

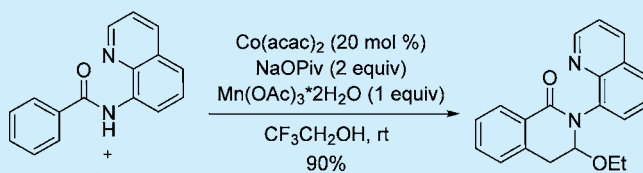
Cobalt-Catalyzed, Aminoquinoline-Directed Coupling of sp^2 C–H Bonds with Alkenes

Liene Grigorjeva and Olafs Daugulis*

Department of Chemistry, University of Houston, Houston, Texas 77204-5003, United States

Supporting Information

ABSTRACT: A method for cobalt-catalyzed, aminoquinoline-directed *ortho*-functionalization of sp^2 C–H bonds with alkenes has been developed. Reactions proceed at room temperature in trifluoroethanol solvent, use oxygen from air as an oxidant, and require $Mn(OAc)_3$ as a cocatalyst. Benzoic, heteroaromatic, and acrylic acid aminoquinoline amides react with ethylene as well as mono- and disubstituted alkenes affording products in good yields. Excellent functional group tolerance is observed; halogen, nitro, ether, and unprotected alcohol functionalities are compatible with the reaction conditions.



Transition-metal catalyzed coupling of sp^2 C–H bonds with alkenes is perhaps one of the earliest synthetically useful C–H bond functionalization reactions.¹ Pioneering reports by Fujiwara,² Lewis,^{3a} and Murali^{3b} have disclosed alkene and arene hydroarylation methodology. Following these discoveries, a substantial number of arene/alkene couplings have been developed. Currently, even directed, selective *meta*-functionalization of arenes is possible.⁴ However, most of the catalytic processes employ scarce second-row transition metal catalysts.⁵ Relatively few papers describe use of cobalt- or nickel-catalyzed arene C–H functionalization by alkenes.⁶ Furthermore, the scope of the transformations is often limited, as acrylates, vinylsilanes, or styrenes are the most commonly employed coupling partners. Use of other functionalized alkenes or olefins that are prone to double bond migration,^{5o} such as 1-butene, is rare.^{5a,n,t,u,6b,d}

In 2005, we introduced 8-aminoquinoline, picolinamide, and 2-pyridinylmethylamine auxiliaries for palladium-catalyzed C–H bond arylation by aryl iodides.^{7a,b} The auxiliaries were subsequently used for copper-catalyzed sp^2 C–H bond sulfonylation, amination, fluorination, and etherification.^{7c–f} Others have extensively used bidentate, monoanionic directing groups for palladium-, ruthenium-, iron-, and copper-catalyzed reactions.⁸ Furthermore, we have recently reported cobalt-catalyzed aminoquinoline- and picolinamide-directed coupling of alkynes with sp^2 C–H bonds.⁹ Excellent functional group tolerance was observed, and both internal and terminal alkynes

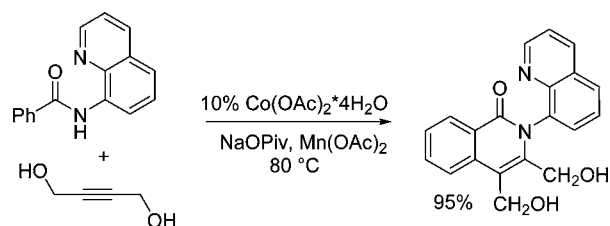
are competent substrates for the coupling. The reaction employs $Co(OAc)_2 \cdot 4H_2O$ as a catalyst, $Mn(OAc)_2$ as a cocatalyst, and oxygen from air as a terminal oxidant (Scheme 1). It is likely that alkenes would also participate in similar coupling reactions, since both alkenes and alkynes can insert into $Co(III)$ –C bonds.¹⁰ Relevant low-valent cobalt-catalyzed, directed hydroarylation of arenes has been described by Yoshikai.^{6c–e} Chatani has reported ruthenium-catalyzed *ortho*-alkylation of aminoquinoline amides by electron-deficient alkenes.^{8d} We report here a method for cobalt-catalyzed, aminoquinoline-directed sp^2 C–H bond coupling with alkenes.

Table 1. Optimization of Reaction Conditions^a

entry	catalyst	cooxidant	<i>t</i> , time	yield of 2, %
1 ^b	$Co(OAc)_2$	$AgNO_3$	80 °C, 16 h	16
2 ^b	$Co(acac)_2$	$AgNO_3$	80 °C, 16 h	66
3	$Co(acac)_2$	none	80 °C, 16 h	15
4 ^c	$Co(acac)_2$	$Mn(OAc)_2$	80 °C, 16 h	41
5 ^c	$Co(acac)_2$	$Mn(OAc)_3 \cdot 2H_2O$	80 °C, 16 h	90
6 ^c	none	$Mn(OAc)_3 \cdot 2H_2O$	80 °C, 16 h	<1
7 ^{c,d}	$Co(acac)_2$	$Mn(OAc)_3 \cdot 2H_2O$	rt, 16 h	93

^aAmide (0.1 mmol), styrene (0.12 mmol), catalyst (0.02 mmol), base (0.2 mmol), CF_3CH_2OH (1 mL), under air. Yield determined by NMR of crude reaction mixtures; 1,1,2-trichloroethane internal standard. ^b $AgNO_3$, 2 equiv. ^c $Mn(OAc)_2$ or $Mn(OAc)_3 \cdot 2H_2O$, 0.5 equiv. ^dReaction open to air.

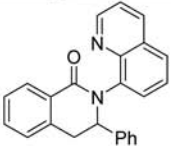
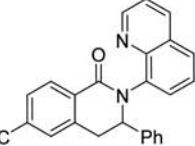
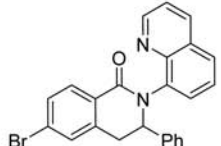
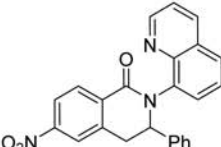
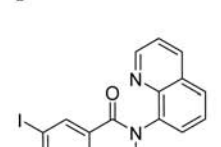
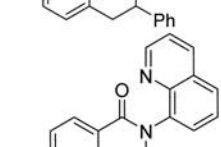
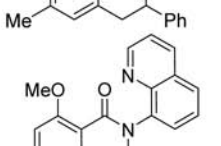
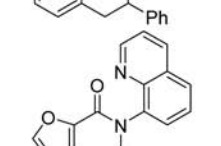
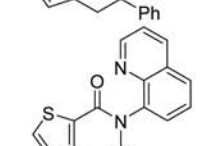
Scheme 1. Coupling with Alkynes



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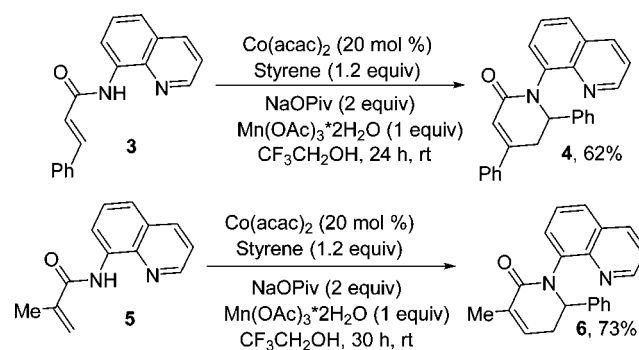
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Table 2. Reaction Scope with Respect to Amides^a

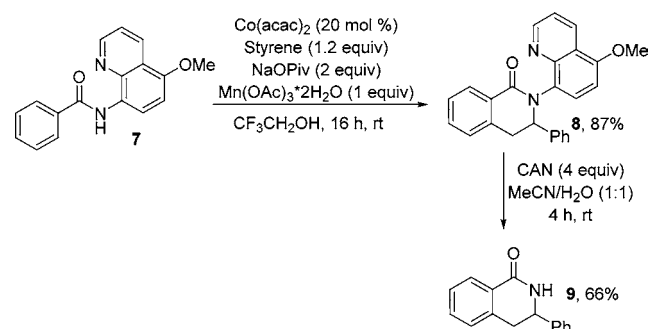
$\text{Ar}-\text{C}(=\text{O})\text{NH}-\text{quinoline} \xrightarrow[\text{CF}_3\text{CH}_2\text{OH, rt}]{\begin{array}{l} \text{Co}(\text{acac})_2 \text{ (20 mol \%)} \\ \text{Styrene (1.2 equiv)} \\ \text{NaOPiv (2 equiv)} \\ \text{Mn}(\text{OAc})_3 \cdot 2\text{H}_2\text{O (0.5 equiv)} \end{array}} \text{Product}$			
entry	Ar	product	yield, %
1	C ₆ H ₅		75
2	4-CF ₃ C ₆ H ₄		70
3	4-BrC ₆ H ₄		64
4	4-NO ₂ C ₆ H ₄		71
5	3-IC ₆ H ₄		61
6	4-MeC ₆ H ₄		80
7 ^b	2-MeOC ₆ H ₄		85
8 ^b	2-furyl		81
9 ^b	2-thiophenyl		75

^aAmide (0.5 mmol), styrene (0.6 mmol), Co(acac)₂ (0.1 mmol), base (1 mmol), Mn(OAc)₃·2H₂O (0.25 mmol), trifluoroethanol (5 mL), reaction vessel open to air. Yields are isolated yields. Please see Supporting Information for details. ^bCooxidant Mn(OAc)₃·2H₂O, 0.5 mmol.

Scheme 2. Vinylamide Reactions



Scheme 3. Removable Directing Group



Based on previous results,⁹ we decided to use readily available cobalt(II) catalysts in trifluoroethanol solvent and sodium pivalate base. The reaction optimization was carried out with respect to the catalyst, reaction temperature, and cooxidant (Table 1). Cobalt(II) acetate is an inferior catalyst compared with Co(acac)₂ (entry 1 vs 2). Silver nitrate (entry 2) and Mn(OAc)₃·2H₂O (entry 5) are competent cooxidants, while Mn(OAc)₂ is somewhat inferior (entry 4). Reaction under air without a cooxidant affords low conversion (entry 3), while the presence of a Co catalyst is essential (entry 6). The reaction can be performed at room temperature, and nearly complete conversion was observed (entry 7).

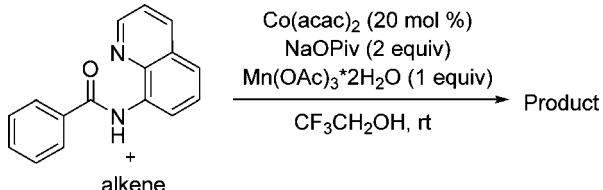
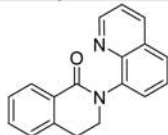
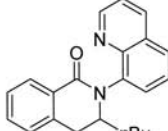
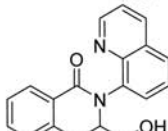
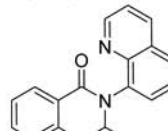
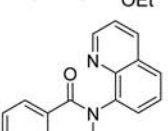
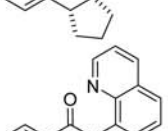
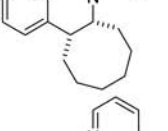
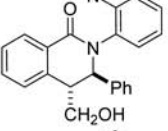
The reaction scope with respect to amides is illustrated in Table 2. Electron-poor (entries 2–5) as well as electron-rich (entries 6, 7) amides are reactive. A number of functionalities, such as a bromine, iodine (entries 3, 5), and nitro moiety (entry 4) are compatible with the reaction conditions. Furthermore, heterocyclic amides such as furane and thiophenecarboxylic acid derivatives (entries 8 and 9) are reactive affording coupling products in good yields. For electron-rich and heterocyclic amides, 1 equiv of cooxidant is necessary to obtain reasonable reaction rates.

The reactions are not limited to aromatic amides. Aminoquinoline amides of cinnamic and methacrylic acids can be coupled with styrene to afford compounds **4** and **6** in good yields (Scheme 2).

Recently, Chen has reported a modified 8-aminoquinoline auxiliary that can be removed by treatment with ceric ammonium nitrate.¹¹ 8-Amino-5-methoxyquinoline benzamide can be coupled with styrene to give product **8** in excellent yield (Scheme 3). The auxiliary can be cleaved affording heterocycle **9** in 66% yield.

The reaction scope with respect to alkenes is presented in Table 3. Ethylene is reactive giving a dihydroisoquinolinone derivative in 72% yield (entry 1). Interestingly, 1-butene affords

Table 3. Reaction Scope with Respect to Alkenes

			
entry	alkene	product	yield, %
1	ethylene		72
2 ^b	1-hexene		89
3	2-propenol		55
4	EtOCH=CH ₂		90
5	cyclopentene		88
6	cis-cyclooctene		73
7 ^c	<i>E</i> -cinnamyl alcohol		53
8 ^c	<i>Z</i> -cinnamyl alcohol		52

^aAmide (0.5 mmol), alkene (0.6 mmol), Co(acac)₂ (0.1 mmol), base (1 mmol), Mn(OAc)₃·2H₂O (0.5 mmol), trifluoroethanol (5 mL), reaction vessel open to air. Yields are isolated yields. Please see Supporting Information for details. ^bRegioisomer ratio 10/1. ^cCobalt(II) acetylacetonate (0.25 mmol), 80 °C.

the product as a 10/1 regioisomer mixture (entry 2) representing a relatively rare example of isomerizable alkene use in C–H/alkene coupling. In all other cases, only a single isomer of product

was observed. The reaction tolerates a free hydroxyl group (entries 3, 7, and 8). Ether is also compatible with the reaction conditions (entry 4). Cyclic disubstituted alkenes such as cyclopentene and cyclooctene can be coupled in good yields (entries 5 and 6). *E*-Cinnamyl alcohol affords the *trans*-product in 53% yield. Interestingly, *Z*-cinnamyl alcohol also gives the *trans*-product in nearly identical yield (entry 8). Unreacted cinnamyl alcohol from entry 8 was recovered as a mixture of *cis* and *trans* isomers.

In conclusion, we have developed a simple method for cobalt-catalyzed, aminoquinoline-directed coupling of sp² C–H bonds with alkenes. Reactions proceed at room temperature in trifluoroethanol solvent, use oxygen from air as an oxidant, and require Mn(OAc)₃ as a cocatalyst. Benzoic, heteroaromatic, and acrylic acid derivatives can be reacted with ethylene as well as mono- and disubstituted alkenes affording products in good yields. Excellent functional group tolerance is observed.

■ ASSOCIATED CONTENT

Supporting Information

Detailed experimental procedures and characterization data for new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: olafs@uh.edu.

Notes

The authors declare no competing financial interest.

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■ REFERENCES

- Reviews: (a) Messaoudi, S.; Brion, J.-D.; Alami, M. *Eur. J. Org. Chem.* **2010**, 6495. (b) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624. (c) Ritleng, V.; Sirlin, C.; Pfeffer, M. *Chem. Rev.* **2002**, *102*, 1731. (d) Bras, J. L.; Muzart, J. *Chem. Rev.* **2011**, *111*, 1170.
- Gao, K.; Yoshikai, N. *Acc. Chem. Res.* **2014**, *47*, 1208.
- Moritani, I.; Fujiwara, Y. *Tetrahedron Lett.* **1967**, 1119.
- (a) Lewis, L. N.; Smith, J. F. *J. Am. Chem. Soc.* **1986**, *108*, 2728. (b) Murai, S.; Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N. *Nature* **1993**, *366*, 529.
- Leow, D.; Li, G.; Mei, T.-S.; Yu, J.-Q. *Nature* **2012**, *486*, 518.
- Selected examples: Ru: (a) Schinkel, M.; Marek, I.; Ackermann, L. *Angew. Chem., Int. Ed.* **2013**, *52*, 3977. (b) Lail, M.; Arrowood, B. N.; Gunnoe, T. B. *J. Am. Chem. Soc.* **2003**, *125*, 7506. (c) Martinez, R.; Chevalier, R.; Darses, S.; Genet, J.-P. *Angew. Chem., Int. Ed.* **2006**, *45*, 8232. (d) Ackermann, L.; Wang, L.; Wolfram, R.; Lygin, A. V. *Org. Lett.* **2012**, *14*, 728. Pd: (e) Jia, C.; Piao, D.; Oyamada, J.; Lu, W.; Kitamura, T.; Fujiwara, Y. *Science* **2000**, *287*, 1992. (f) Zhang, Y.-H.; Shi, B.-F.; Yu, J.-Q. *J. Am. Chem. Soc.* **2009**, *131*, 5072. (g) Wang, D.-H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2011**, *133*, 5767. (h) Miura, M.; Tsuda, T.; Satoh, T.; Pivsa-Att, S.; Nomura, M. *J. Org. Chem.* **1998**, *63*, 5211. (i) Tani, M.; Sakaguchi, S.; Ishii, Y. *J. Org. Chem.* **2004**, *69*, 1221. (j) García-Rubia, A.; Fernández-Ibáñez, M. A.; Arrayás, R. G.; Carretero, J. C. *Chem.—Eur. J.* **2011**, *17*, 3567. (k) Boele, M. D. K.; van Strijdonck, G. P. F.; de Vries, A. H. M.; Kamer, P. C. J.; de Vries, J. G.; van Leeuwen, P. W. N. *M. J. Am. Chem. Soc.* **2002**, *124*, 1586. (l) Dams, M.; De Vos, D. E.; Celen, S.; Jacobs, P. A. *Angew. Chem., Int. Ed.* **2003**, *42*, 3512. (m) Li, Y.; Cai, G.; Fu, Y.; Wan, X.; Shi, Z. *J. Am. Chem. Soc.* **2007**, *129*, 7666. Rh: (n) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2006**,

128, 5604. (o) Lenges, C. P.; Brookhart, M. *J. Am. Chem. Soc.* **1999**, *121*, 6616. (p) Neely, J. M.; Rovis, T. *J. Am. Chem. Soc.* **2013**, *135*, 66. (q) Patureau, F.; Glorius, F. *J. Am. Chem. Soc.* **2010**, *132*, 9982. (r) Rakshit, S.; Grohmann, C.; Besset, T.; Glorius, F. *J. Am. Chem. Soc.* **2011**, *133*, 2350. (s) Tsai, A. S.; Brasse, M.; Bergman, R. G.; Ellman, J. A. *Org. Lett.* **2011**, *13*, 540. (t) Li, X.; Gong, X.; Zhao, M.; Song, G.; Deng, J.; Li, X. *Org. Lett.* **2011**, *13*, 5808. (u) Wang, D.-H.; Engle, K. M.; Shi, B.-F.; Yu, J.-Q. *Science* **2010**, *327*, 315.

(6) Ni: (a) Nakao, Y.; Kashihara, N.; Kanyiva, K. S.; Hiyama, T. *Angew. Chem., Int. Ed.* **2010**, *49*, 4451. Co: (b) Ilies, L.; Chen, Q.; Zeng, X.; Nakamura, E. *J. Am. Chem. Soc.* **2011**, *133*, 5221. (c) Gao, K.; Yoshikai, N. *J. Am. Chem. Soc.* **2011**, *133*, 400. (d) Gao, K.; Yoshikai, N. *Angew. Chem., Int. Ed.* **2011**, *50*, 6888. (e) Lee, P.-S.; Yoshikai, N. *Angew. Chem., Int. Ed.* **2013**, *52*, 1240.

(7) (a) Zaitsev, V. G.; Shabashov, D.; Daugulis, O. *J. Am. Chem. Soc.* **2005**, *127*, 13154. (b) Shabashov, D.; Daugulis, O. *J. Am. Chem. Soc.* **2010**, *132*, 3965. (c) Tran, L. D.; Popov, I.; Daugulis, O. *J. Am. Chem. Soc.* **2012**, *134*, 18237. (d) Tran, L. D.; Roane, J.; Daugulis, O. *Angew. Chem., Int. Ed.* **2013**, *52*, 6043. (e) Truong, T.; Klimovica, K.; Daugulis, O. *J. Am. Chem. Soc.* **2013**, *135*, 9342. (f) Roane, J.; Daugulis, O. *Org. Lett.* **2013**, *15*, 5842.

(8) Selected examples: Ni: (a) Aihara, Y.; Chatani, N. *J. Am. Chem. Soc.* **2014**, *136*, 898. (b) Song, W.; Lackner, S.; Ackermann, L. *Angew. Chem., Int. Ed.* **2014**, *53*, 2477. Fe: (c) Asako, S.; Ilies, L.; Nakamura, E. *J. Am. Chem. Soc.* **2013**, *135*, 17755. Ru: (d) Rouquet, G.; Chatani, N. *Chem. Sci.* **2013**, *4*, 2201. Pd: (e) Zhang, S.-Y.; He, G.; Nack, W. A.; Zhao, Y.; Li, Q.; Chen, G. *J. Am. Chem. Soc.* **2013**, *135*, 2124. (f) He, G.; Chen, G. *Angew. Chem., Int. Ed.* **2011**, *50*, 5192. Cu: (g) Nishino, M.; Hirano, K.; Satoh, T.; Miura, M. *Angew. Chem., Int. Ed.* **2013**, *52*, 4457.

(9) Grigorjeva, L.; Daugulis, O. *Angew. Chem., Int. Ed.* DOI: 10.1002/anie.201404579.

(10) (a) Brookhart, M.; Volpe, A. F., Jr.; Lincoln, D. M.; Horvath, I. T.; Millar, J. M. *J. Am. Chem. Soc.* **1990**, *112*, 5634. (b) Schmidt, G. F.; Brookhart, M. *J. Am. Chem. Soc.* **1985**, *107*, 1443.

(11) He, G.; Zhang, S.-Y.; Nack, W. A.; Li, Q.; Chen, G. *Angew. Chem., Int. Ed.* **2013**, *52*, 11124.