JOC*Note*

Palladium-Catalyzed Direct (Hetero)arylation of Ethyl Oxazole-4-carboxylate: An Efficient Access to (Hetero)aryloxazoles

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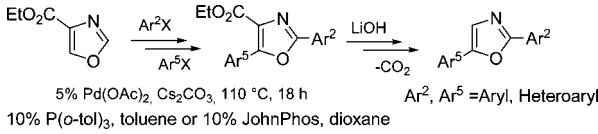

A straightforward route toward 2-(hetero)arylated and 2,5-di(hetero)arylated oxazoles through regiocontrolled palladium-catalyzed direct (hetero)arylation of ethyl oxazole-4-carboxylate with iodo-, bromo-, and chloro(hetero)aromatics followed by a two-step hydrolysis/decarboxylation sequence was described. The method was applied here to a neat synthesis of two 2,5-di(hetero)aryloxazole natural products, balsoxin and texaline.

(Hetero)aryl-substituted oxazoles are common features of a wide range of biologically active natural products. They are also of considerable interest in medicinal chemistry and as organic materials. In recent years, direct (hetero)arylation has emerged as an attractive alternative to the commonly employed cross-coupling reactions because it does not require the rather tricky preliminary preparation of the requisite metallated or halogenated (hetero)arene. Several reviews highlight the broad scope of this strategy, high functional group tolerance, atom economy, and mild reaction conditions.[1] However, this straightforward approach is penalized by the regioselectivity difficulties particularly with the unsubstituted oxazole at positions 2 and 5.[2,3]

As pioneering work, Ohta reported the regioselective C-5 direct heteroarylation of oxazole with 2-chloropyrazine under standard conditions [$Pd(PPh_3)_4$/KOAc/DMF].[2e] The process was further used to introduce the oxazole nucleus at its position 5 on heterocyclic pharmaceutics.[1a] More recently, novel efficient catalyst systems for C-2 arylation of azoles including the challenging oxazole were actively developed. Thus, Bellina and Daugulis reported the first two examples of regioselective direct C-2 phenylation of oxazole with phenyl iodide or 4-methoxyphenyl iodide under base-free conditions[2b] [CuI (2 equiv), 5 mol % $Pd(OAc)_2$] or palladium-free conditions[2c] [5 mol % CuI, ^{t}BuOLi (2 equiv)] providing 2-aryloxazoles in 63% or 23% yields, respectively. Doucet[2d] and Bhanage[2e] designed two novel palladium-bidentate ligand catalysts [$PdCl(C_3H_5)$(dppb) and $Pd(TMHD)_2$] that proved to be effective in C-2 regioselective arylation of oxazole with 4-*tert*-butylbromobenzene, iodobenzene, or 4-methoxyiodobenzene in 69%, 62%, or 63% yields, respectively. To date regioselective direct arylation of oxazole remains sparse compared to the broad range of heterocyclic targets, and there is a need to develop versatile routes to (hetero)aryloxazoles via regioselective direct arylation of oxazoles with halo(hetero)arenes. For this purpose, we recently turned to the commercially available ethyl oxazole-4-carboxylate **1** and we reported the preferential C-2 versus C-5 palladium-catalyzed direct C-H phenylation of **1** with phenyl iodide under standard conditions.[4] In this note, we report new developments of this method on the regiocontrolled C-2 (hetero)arylation of **1** followed by a C-5 (hetero)arylation with various (hetero)aryl halides. This method allows simple and fast access to 2-(hetero)aryl- and 2,5-di(hetero)aryloxazole-4-carboxylates, which are common features of various oxazole-containing natural products such as the thiopeptide antibiotic GE37468A.[5] The removal of the ethyl carboxylate function used as a temporary blocking group was examined to prepare the 2-mono(hetero)aryl- and 2,5-di(hetero)aryloxazoles via a direct coupling strategy, which can be directly run to a innovative synthetic approach toward 2,5-di(hetero)aryloxazole natural products and scintillators.[6]

In the course of the direct phenylation of **1** with phenyl iodide using a combination of $Pd(OAc)_2$ and Cs_2CO_3, we proved that the solvent/ligand pair is of main importance to control the selectivity of the C-2 arylation versus 5-monoarylation and 2,5-

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(2) Examples of C-2 or C-5 regioselective direct (hetero)arylations of oxazole: (a) Derridj, F.; Djebbar, S.; Benali-Baitich, O.; Doucet, H. *J. Organomet. Chem.* **2008**, *693*, 135–144. (b) Nandurkar, N. S.; Bhanushali, M. Y.; Bhor, M. D.; Bhanage, B. M. *Tetrahedron Lett.* **2008**, *49*, 1045–1048. (c) Daugulis, O.; Do, H.-Q. *J. Am. Chem. Soc.* **2007**, *129*, 12404–12405. (d) Bellina, F.; Cauteruccio, S.; Rossi, R. *Eur. J. Org. Chem.* **2006**, 1379–1382. (e) Ohta, A.; Akita, Y.; Ohkuwa, T.; Chiba, M.; Fukunaga, R.; Miyafuyi, A.; Nakata, T.; Tani, N.; Aoyagi, Y. *Heterocycles* **1990**, *31*, 1951–1958.

(3) Examples of C-2 or C-5 direct (hetero)arylations of 5- or 2-monosubstituted oxazoles: (a) Besselière, F.; Mahuteau-Betzer, F.; Gierson, D. S.; Piguel, S. *J. Org. Chem.* **2008**, *73*, 3278–3280. (b) Ohnmacht, S. A.; Mamone, P.; Culshaw, A. J.; Greaney, M. F. *Chem. Commun.* **2008**, *10*, 1241–1243. (c) Hodgett, K. J.; Kershaw, M. T. *Org. Lett.* **2003**, *5*, 2911–2914. (d) Pivsa-Art, S.; Fukui, Y.; Miura, M.; Nomura, M. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 467–473. (e) Pivsa-Art, S.; Fukui, Y.; Miura, M.; Nomura, M. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 467–473.

(4) Hoarau, C.; Du Fou de Kerdaniel, A.; Bracq, N.; Grandclaudon, P.; Couture, A.; Marsais, F. *Tetrahedron Lett.* **2005**, *46*, 8573–8577.

(5) (a) Hughes, R. A.; Moody, C. *Angew. Chem., Int. Ed.* **2007**, *46*, 7930–7954. (b) Bagley, M. C.; Dale, J. W.; Meritt, E. A.; Xiong, X. *Chem. Rev.* **2005**, *105*, 685–714. (c) Yeh, V. S. C. *Tetrahedron* **2004**, *60*, 11995–12402.

(6) (a) Charier, S.; Ruel, O.; Baudin, J.-B.; Alcor, D.; Allemand, J.-F.; Meglio, A.; Jullien, L.; Valeur, B. *Chem. Eur. J.* **2006**, *12*, 1097–1113. (b) Clapham, C.; Sutherland, A. J. *Chem. Commun.* **2003**, 84–85. (c) McCrain, M. C.; Hine, A. V.; Sutherland, A. J. *J. Mater. Chem.* **2003**, *13*, 225–231. (d) Clapham, C.; Sutherland, A. J. *Tetrahedron Lett.* **2000**, *41*, 2253–2256. (e) Diwu, Z.; Zhang, C.; Klaubert, D. H.; Haugland, R. P. *J. Photochem. Photobiol. A: Chem.* **2000**, *131*, 95–100.

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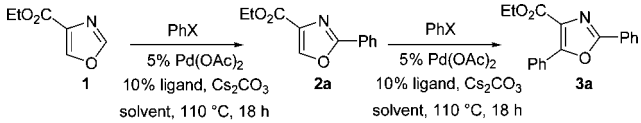
TABLE 1. Direct C-2 and C-5 Phenylation of Ethyl Oxazole-4-carboxylate (1) with Iodo- and Chlorobenzenes[a]

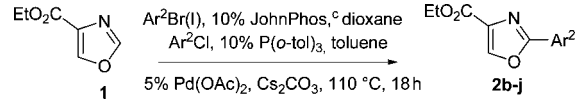


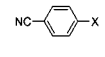
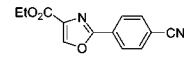
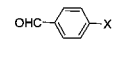
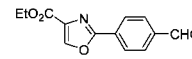
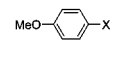
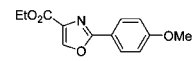
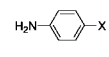
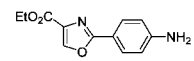
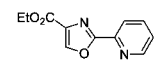
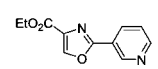
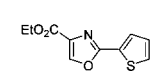
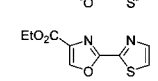
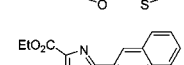
entry	PhX	ligand	dioxane		toluene	
			%-**2a**[b]	%-**3a**[b]	%-**2a**[b]	%-**3a**[b]
1	PhI	P(*o*-tol)$_3$	37[e]	81	86	**96**
2	PhI	JohnPhos[c]	**69**	27	67[f]	49
3	PhI	IMes[d]	88[g]	24	38	12
4	PhCl	P(*o*-tol)$_3$	n.r.	n.r.	44(**71**)[h]	16
5	PhCl	JohnPhos[c]	79	52 (**70**)[h]	n.r.	57 (**69**)[h]
6	PhCl	IMes[d]	n.r.	n.r.	n.r.	n.r.

[a] Reaction conditions: [**1**]/[PhX]/[Pd(OAc)$_2$]/[ligand]/[Cs$_2$CO$_3$] = 0.35:0.35:0.017:0.035:0.7 (in mmol), in dioxane or toluene (1 mL) under N_2 atmosphere at 110 °C for 18 h; n.r. = no reaction. [b] Yield of isolated product over two runs. [c] Buchwald's JohnPhos ligand: 2-(dicyclohexylphosphino)biphenyl. [d] IMes: 1,3-bis-(mesitylimidazolyl)carbene. [e] 16% of **3a** and 10% of ethyl 5-phenyloxazole-4-carboxylate. [f] 15% of **3a**. [g] 11% of **3a**. [h] 0.7 mmol of PhCl.

diarylation of oxazole-4-carboxylates. Bulky ligands greatly favor the formation of ethyl 2-phenyloxazole-4-carboxylate (Table 1, entries 1−3), 86% using P(*o*-tol)$_3$ in toluene, 69% with Buchwald's JohnPhos ligand in dioxane, or 88% with IMes in dioxane. Therefore, the subsequent C-5 phenylation of **2a** to the ethyl 2,5-diphenyloxazole-4-carboxylate **3a** could be achieved with P(*o*-tol)$_3$ either in dioxane (81%) or toluene (96%). With the aim to extend the method to a broad range of (hetero)arene halides, we first checked the direct coupling of phenyl chloride with **1** (Table 1, entries 4−6). We found that Buchwald's JohnPhos ligand in dioxane carried out the two-step C-2 and then C-5 phenylation of **1** to **2a** then **3a** in 79% and 52% yields (entry 5). The use of P(*o*-tol)$_3$ in toluene allowed exclusively the C-2 phenylation of **1** in 71% yield when using a 2-fold excess of phenyl chloride (entry 4). Interestingly, the 2,5-diphenylated compound **3a** was not observed due to the poor efficiency of P(*o*-tol)$_3$ in toluene in subsequent C-5 phenylation of **2a** to **3a** (16%). As consequence of probing C-2 (hetero)arylation of **1** with a number of halo(hetero)arenes, we chose the ligand/solvent pairs that were much more effective in C-2 than in C-5 phenylation of **1** to avoid the side production of the undesired 2,5-diarylated compound. Thus from the results depicted in Table 1 (entries 1−6), two efficient ligand/solvent pairs were retained depending on the (hetero)aryl halide used. The (hetero)arylation of **1** with (hetero)aryl iodides and bromides was carried out with Buchwald's JohnPhos ligand in dioxane, whereas P(*o*-tol)$_3$ in toluene for direct coupling of **1** with (hetero)aryl chlorides was used. The results depicted in Table 2 showed that the selective C-2 (hetero)arylation of **1** could be successfully accomplished with a large number of iodo- and bromo(hetero)arenes leading to the corresponding 2-(hetero)aryloxazole-4-carboxylates **2b**−**j** in 59% to 90% yields range. Most remarkably, almost all (hetero)aryl chlorides proved to be better coupling partners than iodo- and bromo(hetero)arenes for direct coupling since 2-(hetero)aryloxazole-4-carboxylates **2b**−**j** were obtained in higher yields (66−98%). As expected, both 5-(hetero)arylated and 2,5-diarylated products were not formed with 1 equiv of (hetero)aryl halides. Nevertheless, an excess of (hetero)aryl halides could be useful sometimes along with

TABLE 2. Direct C-2 (Hetero)arylation of Ethyl Oxazole-4-carboxylate (1) with Iodo-, Bromo-, and Chloro(hetero)aromatics[a]



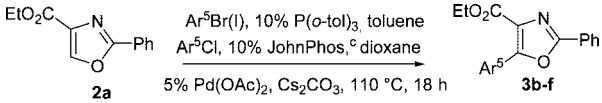
entry	Ar^2X	X	product		yield (%)[b]
1		I		**2b**	65 (91)[d]
2		Cl			85
3		Br		**2c**	33 (60)[d,f]
4		Cl			66
5		I		**2d**	59 (77)[d,g]
6		Cl			29 (68)[e]
7		I		**2e**	78
8		Cl			n.r.
9		I		**2f**	59 (98)[d]
10		Br			87
11		Cl			98
12		I		**2g**	83
13		Br			74 (98)[d]
14		Cl			96
15		I		**2h**	90
16		Cl			97
17		Br		**2i**	77
18		Cl			59 (73)[e]
19		Br		**2j**	84

[a] Reaction conditions: [**1**]/[Ar^2X]/[Pd(OAc)$_2$]/[ligand]/[Cs$_2$CO$_3$] = 0.35:0.35:0.017:0.035:0.7 (in mmol), in dioxane or toluene (1 mL) under N_2 atmosphere at 110 °C for 18 h; n.r. = no reaction. [b] Yield of isolated product over two runs. [c] Buchwald's JohnPhos ligand: 2-(dicyclohexylphosphino)biphenyl. [d] 0.7 mmol of halogeno(hetero)aromatic. [e] [**1**]/[Ar^2X]/[Pd(OAc)$_2$]/[ligand]/[Cs$_2$CO$_3$] = 0.35:0.7:0.035:0.07:0.7 (in mmol). [f] 36% of 2,5 diarylated oxazole. [g] 22% of 2,5 diarylated oxazole.

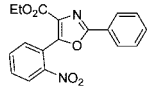
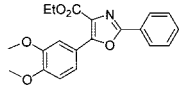
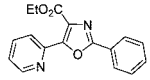
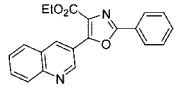
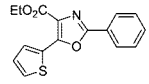
increasing amounts of catalyst (10 mol %) and ligand (20 mol %) to optimize the yield of C-2 (hetero)aryloxazoles versus the side-production of bis-arenes arising from the (hetero)aryl halides homocoupling (entries 1, 3, 5, 6, 9, 13, and 18). It should also be noted that the direct (hetero)arylation of **1** is fully compatible with such reactive functions as cyano and formyl (entries 1−4) as well as the electron-rich amino group of 4-aminoiodobenzene (entry 7). Surprisingly, P(*o*-tol)$_3$ in toluene proved to be an effective ligand in the direct coupling of **1** with the deactivated 4-methoxychlorobenzene (entry 6), whereas the same reaction with 4-aminochlorobenzene remained unsuccessful whatever catalyst was used (entry 8).

The second C-5 (hetero)arylation step of 2-(hetero)aryloxazole-4-carboxylates with various (hetero)aryl halides was then studied. Preliminary results of the C-5 direct phenylation of **2a** with phenyl iodide (Table 1) showed that P(*o*-tol)$_3$ in toluene can be used with (hetero)aryl iodides (entry 1), whereas Buchwald's JohnPhos ligand in dioxane or toluene is better in the case of (hetero)aryl chlorides (entry 5). Under these conditions, the second C-5 coupling step of **2a** with various (hetero)aryl halides led to the expected 5-(hetero)aryl-2-phenyloxazole-4-carboxylates **3b**−**f** in fair to good yields (Table 3). Iodo- and bromo(hetero)arenes proved to be very reactive and allowed good to excellent yields (72−95%) of oxazole-4-carboxylates **3b**−**f**. As with chlorobenzene, 2 equiv of 2-chloropyridine and 2-chlorothiophene were required to produce **3d**

TABLE 3. Direct C-5 (Hetero)arylation of 2-Phenyloxazole-4-carboxylate (2a) with Iodo-, Bromo-, and Chloro(hetero)aromatics[a]



2a **3b-f**

entry	Ar^5X	X	product		yield (%)[b]
1		I		**3b**	84
2		Br		**3c**	84
3		I			95
4		Br		**3d**	72
5		Cl			55,(72)[d]
6		Br		**3e**	88
7		I		**3f**	89
8		Cl			n.r (72)[e]

[a] Reaction conditions: [**2a**]/[Ar^5X]/[$Pd(OAc)_2$]/[ligand]/[Cs_2CO_3] = 0.35:0.35:0.017:0.035:0.7 (in mmol), in dioxane or toluene (1 mL) under N_2 atmosphere at 110 °C for 18 h; n.r. = no reaction. [b] Yield of isolated product over two runs. [c] Buchwald's JohnPhos ligand: 2-(dicyclohexylphosphino)biphenyl. [d] [**2a**]/[Ar^5X]/[$Pd(OAc)_2$]/[ligand]/[Cs_2CO_3] = 0.35:0.7:0.035:0.07:0.7 (in mmol). [e] Toluene as solvent.

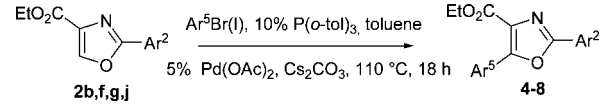
and **3f** in good 72% yields. The same procedure with P(*o*-tol)$_3$ in toluene was further successfully used to prepare 2,5-di(hetero)aryloxazole-4-carboxylates **4**−**8** in good to excellent yields (81−100%) (Table 4).

With a selective C-2 and subsequent C-5 (hetero)arylation process of ethyl oxazole-4-carboxylate **1** in hand, we turned our attention to the preparation of 2-mono(hetero)aryl- and 2,5-di(hetero)aryloxazoles by removal of the ester group through a two-step LiOH-hydrolysis followed by a CuO-induced decarboxylation sequence. This protocol turned out to be very effective especially with sensitive functions such as formyl and cyanide groups and provided the expected (hetero)aryloxazoles **9**−**14** in good (75%) to quantitative yields (Table 5). Some of these 2,5-di(hetero)aryloxazoles are natural products, such as balsoxin **11** and texaline **13** isolated from *Amyris* species of plants in the Caribbean.[7]

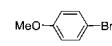
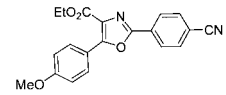
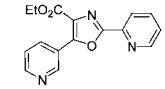
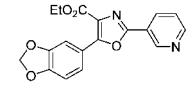
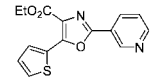
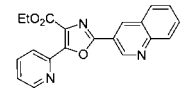
In conclusion, we have developed a general palladium-catalyzed C-2 and subsequent C-5 direct (hetero)arylation process of ethyl oxazole-4-carboxylate **1**. It appeared to be very efficient and general with regard to both halogens (I, Br, Cl) and coupling partners, giving a clean access to a great variety of ethyl 2-(hetero)aryloxazole-4-carboxylates and ethyl 2,5-di(hetero)aryloxazole-4-carboxylates. The carboxylic ester function at C-4 could be then easily removed to readily afford the corresponding 2-(hetero)aryloxazoles and 2,5-di(hetero)aryloxazoles. This first versatile approach toward 2-(hetero)aryloxazoles and 2,5-di(hetero)aryloxazoles based upon a direct C-H arylation strategy was successfully applied to the synthesis of natural 2,5-di(hetero)aryloxazoles. Thus balsoxin and texaline were cleanly prepared in three steps in 54% and 61% overall

(7) (a) Domínguez, X. A.; de la Fuenta, G.; González, A. G.; Reina, M.; Timón, I. *Heterocycles* **1988**, *27*, 35–38. (b) Burke, B.; Parkins, H.; Talbot, A. M. *Heterocycles* **1979**, *12*, 349–351.

TABLE 4. 2,5-Di(hetero)arylated Oxazole-4-carboxylates Synthesis[a]

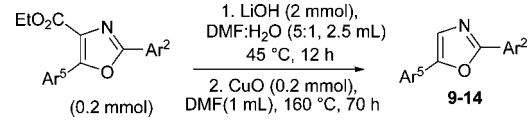


2b,f,g,j **4-8**

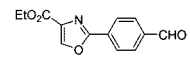
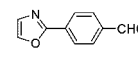
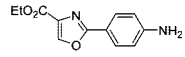
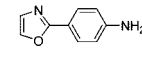
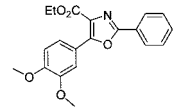
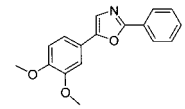
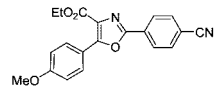
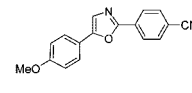
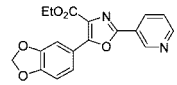
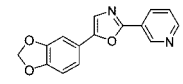
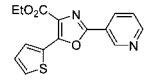
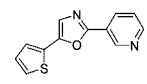
entry	substrate	Ar^5X	product		yield (%)[b]
1	**2b**			**4**	97
2	**2f**			**5**	35 (94)[c]
3	**2g**			**6**	81
4	**2g**			**7**	82
5	**2j**			**8**	56 (100)[c]

[a] Reaction conditions: [**2**]/[Ar^5X]/[$Pd(OAc)_2$]/[ligand]/[Cs_2CO_3] = 0.35:0.35:0.017:0.035:0.7 (in mmol), in dioxane or toluene (1 mL) under N_2 atmosphere at 110 °C for 18 h; n.r. = no reaction. [b] Yield of isolated product over two runs. [c] [**2**]/[Ar^5X]/[$Pd(OAc)_2$]/[ligand]/[Cs_2CO_3] = 0.35:0.7:0.035:0.07:0.7 (in mmol).

TABLE 5. 2-(Hetero)arylated- and 2,5-Di(hetero)arylated Oxazoles Synthesis



(0.2 mmol) **9-14**

entry	substrate	product		yield (%)[a]
1			**9**	82
2			**10**	87
3			**11**	80
4			**12**	97
5			**13**	75
6			**14**	100

[a] Yield of isolated product.

yields, respectively, from **1** using optimized experimental conditions.[8,9]

Experimental Section

General Procedure for C-2 Direct Coupling of Oxazole-4-carboxylate 1 with (Hetero)aryl Iodides and Bromides (Chlorides). To a 10-mL sealed tube were added oxazolecarboxylate **1** (0.35 mmol), (hetero)aryl bromide or iodide (chloride) (0.35 mmol), $Pd(OAc)_2$ (4 mg, 0.017 mmol,), Cs_2CO_3 (231 mg, 0.70 mmol), JohnPhos ($P(o\text{-tol})_3$) (12 mg (11 mg)), 0.035 mmol), and dioxane (toluene) (1 mL). The resulting mixuture was stirred under N_2 at 110 °C. After filtration through Celite and concentration under vacuo, the crude product was purified by flash column chromatography on silica gel using a mixture of ethyl acetate/petrolum ether as the eluent to get 2-arylated oxazolecarboxylates **2b**−**j**.

Ethyl 2-(4-cyanophenyl)oxazole-4-carboxylate (**2b**): white solid (65% (85%)), mp = 123−124 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.40 (t, 3H, J = 7.1 Hz), 4.43 (q, 2H, J = 7.1 Hz), 7.77 (d, 2H, J = 8.7 Hz), 8.22 (d, 2H, J = 8.7 Hz), 8.32 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.3, 62.3, 114.0, 115.0, 118.0, 127.5, 129.0, 130.6, 132.3, 132.8, 144.6, 153.6, 161.6; IR (KBr) υ 1551, 1572, 1654, 1717, 2230, 3100 cm^{-1}. Anal. Calcd for $C_{13}H_{10}N_2O_3$ (242.2): C, 64.46; H, 4.16; N, 11.56. Found: C, 64.63; H, 4.10; N, 11.54.

The characterization data of compounds **2c**−**j** and others detailed C-2 direct arylating procedures are available in Supporting Information.

General Procedure for C-5 Direct Coupling of 2-Aryl Oxazole-4-Carboxylate 2a (2b,f,g,j) with (Hetero)aryl Iodides and Bromides. To a 10-mL sealed tube were added oxazolecarboxylate **2a** (76 mg, 0.35 mmol), (hetero)aryl bromide (0.35 mmol), $Pd(OAc)_2$ (4 mg, 0.017 mmol,), Cs_2CO_3 (231 mg, 0.70 mmol), and $P(o\text{-tol})_3$ (11 mg, 0.035 mmol) in toluene (1 mL). The resulting mixture was stirred under N_2 at 110 °C. After filtration through Celite and concentration under vacuo, the crude product was purified by flash column chromatography on silica gel using a mixture of ethyl acetate/petrolum ether as the eluent to get 2,5-diarylated oxazolecarboxylates **3b**−**f** and **4**−**8**.

Ethyl 2-phenyl-5-(2-nitrophenyl)oxazole-4-carboxylate (**3b**): white solid (84%), mp = 136−137 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.27 (t, 3H, J = 7.2 Hz), 4.32 (q, 2H, J = 7.2 Hz), 7.48−7.50 (m, 3H), 7.66−7.73 (m, 1H), 7.74−7.77 (m, 1H), 7.77−7.79 (m, 1H), 8.11−8.13 (m, 2H), 8.18 (d, 1H, J = 7.9 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 61.7, 122.8, 124.9, 126.2, 127.1, 127.5, 129.0, 130.2, 131.3, 131.5, 132.7, 132.9, 148.6, 151.0, 161.5; IR (KBr) υ 1525, 1576, 1602, 1718, 1743, 2992, 3077 cm^{-1}. Anal. Calcd for $C_{18}H_{14}N_2O_5$ (338.3): C, 63.90; H, 4.17; N, 8.28. Found: C, 63.94; H, 4.03; N, 8.45.

Ethyl 2-(4-cyanophenyl)-5-(4-methoxyphenyl)oxazole-4-carboxylate (**4**): white solid (97%), mp = 192−193 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.41 (t, 3H, J = 6.9 Hz), 3.87 (s, 3H), 4.43 (q, 2H, J = 6.9 Hz), 8.64 (d, 2H, J = 8.6 Hz), 7.76 (d, 2H, J = 8.1 Hz), 8.10 (d, 2H, J = 8.6 Hz), 8.23 (d, 2H, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.4, 55.5, 61.6, 114.0, 114.1, 118.3, 119.1, 127.1, 127.6, 130.3, 130.4, 132.7, 156.4, 157.1, 161.5, 162.1; IR (KBr) υ 1507, 1578, 1610, 1709, 2227, 2837, 2947, 2994 cm^{-1}. Anal. Calcd for $C_{20}H_{16}N_2O_4$ (348.4): C, 68.96; H, 4.63; N, 8.04. Found: C, 69.06; H, 4.85; N, 8.21.

The characterization data of compounds **3c**−**f** and **5**−**8** and other C-5 direct arylating procedures are available in Supporting Information.

Acknowledgment. This work has been supported by the CNRS, the interregional CRUNCH network, INSA, and University of Rouen (I.U.T.).

Supporting Information Available: Experimental procedures and spectroscopic characterization (IR, analytical analysis, ^{1}H, ^{13}C data) of all new (hetero)arylated oxazole-4-carboxylates. The material is available free of charge via the Internet at http://pubs.acs.org.

JO801093N

(8) For balsoxin and texaline synthesis via a combined cross-coupling or condensation and direct arylation approach, see: (a) Hodgett, K. J.; Kershaw, M. T. *Org. Lett.* **2002**, *4*, 2905–2907. (b) References 3a and 3b.

(9) For the unique texaline synthesis via a condensation approach, see: (a) Gildens, A. C.; Boshoff, H. I. M.; Franzblau, S. G.; Barry, C.; Copp, B. R. *Tetrahedron Lett.* **2005**, *46*, 7355–7357.