Published in final edited form as:

J Am Chem Soc. 2015 February 4; 137(4): 1408–1411. doi:10.1021/ja512306a.

Rh-Catalyzed Decarbonylative Coupling with Alkynes via C–C Activation of Isatins

Rong Zeng and Guangbin Dong*

Department of Chemistry, University of Texas at Austin, Austin, Texas 78712, United States

Abstract

Herein we report a [5+2-1] transformation through catalytic decarbonylative coupling between isatins and alkynes, which provides a unique way to synthesize 2-quinolinone derivatives. A broad range of alkynes can be coupled efficiently with high regioselectivity. This reaction is proposed to go through C–C activation of isatins, followed by decarbonylation and alkyne insertion. Directing group (DG) plays a critical role in this transformation. Assisted by the DG, the C–C cleavage of isatins occurs at room temperature.

Graphical Abstract

Cycloaddition reactions, the [X+Y(+Z)] transformation, are a powerful way to construct rings by uniting multiple π systems.¹ Alternatively, a complementary strategy is through cleavage of a C–C bond² in a cyclic compound followed by insertion of a 2π -unsaturated unit (e.g. olefins or alkynes). In particular, when cyclic ketones are employed as the substrates, C–C cleavage accompanied by CO extrusion and 2π -insertion offers a distinct approach to build ring structures, because it represents a unique [X+Y-1] transformation.^{3,4} While Murakami/Ito demonstrated stoichiometric and catalytic decarbonylation of strained and unstrained cyclic ketones leading to ring contraction two decades ago,⁵ such transformations coupled with 2π -insertion have been much underdeveloped to date. The intermolecular decarbonylative couplings of cyclobutenediones and cyclobutenones with norbornene and ethylene were first reported by Kondo/Mitsudo (Scheme 1A).^{6a-6b} Yamamoto later developed a related intramolecular coupling between squaric acid-derivatives and olefins.^{6c} Very recently, our group described a decarbonylative coupling of benzocyclobutenones with alkynes to prepare fused indene compounds (Scheme 1B).⁷

Corresponding Author: gbdong@cm.utexas.edu.

Supporting Information Experimental procedures; spectral data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

Notes: The authors declare no competing financial interests.

While efficient, these [4+2-1] reactions are limited to highly strained four-membered ring ketones. An intriguing question is whether less strained systems, such as five- or six-membered rings, can be used as the substrates for the decarbonylative C–C activation/ 2π -insertion reaction, which, to the best of our knowledge, has not been explored previously. Herein, as an exploratory study, we describe our development of a catalytic [5+2-1] transformation⁸ through directed C–C activation of isatins,⁹ a five-membered ring ketone, followed by decarbonylation and intermolecular alkyne insertion (Scheme 1C). This method provides a distinct strategy to synthesize various 2-quinolinone derivatives from isatins.

Compared to four-membered ring compounds, one key concern of activating a less-strained C–C bond is the competing C–H activation. While a C–C σ bond is generally weaker than a C–H bond, C–H activation is often kinetically more favorable.¹⁰ As illustrated in Scheme 2, when isatin **1** is employed as the substrate, both C–H and C–C activation pathways are possible, leading to either *ortho*-vinylation or decarbonylative ring expansion. Given that directed addition of aryl C–H bonds across alkenes or alkynes is known to be efficient,¹¹ selective activation/subsequent functionalization of the C–C bond in isatins can be challenging.¹²

(1)

To address the above challenge, we hypothesize that, through *control of the orientation of the directing group* (DG),¹³ it is likely that a chemoselective activation of the C–C bond can be achieved. Given that the carbonyl group is significantly larger than the hydrogen, increasing steric hindrance on the “back” site of the DG should minimize the conformation that leads to C–H activation (e.g. Eq 1). To examine this hypothesis, two DGs with different steric properties were evaluated initially (Eq 2). While both provided the desired 2-quinolinone products, the 3-methyl-2-pyridyl group¹⁴ (isatin **1a**) showed superior selectivity compared to the corresponding 2-pyridyl group (**1b**). For example, under the optimized reaction conditions (“standard conditions”), isatin **1a** afforded the desired decarbonylative ‘cut and sew’ product **3aa** in 88% yield without any observable C–H activation products; in contrast, with 2-pyridyl as the DG, a significant amount of C–H vinylation (including 4% C–H-activation only and 3% sequential C–C/C–H-activation products)¹⁵ and decomposition products were formed.

Control experiments were subsequently conducted to understand the role of each reactant (Table 1). In the absence of the Rh catalyst, no desired product was observed (Entry 2). Use of Wilkinson's catalyst $[\text{Rh}(\text{PPh}_3)_3\text{Cl}]$ instead gave only 8% of the desired product together with high recovery of the starting material (Entry 3). Other Rh(I) catalysts, such as

[Rh(coe)₂Cl]₂, [Rh(C₂H₄)₂Cl]₂ and [Rh(CO)₂Cl]₂, showed lower efficiency (Entries 4-6). Employment of other metals, such as Ru₃(CO)₁₂ and Co₂(CO)₈, didn't afford any desired product (Entries 7 and 8). Addition of phosphine ligands all inhibited the reaction to various extents (Entries 9-11). Solvent effect was also surveyed: toluene proved less effective (Entry 12); DCE completely decomposed the starting material (Entry 13); dioxane worked almost equally well as chlorobenzene affording 2-quinolinone **3aa** in 84% yield (Entry 14). Decreasing the temperature to 150 °C resulted in lower conversion (Entry 15).

The reaction scope was first tested using substrate **1a** with different alkynes under the optimized conditions (Table 2). Both aryl and alkyl substituted internal alkynes with various electronic properties all worked very well affording high yields of the corresponding 2-quinolinones. Heterocycles, such as pyridine (**2d**) and thiophene (**2e**), are tolerated; unprotected alcohols, esters and ketones are also compatible due to the pH and redox neutral conditions. For unsymmetrical internal alkynes, good to excellent regioselectivity was observed. It is interesting to note that the major regioisomer tends to have the more sterically hindered substituent at the 4-position of the 2-quinolinone, though the exact reason is unclear. The structures of the major regioisomers were further confirmed by 1D-NOESY study and/or X-ray crystallography. Terminal alkynes,¹⁶ such as 1-decyne **2h**, can also be used as the coupling partner albeit giving a relatively lower yield (50% for the major regioisomer) and a moderate selectivity (6/1).

The scope of the isatins and DGs was next investigated and compared (Table 3). Besides pyridine-based groups, other DGs are also effective, such as 1*H*-indazol-1-yl (**3ca**) and oxazolynyl groups (**3da** and **3ha**).¹⁷ As expected, while no *ortho*-C–H activation was observed with the 1*H*-indazol-1-yl DG, about 6% yield of *ortho*-C–H vinylation product was found with the less hindered oxazolynyl DG. Isatin substrates with a methyl group at C-5 position led to the corresponding product **3ea** in 92% yield. In addition, the *N*-benzyl protected isatin worked equally well (**3fa**). Finally, the 7-*aza*-isatin compound was also found to be a viable substrate, giving an interesting 1,8-naphthyridinone (**3ga**) as the product.

Regarding the mechanistic features, a key question is why the reaction requires a relatively high temperature to take place? Consequently, it is natural to be concerned about the ease of oxidative addition of Rh into the isatin C–C bonds. To probe the mechanism, reaction of isatin **1a** with stoichiometric [Rh(C₂H₄)₂Cl]₂ was investigated (Scheme 3). Interestingly, the C–C cleavage occurred smoothly even at room temperature (rt).¹⁸ The red color of isatin disappeared and a light yellow solid slowly precipitated, which is presumably a chlorine-bridged oligomer (or dimer). This Rh complex was then treated with excess pyridine, affording a mixture of two diastereomers (**M1** and **M2**), which are more soluble and can be separated using silica-gel flash chromatography. Another reason of adding pyridine is to mimic the real reaction conditions in which excess substrate (pyridine-like) is present. Both **M1** and **M2** are expected to be the products after C–C activation and CO deinsertion, the structures of which were confirmed through NMR, IR and HRMS. The Rh–CO stretching frequencies for **M1** and **M2** are 2067 and 2044 cm^{–1} respectively. In addition, the structure of **M1** was further unambiguously confirmed by X-ray crystallography.¹⁹ It is worthy to note that when the parent *N*-methylisatin (without DG) was used as the substrate, no C–C

activation product was observed under either the catalytic or stoichiometric-metal conditions.²⁰

Reaction of complex **M1** and **M2** with alkyne **2a** was next studied. It is not surprising to find that alkyne insertion did not occur when the temperature was below 130 °C. Nevertheless, at 160 °C the quinolinone product (**3aa**) was isolated in 59% yield. Similar experiments have also been conducted using the C–C cleavage complex (the precursor for **M1/M2**) in the absence of added pyridine. Again, its decarbonylative coupling with alkyne **2a** showed no significant reactivity below 130 °C. In addition, complex **M1** was found to catalyze the reaction giving a good yield of the product (Eq 3).

(3)

From these studies, the following information can be obtained. First, the observations are consistent with the proposed mechanism involving directed C–C activation (Scheme 2, left cycle). Second, the DG plays a critical role in assisting the C–C activation. Third, there is a remarkable reaction-temperature difference between the C–C activation and the following steps in stoichiometric metal settings. More in-depth mechanistic study is still ongoing.

In summary, we have developed a Rh-catalyzed [5+2-1] transformation through catalytic C–C activation of isatins followed by decarbonylative coupling with alkynes. A range of isatin and alkyne substrates are suitable for this reaction providing the corresponding poly-substituted 2-quinolinones in good to excellent yields. The reaction conditions are both pH and redox neutral, which is the key for the tolerance of various functional groups and heterocycles. The activation of the C–C bond in a relatively less strained cyclic ketone followed by 2 π -insertion should have broad implications beyond this work. Efforts on expanding the reaction scope with alkenes and developing C–C activation of less strained ketones in the absence of auxiliary DGs are currently undertaken in our laboratory.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We thank UT Austin and CPRIT for a startup fund, NIGMS (R01GM109054-01) and the Welch Foundation (F 1781) for research grants. GD is a Searle Scholar. Prof. P. Liu from University of Pittsburgh is acknowledged for DFT calculation of the ring strain of isatin. We thank Ms R. E. Whittaker for checking the reproducibility of the experiment, and Dr. M. C. Young for proofreading the manuscript. We are also grateful to Johnson Matthey for a generous donation of Rh.

References

1. For selected books on cycloadditions, see: Kobayashi S, Jørgensen KA. Cycloaddition Reactions in Organic Synthesis. Wiley-VCH Verlag GmbH 2001; Curran DP, Lautens M, Harmata M. Advances in Cycloaddition. 1-6 JAI, Press Inc 1988-1999; For selected reviews on cycloadditions, see: Yu ZX, Wang Y, Wang Y. Chem Asian J. 2010; 5:1072. [PubMed: 20432504] Schore NE. Chem Rev. 1988; 88:1081. Murakami M. Angew Chem Int Ed. 2003; 42:718. Perreault S, Rovis T. Chem Soc Rev. 2009; 38:3149. [PubMed: 19847348] Varela JA, Saá C. Chem Rev. 2003; 103:3787. [PubMed: 12964884] Ylijoki KEO, Stryker JM. Chem Rev. 2012; 113:2244. [PubMed: 23153111] Heller B, Hapke M. Chem Soc Rev. 2007; 36:1085. [PubMed: 17576476]
2. For selected reviews on transition-metal-mediated C–C bond activations, see: Jones WD. Nature. 1993; 364:676. Murakami M, Ito Y. Top Organomet Chem. 1999; 3:97. Rybtchinski B, Milstein D. Angew Chem Int Ed. 1999; 38:870. Perthuisot C, Edelbach BL, Zubris DL, Simhai N, Iverson CN, Müller C, Satoh T, Jones WD. J Mol Catal A. 2002; 189:157. van der Boom ME, Milstein D. Chem Rev. 2003; 103:1759. [PubMed: 12744693] Jun CH. Chem Soc Rev. 2004; 33:610. [PubMed: 15592626] Satoh T, Miura M. Top Organomet Chem. 2005; 14:1. Jun CH, Park JW. Top Organomet Chem. 2007; 24:117. Necas D, Kotora M. Curr Org Chem. 2007; 11:1566. Crabtree RH. Chem Rev. 1985; 85:245. Kondo T, Mitsudo TA. Chem Lett. 2005; 34:1462. Ruhland K. Eur J Org Chem. 2012; 2683. Korotvicka A, Necas D, Kotora M. Curr Org Chem. 2012; 16:1170. Seiser T, Saget T, Tran DN, Cramer N. Angew Chem Int Ed. 2011; 50:7740. Murakami M, Matsuda T. Chem Commun. 2011; 47:1100. Dermenci A, Coe PW, Dong G. Org Chem Front. 2014; 1:567. Dong G. C–C bond activation in Topics in Current Chemistry. Springer-Verlag Berlin Heidelberg 2014; 346
3. For a recent review of decarbonylative C–C bond formation, see: Dermenci A, Dong G. Sci China, Chem. 2013:685.
4. For representative works of catalytic C–C activation with subsequent insertion of olefins or alkynes without decarbonylation, see: for biphenylenes: Edelbach BL, Lachicotte RJ, Jones WD. Organometallics. 1999; 18:4040. For cyclobutenones: Huffman MA, Liebeskind LS. J Am Chem Soc. 1990; 112:8617. For cyclobutenediones: South MS, Liebeskind LS. J Am Chem Soc. 1984; 106:4181. For cyclobutanones: Murakami M, Itahashi T, Ito Y. J Am Chem Soc. 2002; 124:13976. [PubMed: 12440879] For linear ketones: Wentzel MT, Reddy VJ, Hyster TK, Douglas CJ. Angew Chem Int Ed. 2009; 48:6121. Dreis AM, Douglas CJ. J Am Chem Soc. 2009; 131:412. [PubMed: 19105696] For cyclopropanes: Narasaka K, Koga Y. Chem Lett. 1999; 28:705. For cyclopropenes: Li C, Zhang H, Feng J, Zhang Y, Wang J. Org Lett. 2010; 12:3082. [PubMed: 20536190] For vinylcyclopropanes: Jiao L, Lin M, Zhuo LG, Yu ZX. Org Lett. 2010; 12:2528. [PubMed: 20465285] Wender PA, Takahashi H, Witulski B. J Am Chem Soc. 1995; 117:4720. For amino cyclopropanes: Shaw MH, Melikhova EY, Kloer DP, Whittingham WG, Bower JF. J Am Chem Soc. 2013; 135:4992. [PubMed: 23488745] For cyclobutenols: Ishida N, Sawano S, Masuda Y, Murakami M. J Am Chem Soc. 2012; 134:17502. [PubMed: 23043426] For methylenecyclopropanes: Weintz HJ, Binger P. Tetrahedron Lett. 1985; 26:4075. For C–CN bond cleavage: Nakao Y, Oda S, Hiyama T. J Am Chem Soc. 2004; 126:13904. [PubMed: 15506734]
5. Murakami M, Amii H, Ito Y. Nature. 1994; 370:540. Murakami M, Amii H, Shigeto K, Ito Y. J Am Chem Soc. 1996; 118:8285. Matsuda T, Shigeno M, Murakami M. Chem Lett. 2006; 35:288. For a seminal example of decarbonylation of linear diketones, see: Kaneda K, Azuma H, Wayaku M, Tehanishi S. Chem Lett. 1974; 3:215.
6. Kondo T, Nakamura A, Okada T, Suzuki N, Wada K, Mitsudo TA. J Am Chem Soc. 2000; 122:6319. Kondo T, Taguchi Y, Kaneko Y, Niimi M, Mitsudo TA. Angew Chem Int Ed. 2004; 43:5369. Yamamoto Y, Kuwabara S, Hayashi H, Nishiyama H. Adv Synth Catal. 2006; 348:2493. A related decarbonylative ring expansion of cyclobutanones, see: Wender PA, Carrea AG, Sato Y, Sun R. J Am Chem Soc. 2000; 122:7815.
7. Chen PH, Xu T, Dong G. Angew Chem Int Ed. 2014; 53:1674.
8. It is noteworthy that related [5+2-1] transformations through cleavage of polarized C–O, C–N and very recently C–S bonds were first reported by Matsubara and Kurahashi using Ni catalysts, see: Kajita Y, Kurahashi T, Matsubara S. J Am Chem Soc. 2008; 130:17226. [PubMed: 19049285] Kajita Y, Matsubara S, Kurahashi T. J Am Chem Soc. 2008; 130:6058. [PubMed: 18412348] Fujiwara K, Kurahashi T, Matsubara S. Org Lett. 2010; 12:4548. [PubMed: 20863073] Fujiwara K, Kurahashi T, Matsubara S. Chem Lett. 2011; 40:322. Inami T, Baba Y, Kurahashi T, Matsubara S.

- Org Lett. 2011; 13:1912. [PubMed: 21381687] Inami T, Kurahashi T, Matsubara S. Chem Commun. 2011; 47:9711. Ochi Y, Kurahashi T, Matsubara S. Org Lett. 2011; 13:1374. [PubMed: 21332138] Inami T, Kurahashi T, Matsubara S. Org Lett. 2014; 16:5660. [PubMed: 25347619] For the Ni-catalyzed [6+2-2] transformations through denitrogenation, see: Miura T, Yamauchi M, Murakami M. Org Lett. 2008; 10:3085. [PubMed: 18558759] Yamauchi M, Morimoto M, Miura T, Murakami M. J Am Chem Soc. 2009; 132:54. [PubMed: 20000760] Miura T, Morimoto M, Yamauchi M, Murakami M. J Org Chem. 2010; 75:5359. [PubMed: 20604510] Miura T, Yamauchi M, Kosaka A, Murakami M. Angew Chem Int Ed. 2010; 49:4955.
9. A DFT calculation (M06-2X/6-311+G(d,p)//M06-2X/6-31G(d)) indicates that ring strain of the parent isatin is around 11 kcal/mol.
10. For seminal examples, see Periana RA, Bergman RG. J Am Chem Soc. 1986; 108:7346. Gozin M, Weisman A, Ben-David Y, Milstein D. Nature. 1993; 364:699.
11. For selected reviews, see: Kakiuchi F, Murai S. Acc Chem Res. 2002; 35:826. [PubMed: 12379135] Ritleng V, Sirlin C, Pfeffer M. Chem Rev. 2002; 102:1731. [PubMed: 11996548] Kakiuchi F, Kochi T. Synthesis. 2008;3013. Foley NA, Lee JP, Ke Z, Gunnoe TB, Cundari TR. Acc Chem Res. 2009; 42:585. [PubMed: 19296659] Kitamura T. Eur J Org Chem. 2009;1111. Colby DA, Bergman RG, Ellman JA. Chem Rev. 2010; 110:624. [PubMed: 19438203] Yoshikai N. Synlett. 2011:1047. Colby DA, Tsai AS, Bergman RG, Ellman JA. Acc Chem Res. 2012; 45:814. [PubMed: 22148885]
12. For a Rh(III)-catalyzed selective C–C cleavage vs C–H activation via β -C elimination followed by Heck coupling, see: Li H, Li Y, Zhang XS, Chen K, Wang X, Shi ZJ. J Am Chem Soc. 2011; 133:15244. [PubMed: 21875139]
13. Shi and coworkers reported the first pyridine-directed decarbonylation of aryl ketones, see: Lei ZQ, Li H, Li Y, Zhang XS, Chen K, Wang X, Sun J, Shi ZJ. Angew Chem Int Ed. 2012; 51:2690.
14. For selected examples using 3-methyl-2-pyridyl group as efficient directing group for C–H functionalization, see: Kalyani D, Deprez NR, Desai LV, Sanford MS. J Am Chem Soc. 2005; 127:7330. [PubMed: 15898779] Hull KL, Lanni EL, Sanford MS. J Am Chem Soc. 2006; 128:14047. [PubMed: 17061885] Kalyani D, Dick AR, Anani WQ, Sanford MS. Organic Letters. 2006; 8:2523. [PubMed: 16737304] Chen X, Goodhue CE, Yu JQ. J Am Chem Soc. 2006; 128:12634. [PubMed: 17002342] Chen X, Hao XS, Goodhue CE, Yu JQ. J Am Chem Soc. 2006; 128:6790. [PubMed: 16719450] Deprez NR, Sanford MS. J Am Chem Soc. 2009; 131:11234. [PubMed: 19621899] Guo X, Deng G, Li CJ. Adv Synth Cat. 2009; 351:2071. Zhao X, Dimitrijević E, Dong VM. J Am Chem Soc. 2009; 131:3466. [PubMed: 19243177] Li Y, Li BJ, Wang WH, Huang WP, Zhang XS, Chen K, Shi ZJ. Angew Chem Int Ed. 2011; 50:2115. Feng CG, Ye M, Xiao KJ, Li S, Yu JQ. J Am Chem Soc. 2013; 135:9322. [PubMed: 23755825]
15. Their presence was confirmed by crude ^1H NMR and LC-MS.
16. Phenyl acetylene was found not stable under the reaction conditions only leading to a complex mixture. Nevertheless, still ca. 20% of the desired product was observed by crude ^1H NMR, but its pure form was difficult to isolate.
17. Use of ester, amide or triazole as DGs did not provide any desired quinolinone product.
18. For seminal studies on directed C–C activation of ketones with stoichiometric Rh, see: Suggs JW, Cox SDJ. Organomet Chem. 1981; 221:199. Suggs JW, Jun CH. J Am Chem Soc. 1984; 106:3054. Suggs JW, Jun CH. J Am Chem Soc. 1986; 108:4679. Suggs JW, Jun CH. J Chem Soc Chem Commun. 1985:92.
19. Complex **M2** was found to be less stable than **M1**; slight decomposition of **M2** was observed during purification.
20. Similarly, the Rh-mediated C–C cleavage using other DGs has been examined. For isatins **1b** (pyridyl) and **1d** (oxazolynyl), the C–C activation also proceeded at room temperature within 16h; however, the reaction with substrate **1c** (1H-indazol-1-yl) did not occur until 50 °C. Isolation of the pure Rh-CO complexes for all these cases proved nontrivial, but their characteristic Rh-CO IR stretching frequencies can be observed. For more details, see supporting information.

a. Cyclobuten-(di)one: [4+2-1]-type products

Kondo; Mitsudo; Yamamoto

b. Benzocyclobutenone: [4+2-1]-type products **c. This work: Isatins: [5+2-1]-type products**

Scheme 1. Decarbonylative C–C activation of cyclic ketones with insertion of an unsaturated moiety

Scheme 2. Reaction pathways: C-C vs C-H activation

Scheme 3. Mechanistic exploration

Table 1

Control experiments^a

entry	change from standard conditions ^c for 1a	conversion	yield of 3aa
1	None	>99%	88%
2	Without Rh catalyst	14%	-
3	$\text{Rh}(\text{PPh}_3)_3\text{Cl}$ instead of $[\text{Rh}(\text{cod})\text{Cl}]_2$	22%	8%
4	$[\text{Rh}(\text{coe})_2\text{Cl}]_2$ instead of $[\text{Rh}(\text{cod})\text{Cl}]_2$	93%	73%
5	$[\text{Rh}(\text{C}_2\text{H}_4)_2\text{Cl}]_2$ instead of $[\text{Rh}(\text{cod})\text{Cl}]_2$	73%	69%
6	$[\text{Rh}(\text{CO})_2\text{Cl}]_2$ instead of $[\text{Rh}(\text{cod})\text{Cl}]_2$	73%	62%
7	$\text{Ru}_3(\text{CO})_{12}$ instead of $[\text{Rh}(\text{cod})\text{Cl}]_2$	73%	trace
8	$\text{Co}_2(\text{CO})_8$ instead of $[\text{Rh}(\text{cod})\text{Cl}]_2$	14%	-
9	Additional 20 mol% of PCy_3 was added	75%	23%
10	Additional 20 mol% of $\text{P}(\text{C}_6\text{H}_3(\text{CF}_3)_2)_3$ was added	24%	-
11	Additional 20 mol% of dppb was added	40%	15%
12	Toluene instead of PhCl	57%	29%
13	DCE instead of PhCl	>99%	-
14	1,4-Dioxane instead of PhCl	>99%	84%
15	Temperature was 150 °C	56%	43%

^a All yields and conversions were determined by crude ¹H NMR using 1,1,2,2-tetrachloroethane as the internal standard.

^b 4% of *ortho*-C–H vinylation product and 3% of sequential C–H/C–C activation product were observed.

^c The standard reactions were conducted with **1a** (0.04 mmol), **2a** (0.048 mmol, 1.2 equiv), $[\text{Rh}(\text{cod})\text{Cl}]_2$ (0.002 mmol, 5 mol%), and PhCl (1 mL) in a 4 mL vial at 160 °C. ^c

Table 2
Substrate scope with different alkynes^a

^a All yields are isolated yields; regioselectivity of the products was determined by crude ¹H NMR.

^b Isolated yield for the *major regioisomer* only.

Table 3
Substrate scope with different amines^a

^a All yields are isolated yields.

^b 4% of *ortho*-C–H vinylation product and 3% of sequential C–H/C–C activation product were observed.

^c 6% of *ortho*-C–H vinylation product was observed.

^d 2.0 equiv of alkyne **2a** was used.

^e The reaction conversion was 83%, determined by crude ¹H NMR.