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Ortho-Selective Direct Cross-Coupling Reaction of 2-Aryloxazolines and 2-Arylimidazolines with Aryl and Alkenyl Halides Catalyzed by Ruthenium Complexes

Shuichi Oi,* Emi Aizawa, Yukako Ogino, and Yoshio Inoue*

Department of Biomolecular Engineering, Graduate School of Engineering, Tohoku University, Sendai 980-8579, Japan

oishu@aporg.che.tohoku.ac.jp

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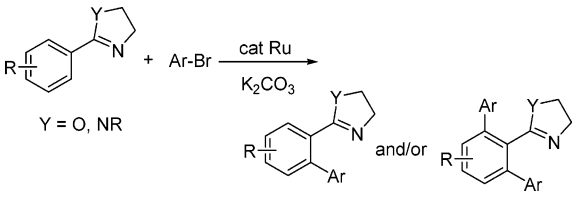

The ortho position of the aromatic ring in 2-aryloxazolines and 2-arylimidazolines is selectively arylated and alkenylated with organic halides in the presence of a ruthenium(II)−phosphine complex. In the case of unsubstituted and para-substituted phenyloxazolines, 1:2 coupled products were obtained preferentially, while 1:1 coupled products were obtained in the case of meta-substituted phenyloxazolines and *N*-acylarylimidazolines. The reaction is proposed to proceed via the generation of an organoruthenium intermediate, formed by oxidative addition of the organic halide, and ortho-ruthenation directed by the coordination of the 2-oxazolinyl or 2-imidazolinyl group to the ruthenium center.

Introduction

There has been much interest in direct transition-metal-catalyzed C−C bond formation of aromatic compounds involving activation of normally unreactive aromatic C−H bonds, particularly in terms of synthetic and atom efficiency.[1] This has proven particularly effective in reactions involving the addition of aromatic C−H bonds to carbon−carbon multiple bonds, such as alkenes and alkynes,[2−4] and the ortho carbonylation of aromatic rings with carbon monoxide.[5] The direct coupling of aromatic C−H bonds with aryl halides and arylmetal compounds also presents a useful pathway for the synthesis of biaryls and teraryls. The arylation of various aromatic compounds, such as phenolic compounds,[6] benzyl phenyl ketones,[7] benzanilides,[8] and heteroaromatic compounds,[9] with aryl halides in the presence of a suitable transition-metal catalyst has been reported. The ruthenium-catalyzed coupling of aryl ketones with aryl-

(1) (a) Fujiwara, Y.; Jintoku, T.; Takaki, K. *CHEMTECH* **1990**, 636. (b) Trost, B. M. *Science* **1991**, *278*, 1471. (c) Shilov, E.; Shul'pin, G. B. *Chem. Rev.* **1997**, *97*, 2879. (d) Dyker, G. *Angew. Chem., Int. Ed.* **1999**, *38*, 1698.

(2) Review: Kakiuchi, F.; Murai, S. In *Topics in Organometallic Chemistry*; Murai, S., Ed.; Springer: Berlin, 1999; Vol. 3, pp 47−79.

(3) (a) Jun, C. H.; Chung, K. Y.; Hong, J. B. *Org. Lett.* **2001**, *3*, 785. (b) Lail, M.; Arrowood, B. N.; Gunnoe, T. B. *J. Am. Chem. Soc.* **2003**, *125*, 7506. (c) Oxgaard, J.; Muller, R. P.; Goddard, W. A.; Periana, R. A. *J. Am. Chem. Soc.* **2004**, *126*, 352. (d) Tan, K. L.; Park, S.; Ellman, J. A.; Bergman, R. G. *J. Org. Chem.* **2004**, *69*, 7329.

(4) (a) Jia, C.; Lu, W.; Oyamada, J.; Kitamura, T.; Matsuda, K.; Irie, M.; Fujiwara, Y. *J. Am. Chem. Soc.* **2000**, *122*, 7252. (b) Lim, Y. G.; Lee, K. H.; Koo, B. T.; Kang, J. B. *Tetrahedron Lett.* **2001**, *42*, 7609. (c) Tsukada, N.; Mitsuboshi, T.; Setoguchi, H.; Inoue, Y. *J. Am. Chem. Soc.* **2003**, *125*, 12102.

(5) (a) Moore, E.; Pretzer, W. R.; O'Connell, T. J.; Harris, J.; LaBounty, L.; Chou, L.; Grimmer, S. S. *J. Am. Chem. Soc.* **1992**, *114*, 5888. (b) Chatani, N.; Ie, Y.; Kakiuchi, F.; Murai, S. *J. Org. Chem.* **1997**, *62*, 2604. (c) Fukuyama, T.; Chatani, N.; Kakiuchi, F.; Murai, S. *J. Org. Chem.* **1997**, *62*, 5647. (d) Ie, Y.; Chatani, N.; Ogo, T.; Marshall, D. R.; Fukuyama, T.; Kakiuchi, F.; Murai, S. *J. Org. Chem.* **2000**, *65*, 1475. (e) Asaumi, T.; Chatani, N.; Matsuo, T.; Kakiuchi, F.; Murai, S. *J. Org. Chem.* **2003**, *68*, 7538.

(6) (a) Satoh, T.; Kawamura, Y.; Miura, M.; Nomura, M. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1740. (b) Satoh, T.; Inoh, J.-I.; Kawamura, Y.; Kawamura, Y.; Miura, M.; Nomura, M. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 2239. (c) Kawamura, Y.; Satoh, T.; Miura, M.; Nomura, M. *Chem. Lett.* **1999**, 961. (d) Bedford, R. B.; Coles, S. J. Hursthouse, M. B.; Limmert, M. E. *Angew. Chem., Int. Ed. Engl.* **2003**, *42*, 112. (e) Bedford, R. B.; Limmert, M. E. *J. Org. Chem.* **2003**, *68*, 8669. (f) Oi, S.; Watanabe, S.; Fukita, S.; Inoue, Y.; *Tetrahedron Lett.* **2003**, *44*, 8665.

(7) Satoh, T.; Kametani, Y.; Terao, Y.; Miura, M.; Nomura, M. *Tetrahedron Lett.* **1999**, *40*, 5345.

(8) Kametani, Y.; Satoh, T.; Miura, M.; Nomura, M. *Tetrahedron Lett.* **2000**, *41*, 2655.

(9) Reviews: (a) Miura, M.; Nomura, M. In *Topics in Current Chemistry* Miyaura, N., Ed.; Springer: Berlin, 2002; Vol. 219, pp 211−241. (b) Hassan, J.; Sévignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359. (c) Zificsak, C. A.; J. H. Dennis *Tetrahedron* **2004**, *60*, 8991.

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boronates[10] has also been reported. With regard to arylmetal compounds, we have reported the ortho arylation of pyridylarenes with tetraarylstannanes in the presence of a catalytic amount of a rhodium−phosphine complex.[11] This reaction has since been extended to the direct ortho arylation of pyridylarenes and aromatic imines using readily available and inexpensive aryl halides, in the presence of a ruthenium(II)−phosphine complex.[12] In these reactions, coordination of the pyridyl or imino group to the transition-metal complex directs metalation to the ortho position of the aromatic ring.[2] The 2-oxazolinyl group is known to act as an ortho-directing group for aromatic C−H bond activation in the presence of transition-metal complexes. Indeed, 2-aryloxazolines are reported to undergo ruthenium-catalyzed carbonylation with carbon monoxide[5d] and silylation with trialkylsilanes.[13] The 2-oxazolinyl group is also very useful from the standpoint that it can be easily converted to other functional groups, such as carboxylic acids.[14] In this paper, we report the successful ruthenium-catalyzed ortho-selective direct coupling of 2-aryloxazolines, and their analogous 2-arylimidazolines, with aryl and alkenyl halides.

Results and Discussion

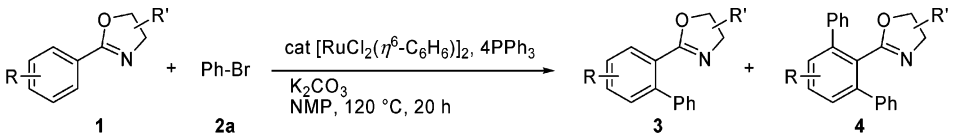
The results of the direct coupling reactions of various 2-aryloxazolines with bromobenzene are shown in Table 1. The reaction between 2-phenyl-2-oxazoline (**1a**, 0.5 mmol) and a slight excess of bromobenzene (**2a**, 0.6 mmol), in the presence of 2.5 mol % of $[RuCl_2(\eta^6\text{-}C_6H_6)]_2$, PPh_3 (0.05 mmol, P:Ru ratio = 2:1), and K_2CO_3 (1.0 mmol) in *N*-methylpyrrolidinone (NMP) at 120 °C for 20 h, afforded a 60% yield of a mixture comprising the expected 1:1 ortho-coupled product **3aa** and 1:2 ortho-coupled product **4aa** in a 25:75 ratio (entry 1). The preferential formation of **4aa** was further enhanced when 2.5 equiv of bromobenzene was used, affording the 1:2 ortho-coupled product as the sole product in quantitative yield (entry 2). To investigate the influence of the oxazoline ring substituents on the distribution of the 1:1 and 1:2 product formations, the reactions of 5,5-dimethyl-2-phenyl-2-oxazoline (**1b**) and 4,4-dimethyl-2-phenyl-2-oxazoline (**1c**) were examined. In the reaction of **1b** with 1.2 equiv of bromobenzene, it was found that the two methyl groups in the 5-position of the oxazoline ring had no effect on either the product yield or distribution, resulting in the formation of products **3ba** and **4ba** in a 31:69 ratio in 62% yield (entry 3). On the other hand, the reaction of **1c**, having two methyl groups in the 4-position of the oxazoline ring, with 1.2 equiv of bromobenzene gave the 1:1 coupled product **3ca** exclusively, with a yield as low as 11% (entry 4). In this case, the steric hindrance associated with the two methyl groups is thought to be sufficient to inhibit coordination of the nitrogen atom to the ruthenium complex. The reaction of the aryloxazoline compound having a methyl group in the ortho position of the benzene ring **1d** with 1.2 equiv of **2a** resulted in the exclusive formation of the 1:1 coupled product **3da** in 92% yield (entry 5). The reaction of **1e**, having a methyl group in the para position, with **2a** favored formation of a 1:2 coupled product, as in the case of **1a**. When **1e** was reacted with 1.2 equiv of **2a**, the corresponding 1:1 and 1:2 coupled products (**3ea** and **4ea**) were obtained in a ratio of 15:85 (59% yield, entry 6), while the same reaction using 2.5 equiv of **2a** afforded **3ea** and **4ea** in a ratio of 4:96 (81% yield, entry 7). On the other hand, the reaction of aryloxazoline having a methyl group in the meta position **1f** with 1.2 equiv of **2a** resulted in the preferential formation of the 1:1 coupled product in a **3fa**:**4fa** ratio of 85:15, with a combined yield of 73% (entry 8). Interestingly, the same reaction using 2.5 equiv of **2a** did not alter either the yield or the product ratio (entry 9). Here, it is assumed that the steric hindrance associated with the meta-methyl group was sufficient to inhibit the second arylation. Similarly, the reaction of the *m*-trifluoromethyl-substituted aryloxazoline **1g** gave the 1:1 coupled product **3ga** exclusively in 91% yield (entry 10). The reaction of 1-naphthyloxazoline **1h** with 1.2 equiv of **2a** resulted in the preferential formation of the 1:1 coupled product, in which the aryl substituent was located in the 2-position **3ha**. The corresponding 1:2 coupled product **4ha** was produced with aryl groups located in the 2- and 8-positions (entry 11). The reaction of **1h** with 2.5 equiv of **2a** also resulted in the preferential formation of the 1:1 coupled product **3ha** in a slightly higher ratio (78:22) (99% yield, entry 12). The reaction of 2-naphthyloxazoline **1i** with 1.2 equiv of **2a** gave a mixture of **3ia** and **4ia** in a ratio of 64:36 (88% yield, entry 13), while the same reaction with 2.5 equiv of **2a** demonstrated an increased preference for the 1:2 coupled product **4ia** (46:54, entry 14).

The reaction of the *o*-methyl-substituted aryloxazoline **1d** with various aryl bromides (1.2 equiv) was also examined (Table 2). 4-Methoxy- and 2-methoxybromobenzene (**2b** and **2c**), 4-acetylbromobenzene **2d**, and 2-methylbromobenzene **2e** all reacted smoothly with **1d**, giving the corresponding ortho 1:1 coupled products in good to excellent yield (entries 1−4). 1-Bromonaphthalene **2g** was also found to react well with **1d**, affording the product **3dg** in 73% yield (entry 5). The sterically hindered 2,6-dimethylbromobenzene (**2f**), on the other hand, failed to react with **1d** (entry 6), while the corresponding reaction between the hindered 1-bromo-2-methylnaphthalene **2h** and **1d** gave the product **3dh** in a moderate yield of 44% (entry 7).

The ruthenium-catalyzed direct coupling of aryloxazolines with alkenyl bromides was also deemed possible; however, isomerization of the olefinic moiety was observed in all cases (Table 3). When (*E*)-1-bromo-1-propene ((*E*)-**5a**) was reacted with **1d** under the same reaction conditions used for aryl bromides, 53% yield of the coupled product **6da** was obtained in an *E*/*Z* ratio of 91:9 (entry 1). The use of (*Z*)-**5a** instead of (*E*)-**5a** also resulted in the preferential formation of the (*E*)-**6da** in a similar *E*/*Z* ratio (90:10, 63% yield). The reaction of **1d** with an *E*/*Z* (85:15) mixture of β-bromostyrene **5b** gave the product **6db** with an *E*/*Z* ratio of 97:3 (93% yield, entry

(10) Kakiuchi, F.; Kan, S.; Igi, K.; Chatani, N.; Murai, S. *J. Am. Chem. Soc.* **2003**, *125*, 1698.
(11) Oi, S.; Fukita, S.; Inoue, Y. *Chem. Commun.* **1998**, 2439.
(12) (a) Oi, S.; Fukita, S.; Hirata, N.; Watanuki, N.; Miyano, S.; Inoue, Y. *Org. Lett.* **2001**, *3*, 2579. (b) Oi, S.; Ogino, Y.; Fukita, S.; Inoue, Y. *Org. Lett.* **2002**, *4*, 1783.
(13) Kakiuchi, F.; Matsumoto, M.; Tsuchiya, K.; Igi, K.; Hayamizu, T.; Chatani, N.; Murai, S. *J. Organomet. Chem.* **2003**, *686*, 134.
(14) Reviews: (a) Reuman, M.; Meyers, A. I. *Tetrahedron* **1985**, *41*, 837. (b) Gant, T. G.; Meyers, A. I. *Tetrahedron* **1994**, *50*, 2297.

TABLE 1. Ruthenium-Catalyzed Ortho-Selective Direct Arylation of Various 2-Aryloxazolines 1 with Bromobenzene (2a)[a]

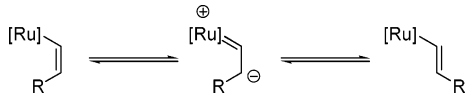


entry	aryloxazoline **1**	equiv of **2a**	product **3**	product **4**	total yield (%)	ratio (**3**:**4**)
1	(**1a**)	1.2	(**3aa**)	(**4aa**)	60	25:75
2		2.5			100	0:100
3	(**1b**)	1.2	(**3ba**)	(**4ba**)	62	31:69
4	(**1c**)	1.2	(**3ca**)		11	100:0
5	(**1d**)	1.2	(**3da**)	—	92	—
6	(**1e**)	1.2	(**3ea**)	(**4ea**)	59	15:85
7		2.5			81	4:96
8	(**1f**)	1.2	(**3fa**)	(**4fa**)	73	85:15
9		2.5			73	85:15
10	(**1g**)	1.2	(**3ga**)		91	100:0
11	(**1h**)	1.2	(**3ha**)	(**4ha**)	90	86:14
12		2.5			99	78:22
13	(**1i**)	1.2	(**3ia**)	(**4ia**)	88	64:36
14		2.5			93	46:54

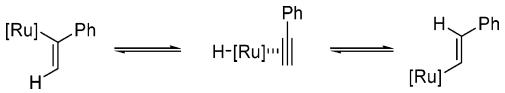
[a] Reactions were carried out using 0.5 mmol of **1**, 0.6 or 1.25 mmol of **2a**, 0.0125 mmol of $[RuCl_2(\eta^6\text{-}C_6H_6)]_2$, and 0.05 mmol of PPh_3 in 1 mL of NMP at 120 °C for 20 h under N_2.

3). The reaction of α-bromostyrene (**5c**) with **1d**, on the other hand, gave only 9% of the expected α-styryl product **6dc**. Interestingly, the major product of this reaction was the formation of the (*E*)-*β*-styryl product **6db**, in an *E*/*Z* ratio of 96:4 (43% yield, entry 4). Although the exact mechanism has not yet been fully determined, it is most likely that isomerization occurs on the alkenylruthenium intermediate. The isomerization between (*E*)- and (*Z*)-alkenylruthenium complexes is best explained by the formation of a zwitterionic carbenoid complex (Scheme 1), as proposed for the transition-metal-catalyzed trans-hydrosilylation.[15] An example of the isomerization reaction between α- and *β*-styrylruthenium complexes was reported by Torres et al., in which isomerization was proposed to occur via an *η*-alkyne hydrido species (Scheme 2).[16]

SCHEME 1



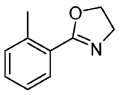
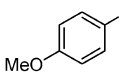
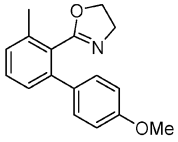
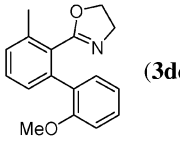
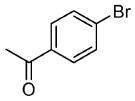
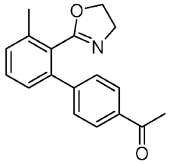
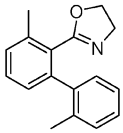
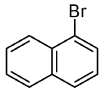
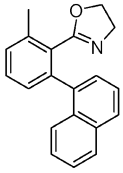
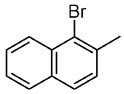
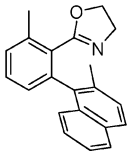
SCHEME 2



(15) (a) Tanke, R. S.; Crabtree, R. H. *J. Am. Chem. Soc.* **1990**, *112*, 7984. (b) Ojima, I.; Clos, N.; Donovan, R. J.; Ingallina, P. *Organometallics* **1990**, *9*, 3127.

(16) Torres, M. R.; Vegas, A.; Santos, A. *J. Organomet. Chem.* **1986**, *309*, 169.

TABLE 2. Ruthenium-Catalyzed Ortho-Selective Direct Arylation of 2-(2-Methylphenyl)-2-oxazoline (1d) with Various Aryl Bromides 2[a]

entry	aryloxazoline **1**	arylbromide **2**	product **3**	yield (%)
1	 (**1d**)	 (**2b**)	 (**3db**)	94
2	**1d**	 (**2c**)	 (**3dc**)	71
3	**1d**	 (**2d**)	 (**3dd**)	98
4	**1d**	 (**2e**)	 (**3de**)	85
5	**1d**	 (**2g**)	 (**3dg**)	73
6	**1d**	 (**2f**)	—	0
7	**1d**	 (**2h**)	 (**3dh**)	44

[a] Reactions were carried out using 0.5 mmol of **1d**, 0.6 mmol of **2**, 0.0125 mmol of $[RuCl_2(\eta^6\text{-}C_6H_6)]_2$, and 0.05 mmol of PPh_3 in 1 mL of NMP at 120 °C for 20 h under N_2.

Next, arylimidazolines were employed in an effort to assess the effects of transition-metal-catalyzed direct cross-coupling on aryloxazoline analogues with aryl halides (Table 4). The reaction of 2-phenyl-2-imidazoline (**7a**) with 1.2 equiv of bromobenzene under the same reaction conditions as those for aryloxazolines gave the expected 1:1 and 1:2 ortho-coupled products (**8aa** and **9aa**) in a ratio of 31:69 (64% yield, entry 1). These products were isolated in the *N*-acetyl form by treatment with acetyl anhydride. As in the case of phenyloxazoline **1a**, the 1:2 coupling reaction occurred preferentially. This was further confirmed in the corresponding reaction with 2.5 equiv of bromobenzene, which afforded the 1:2 coupled species **9aa** as the sole product in good yield (90%, entry 2). The reaction of *N*-acyl derivatives was therefore examined in order to ascertain the effects of the *N*-acyl substituent, which is expected to block the second coupling reaction. Indeed, the reaction of *N*-acetyl-2-phenyl-2-imidazoline (**7b**) with 1.2 equiv of bromobenzene gave the 1:1 coupled product **8ba** preferentially, in a ratio of 89:11 (76% total yield, entry 3). Similarly, the *N*-pivaloyl **7c** and *N*-benzoyl **7d** derivatives resulted in the preferential formation of the 1:1 coupled products **8ca** (86:14, 84% total yield, entry 4) and **8da** (77:23, 88% total yield, entry 5), respectively. The corresponding reaction between an *N*-tosyl derivative **7e** with bromobenzene, however, failed to proceed (entry 6) due to the effects of the strong electron-withdrawing tosyl group, which is thought to decrease the ability of the imidazoline nitrogen to coordinate the ruthenium complex.

The combination of the *N*-acylarylimidazolines with ortho-substituted bromobenzenes afforded the 1:1 coupled products exclusively. Thus, the steric hindrance associated with both the acyl group and the ortho-substituted bromobenzene compounds is assumed to prevent the second coupling reaction from occurring. For example, the reaction of **7b** with 2-methoxybromobenzene (**2c**) afforded the 1:1 species **8bc** as the sole product in 71% yield. Similarly, the reaction of **7c** with 2-methylbromobenzene (**2e**) gave **8ce** in 48% yield (Scheme 3).

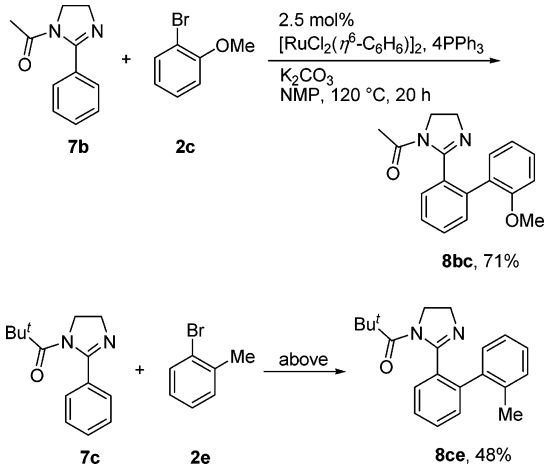
In a further step, the arylated and alkenylated 2-aryloxazolines and 2-arylimidazolines products can be readily converted to the corresponding carboxylic acids, ketones, and aldehydes, providing a facile pathway for the forma-

TABLE 3. Ruthenium-Catalyzed Ortho-Selective Direct Alkenylation of 2-(2-Methylphenyl)-2-oxazoline (1d) with Various Alkenyl Bromides 5[a]

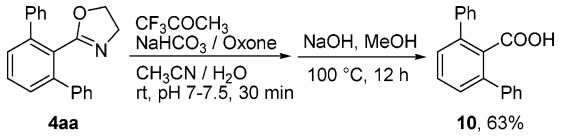
entry	substrate **1**	alkenylbromide **5**	product **6**	yield (%)
1	**1d**	((*E*)-**5a**)	(**6da**)	53 (*E*/*Z* = 91:9)
2	**1d**	((*Z*)-**5a**)	(**6da**)	63 (*E*/*Z* = 90:10)
3	**1d**	(**5b**) (*E*/*Z* = 85:15)	(**6db**)	93 (*E*/*Z* = 97:3)
4	**1d**	(**5c**)	(**6dc**)	9
			(**6db**)	43 (*E*/*Z* = 96:4)

[a] Reactions were carried out using 0.5 mmol of **1d**, 1.5 mmol of **5**, 0.02 mmol of $[RuCl_2(\eta^6\text{-}C_6H_6)]_2$, and 0.08 mmol of PPh_3 in 1 mL of NMP at 120 °C for 20 h under N_2.

SCHEME 3

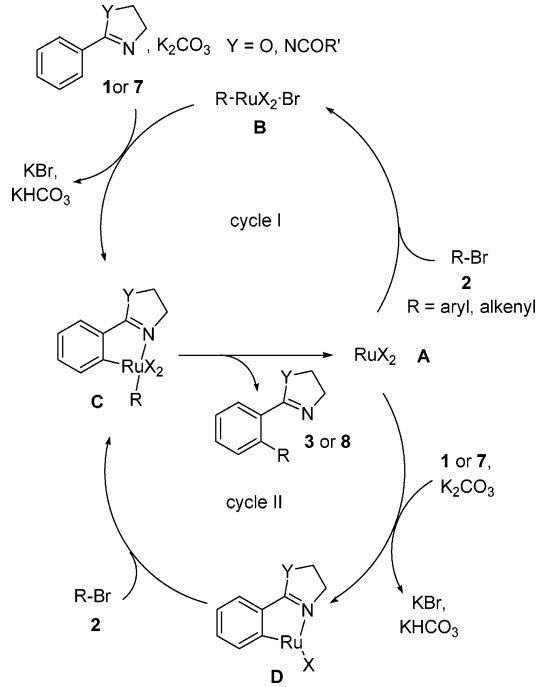


SCHEME 4



tion of *o*-aryl and diaryl aromatic compounds.[17−21] For example, treatment of 2-(2,6-diphenylphenyl)-2-oxazoline (**4aa**) with 1,1,1-trifluoroacetone, Oxone, and then sodium hydroxide[17] gave 2,6-diphenylbenzoic acid (**10**) in 63% yield (Scheme 4).

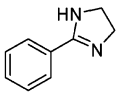
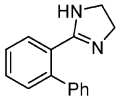
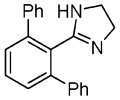
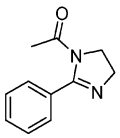
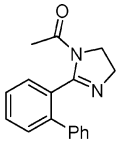
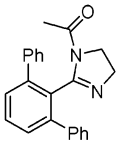
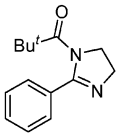
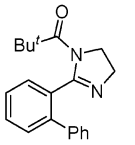
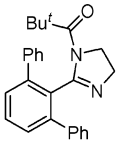
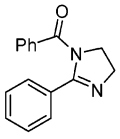
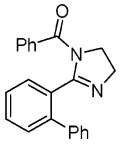
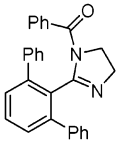
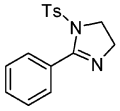
SCHEME 5. Possible Reaction Pathways



Although there is little experimental evidence at present to determine the exact reaction pathway for the direct cross-coupling process, the following two steps are believed to play some part in the catalytic pathway: (i) oxidative addition of the aryl or alkenyl halide to the ruthenium complex, to afford an aryl- or alkenylruthenium intermediate, and (ii) ortho-ruthenation of the aromatic ring directed by coordination of the oxazoline or imidazoline nitrogen to the ruthenium atom. Of the several possible reaction mechanisms, the two most likely pathways are shown in Scheme 5. In cycle I, the oxidative addition of the aryl or alkenyl halide **2** to a suitable ruthenium(II) complex **A** generates an aryl- or alkenyl-

(17) Yang, D.; Yip, Y.-C.; Wang, X.-C. *Tetrahedron Lett.* **1997**, *38*, 7083.
(18) Meyers, A. I.; Temple, D. L.; Haidukewych, D. Mihelich, E. D. *J. Org. Chem.* **1974**, *39*, 2787.
(19) Anderson, M. W.; Jones, R. C. F. *J. Chem. Soc., Perkin Trans. 1* **1986**, 205.
(20) Anderson, M. W.; Jones, R. C. F. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1995.
(21) Shi, Z.; Gu, H. *Synth. Commun.* **1997**, *27*, 2701.

TABLE 4. Ruthenium-Catalyzed Ortho-Selective Direct Arylation of Various 2-Arylimidazolines 7 with Bromobenzene (2a)[a]

entry	arylimidazoline **7**	equiv of **2a**	product **8**	product **9**	total yield (%)	ratio (**8**:**9**)
1	 (**7a**)	1.2	 (**8aa**)	 (**9aa**)	64[b]	31:69
2	**7a**	2.5	**8aa**	**9aa**	90[b]	0:100
3	 (**7b**)	1.2	 (**8ba**)	 (**9ba**)	76	89:11
4	 (**7c**)	1.2	 (**8ca**)	 (**9ca**)	84	86:14
5	 (**7d**)	1.2	 (**8da**)	 (**9da**)	88	77:23
6	 (**7e**)	1.2			0	

[a] Reactions were carried out using 0.5 mmol of **7**, 0.6 or 1.25 mmol of **2a**, 0.0125 mmol of $[RuCl_2(\eta^6\text{-}C_6H_6)]_2$, and 0.05 mmol of PPh_3 in 1 mL of NMP at 120 °C for 20 h under N_2. [b] Products were isolated after acetylation.

ruthenium intermediate **B**. Ortho-ruthenation of the aryloxazoline **1** or arylimidazoline **7** with **B** gives the corresponding ruthenacycle **C**. The coupled product **3** or **8** is then formed through reductive elimination from **C**, with the simultaneous regeneration of **A**. In cycle II, the aryloxazoline **1** or arylimidazoline **7** reacts with a suitable ruthenium(II) complex **A** to generate a ruthenacycle **D**. Subsequently, the oxidative addition of the aryl or alkenyl halide **2** to **D** affords a second ruthenacycle **C**, from which the coupled product **3** or **8** is formed through reductive elimination. The nitrogen atom-directed ortho-metalation of aromatic rings is well-known for a wide range of transition metals[22] and is the most likely mechanism in this reaction.

Conclusion

The ruthenium-catalyzed direct coupling of 2-aryl-oxazolines and 2-arylimidazolines with aryl and alkenyl halides is described. These reactions were found to occur regioselectively at the ortho position(s) of the aromatic ring. In the case of unsubstituted and para-substituted phenyloxazolines, both 1:1 and 1:2 coupled products were obtained. Reactions involving the meta-substituted phenyloxazolines and *N*-acylarylimidazolines with organic halides produced the 1:1 coupled species as the major product. This methodology provides not only a straightforward route for the direct arylation and alkenylation of 2-aryloxazolines and 2-arylimidazolines with organic halides, but also a facile method for preparing *o*-aryl and diaryl aromatic compounds, since the oxazolinyl and imidazolinyl groups can be readily converted to various functional groups.

Experimental Section

Direct Coupling Reaction of 2-Phenyl-2-oxazoline (1a) with Bromobenzene (2a). A mixture of **1a** (74.0 mg, 0.503 mmol), **2a** (196.2 mg, 1.25 mmol), K_2CO_3 (138.6 mg, 1.0 mmol), PPh_3 (13.1 mg, 0.05 mmol), and $[RuCl_2(\eta^6\text{-}C_6H_6)]_2$ (6.3 mg, 0.0126 mmol) in 1 mL of dried NMP was stirred at 120 °C for 20 h. The reaction mixture was diluted with 30 mL of Et_2O, washed with water (20 mL × 3), and dried over Na_2SO_4. After the solvent was removed in vacuo, the residue was purified by silica gel flash chromatography (hexanes−EtOAc, 2:1) to give the 1:2 coupled product **4aa** (150.5 mg, 0.503 mmol): mp 140.6−141.2 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ (ppm) 7.52 (t, J = 7.7 Hz, 1H), 7.45 (dt, J = 7.3, 1.8 Hz, 4H), 7.39 (d, J = 7.7 Hz, 2H), 7.38 (td, J = 7.3, 1.8 Hz, 4H), 7.32 (tt, J = 7.3, 1.8 Hz, 2H), 3.88 (t, J = 9.4 Hz, 2H), 3.58 (t, J = 9.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm) 163.9, 142.4, 140.9, 129.5, 128.8, 128.6, 128.0, 127.6, 127.2, 67.3, 55.1; IR (KBr) 2893, 1655, 1040, 758 cm^{-1}. Anal. Calcd for $C_{21}H_{17}NO$: C, 84.25; H, 5.72; N, 4.68. Found: C, 84.03; H, 5.85; N, 4.63.

All coupling reactions except entries 1 and 2 (Table 4) were performed using the same procedure.

Direct Coupling Reaction of 2-Phenyl-2-imidazoline (7a) with Bromobenzene (2a). A mixture of **7a** (74.0 mg, 0.503 mmol), **2a** (196.2 mg, 1.25 mmol), K_2CO_3 (138.6 mg, 1.0 mmol), PPh_3 (13.1 mg, 0.05 mmol), and $[RuCl_2(\eta^6\text{-}C_6H_6)]_2$ (6.3 mg, 0.0126 mmol) in 1 mL of dried NMP was stirred at 120 °C for 20 h. After the reaction mixture was cooled to room temperature, acetic anhydride (102.1 mg, 1.0 mmol) and THF (1 mL) were added, and the mixture was stirred at 50 °C for 2 h. The reaction mixture was diluted with 30 mL of EtOAc, washed with water (20 mL × 3), and dried over Na_2SO_4. After the solvent was removed in vacuo, the residue was purified by silica gel flash chromatography (EtOAc) to give the acety-

(22) Review: Omae, I. *Coord. Chem. Rev.* **2004**, *248*, 995.

lated 1:2 coupled product **8ba** (152.7 mg, 0.449 mmol): ^{1}H NMR ($CDCl_3$, 250 MHz) δ (ppm) 7.54−7.33 (m, 9H), 4.08−3.82 (m, 2H), 3.81−3.40 (m, 2H), 1.55 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm) 166.8, 140.4, 132.7, 131.9, 131.8, 131.71, 131.70, 130.9, 130.7, 130.2, 129.7, 128.9, 128.5, 128.3, 128.21, 128.20, 127.4, 52.5, 47.3, 23.2; IR (neat) 3244, 1638, 1557, 742, 699 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{17}N_2O$ ($M + H^+$) 265.1335, found 265.1336.

Synthesis of 2,6-Diphenylbenzoic Acid (10) from 4aa.[17] To a mixture of **4aa** (29.9 mg, 0.10 mmol) and 1,1,1-trifluoroacetone (0.2 mL, 2.2 mmol) in acetonitrile (1.5 mL) and aqueous Na_2·EDTA solution (1 mL, 4×10^{-4} M) was added successive portions of a mixture of $NaHCO_3$ (0.78 g, 9.3 mmol) and Oxone (1.84 g, 3.0 mmol) over a period of 25 min. The mixture was stirred at room temperature for 30 min. The reaction mixture was poured into water (20 mL), extracted with CH_2Cl_2 (20 mL × 3), and dried with Na_2SO_4. After the solvent was removed, the residue was dissolved in methanol (1 mL). To this solution was added 30% aqueous NaOH solution (3 mL) and the mixture was refluxed for 16 h. The reaction mixture was diluted with water (20 mL) and washed with CH_2Cl_2 (10 mL). The aqueous layer was acidified by 2 N HCl, extracted with EtOAc (20 mL × 3), and dried over $MgSO_4$. Solvent removal in vacuo afforded a white solid **10** (17.4 mg, 0.063 mmol): mp 187.6−188.4 °C (lit.[23] mp 184 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.52 (t, $J = 7.5$ Hz, 1H), 7.43−7.35 (m, 12H); ^{13}C NMR($CDCl_3$, 100 MHz) δ (ppm) 173.5, 140.3, 140.2, 129.6, 129.0, 128.4, 128.3, 127.6, 119.6; IR (KBr) 2923, 1698, 1299 cm^{-1}.

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Supporting Information Available: General experimental methods and analytical data for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

JO050031I

(23) T. Mukai, H. Tsuruta, T. Nozoe, *Nippon Kagaku Zasshi* **1968**, *89*, 991; *Chem. Abstr.* **1969**, *70*, 96367.