lett.* **2012**, *14*, 170. (b) Ueda, S.; Su, M.; Buchwald, S. L. *J. Am. Chem. Soc.* **2011**, 133: DOI: 10.1021/ja2102373. (c) For a review on Pd-catalyzed C–N bond formation, see: Wolfe, J.; Wagaw, S.; Marcoux, J.-F.; Buchwald, S. L. *Acc. Chem. Res.* **1998**, *31*, 805.

(10) (a) For a recent example, see: Li, Z.; Zhang, Y.; Liu, Z.-Q. *Org. Lett.* **2012**, *14*, 74. (b) For a recent review on C–H functionalization via palladium catalysis, see: Engle, K. M.; Mei, T.-S.; Wasa, M.; Yu, J.-Q. *Acc. Chem. Res.* **2011**, DOI: 10.1021/ar200185g.

(11) For a very recent example of enantioselective Pd-catalyzed allylic alkylation of lactams, see: Behenna, D. C.; Liu, Y.; Yurino, T.; Kim, J.; White, D. E.; Virgil, S. C.; Stoltz, B. M. *Nature Chem.* **2011**, DOI:10.1038/nchem.1222.

(12) For selected examples, see: (a) Luo, Y.; Wu, J. *Chem. Commun.* **2011**, *47*, 11137. (b) Luo, Y.; Pan, X.; Wu, J. *Org. Lett.* **2011**, *13*, 1150. (c) Ren, H.; Luo, Y.; Ye, S.; Wu, J. *Org. Lett.* **2011**, *13*, 2552. (d) Luo, Y.; Wu, J. *Org. Lett.* **2011**, *13*, 5858. (e) Cao, J.; Xu, Y.; Kong, Y.; Gui, Y.; Hu, Z.; Wang, G.; Deng, Y.; Lai, G. *Org. Lett.* **2012**, *14*, 38.

(13) Initially, CuI was tried as the catalyst under various conditions, but only trace amount of **1a** was observed.

(14) Other 2-(2-halophenoxy)alkanoates used in this work were prepared in excellent yields (95–98%) under the similar conditions.

(15) For references on synthesis of 2-(2-halophenoxy)alkanoate **3**, see: (a) Lu, G.; Portscheller, J. L.; Malinakova, H. C. *Organometallics* **2005**, *24*, 945. (b) Sathisha, K. R.; Khanum, S. A.; Chandra, J. N.; Ayisha, F.; Balaji, S.; Marathe, G. K.; Gopal, S.; Rangappa, K. S. *Bioorg. Med. Chem.* **2011**, *19*, 211. (c) Portscheller, J. L.; Malinakova, H. C. *Org. Lett.* **2002**, *4*, 3679.

(16) **General Procedure for the Synthesis of 4*H*-Benz[1,4]oxazin-3-ones**: To a 10-mL pressurized process vial were added magnetic stir bar, $Pd(OAc)_2$ (6.8 mg, 0.03 mmol, 10 mol%), (±)-BINAP (18.7 mg, 0.03 mmol, 10 mol%), ethyl 2-(2-halophenoxy)alkanoates (0.30 mmol), and Cs_2CO_3 (195 mg, 0.6 mmol). The loaded vial was then sealed with a rubber cap. The vial was evacuated and backfilled with nitrogen through the cap (this procedure was repeated several times). The anhyd and degassed toluene (3 mL) and aryl amine (0.45 mmol) were added by syringe through the cap. The resultant mixture was heated at 90 °C for 24 h in an oil bath, and then filtrated through Celite with washing with EtOAc. The combined filtrate was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel, eluting with EtOAc and petroleum ether (60–90 °C) to afford **1**.[17,18] The structures and yields of the products are given in Tables 2 and 3.

(17) Physical and spectroscopic data for 4-naphthanyl-4*H*-benz[1,4]oxazin-3-one (**1n**): yellow crystalline solid; mp 146–147 °C; R_f 0.55 (EtOAc–hexane, 25%). IR (film): 1682, 1370 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.95 (d, *J* = 8.0 Hz, 1 H), 7.91 (d, *J* = 8.0 Hz, 1 H), 7.55–7.61 (m, 2 H), 7.39–7.49 (m, 3 H), 7.07 (d, *J* = 8.0 Hz, 1 H), 6.94 (dd, *J* = 8.4, 8.4 Hz, 1 H), 6.70 (dd, *J* = 8.0, 8.0 Hz, 1 H), 6.20 (d, *J* = 8.0 Hz, 1 H), 4.91, 4.84 (AB q, *J* = 15.6, 15.6 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.6, 144.8, 134.9, 132.3, 130.7, 130.1, 129.8, 128.8, 127.55, 127.52, 126.8, 126.0, 124.2,

122.9, 122.4, 117.1, 116.9, 68.3. MS (+ESI): *m*/*z* = 298 (53) [M + Na^+], 572 (100) [2 M + Na^+]. Anal. Calcd for $C_{18}H_{13}NO_2$: C, 78.53; H, 4.76; N, 5.09. Found: C, 78.56; H, 4.79; N, 4.98.

(18) Physical and spectroscopic data for 2-ethyl-4-(4-methylphenyl)-4*H*-benz[1,4]oxazin-3-one (**1r**): yellowish crystalline solid; mp 95–96 °C; R_f 0.72 (EtOAc–hexane, 25%). IR (film): 1689, 1368 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.34 (d, *J* = 8.0 Hz, 2 H), 7.16 (d, *J* = 8.0 Hz, 2 H), 7.06 (dd, *J* = 8.0, 1.2 Hz, 1 H), 6.99 (ddd, *J* = 8.0, 8.0, 1.6 Hz, 1 H), 6.85 (ddd, *J* = 8.0, 8.0, 1.6 Hz, 1 H), 6.44 (dd, *J* = 8.0, 1.2 Hz, 1 H), 4.66 (dd, *J* = 8.4, 4.4 Hz, 1 H), 2.44 (s, 3 H), 1.95–2.10 (m, 2 H), 1.16 (t, *J* = 7.6 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.3, 143.8, 138.7, 133.6, 130.8, 130.6 (2 ×), 128.5 (2 ×), 123.9, 122.2, 117.3, 116.6, 78.8, 23.9, 21.3, 9.6. MS (+ESI): *m*/*z* = 290 (28) [M + Na^+], 557 (100) [2 M + Na^+]. Anal. Calcd for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.36; H, 6.39; N, 5.37.

