JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
Communication
pubs.acs.org/JACS

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

Rong Zeng and Guangbin Dong*

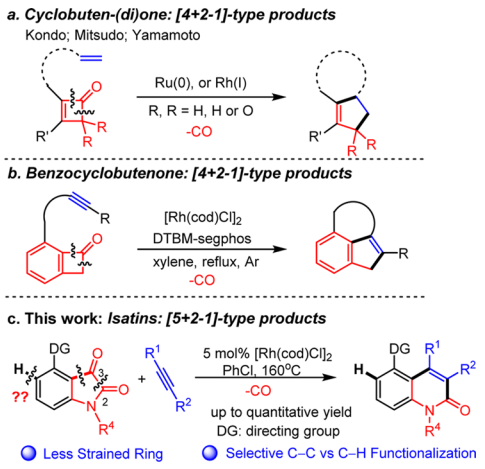
Department of Chemistry, University of Texas at Austin, Austin, Texas 78712, United States

Supporting Information

ABSTRACT: Herein we report a [5 + 2 − 1] transformation though 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.

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 bond[2] 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,b]

Scheme 1. Decarbonylative C−C Activation of Cyclic Ketones with Insertion of an Unsaturated Moiety

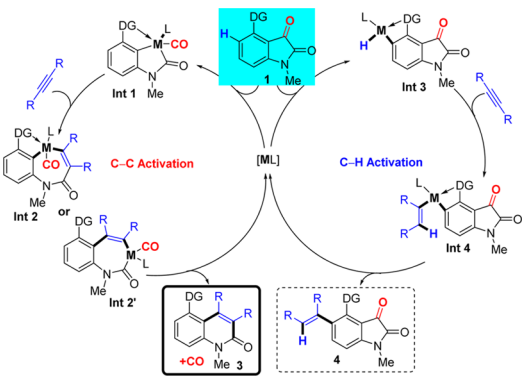


Yamamoto later developed a related intramolecular coupling between squaric acid derivatives and olefins.[6c] Very recently, our group described a decarbonylative coupling of benzocyclobutenones with alkynes to prepare fused indene compounds (Scheme 1B).[7] While efficient, these [4 + 2 − 1] reactions 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] transformation[8] 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]

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

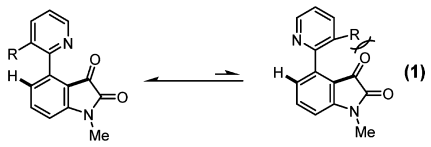
Scheme 2. Reaction Pathways: C−C vs C−H Activation



Received: December 2, 2014
Published: January 8, 2015

DOI: 10.1021/ja512306a
J. Am. Chem. Soc. 2015, 137, 1408−1411

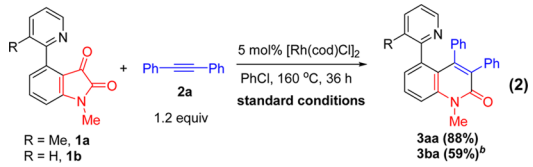
achieved. Given that the carbonyl group is significantly larger than the hydrogen, increasing steric hindrance on the "back" site of the DG should minimize the conformation that leads to C−H activation (e.g., eq 1). To examine this hypothesis, two DGs with



different steric properties were evaluated initially (eq 2). While both provided the desired 2-quinolinone products, the 3-methyl-2-pyridyl group[14] (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

Table 1. Control Experiments[a]



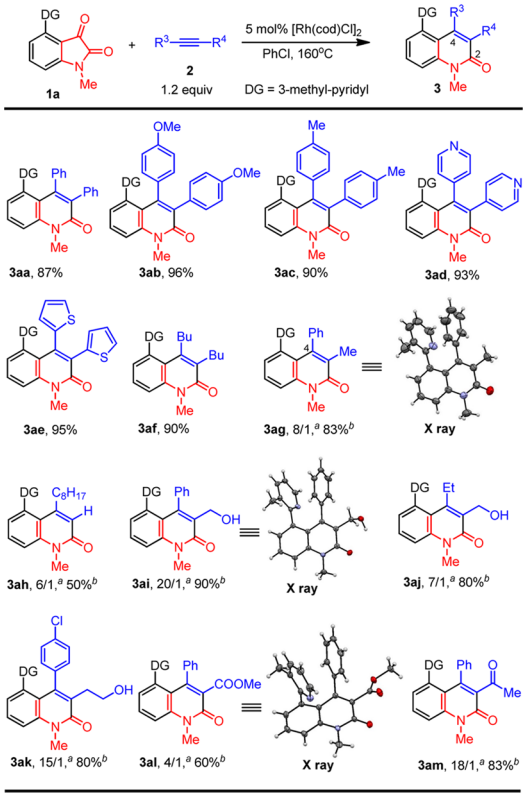
entry	change from standard conditions[c] for **1a**	conversion	yield of **3aa**
1	none	>99%	**88%**
2	without Rh catalyst	14%	–
3	$Rh(PPh_3)_3Cl$ instead of $[Rh(cod)Cl]_2$	22%	8%
4	$[Rh(coe)_2Cl]_2$ instead of $[Rh(cod)Cl]_2$	93%	73%
5	$[Rh(C_2H_4)_2Cl]_2$ instead of $[Rh(cod)Cl]_2$	73%	69%
6	$[Rh(CO)_2Cl]_2$ instead of $[Rh(cod)Cl]_2$	73%	62%
7	$Ru_3(CO)_{12}$ instead of $[Rh(cod)Cl]_2$	73%	trace
8	$Co_2(CO)_8$ instead of $[Rh(cod)Cl]_2$	14%	–
9	additional 20 mol % of PCy_3 was added	75%	23%
10	additional 20 mol % of $P(C_6H_3(CF_3)_2)_3$ 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 ^{1}H 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), $[Rh(cod)Cl]_2$ (0.002 mmol, 5 mol %), and PhCl (1 mL) in a 4 mL vial at 160 °C.

catalyst, no desired product was observed (entry 2). Use of Wilkinson's catalyst $[Rh(PPh_3)_3Cl]$ instead gave only 8% of the desired product together with high recovery of the starting material (entry 3). Other Rh(I) catalysts, such as $[Rh(coe)_2Cl]_2$, $[Rh(C_2H_4)_2Cl]_2$, and $[Rh(CO)_2Cl]_2$, showed lower efficiency (Entries 4−6). Employment of other metals, such as $Ru_3(CO)_{12}$ and $Co_2(CO)_8$, did not 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).

Table 2. Substrate Scope with Different Alkynes[a]



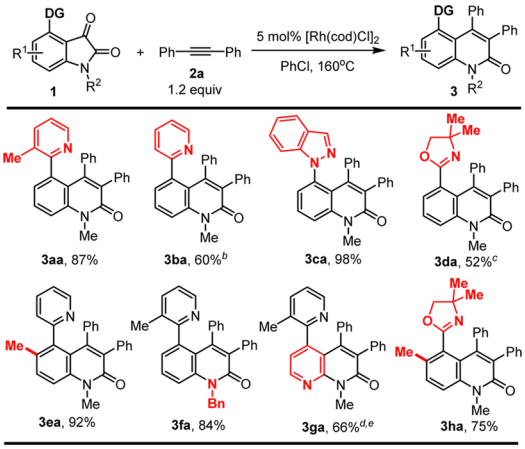
[a]All yields are isolated yields; regioselectivity of the products was determined by crude ^{1}H NMR. [b]Isolated yield for the *major regioisomer only*.

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 oxazolinyl 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 oxazolinyl DG. Isatin substrates with a methyl group at C-5 position

DOI: 10.1021/ja512306a
J. Am. Chem. Soc. 2015, 137, 1408−1411

Table 3. Substrate Scope with Different Amines[a]

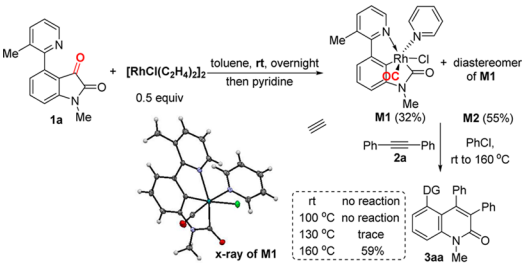


[a]All yields are isolated yields. [b]4% of *ortho*-C−H vinylation product and 3% of sequential C−H/C−C activation product were observed. [c]6% of *ortho*-C−H vinylation product was observed. [d]2.0 equiv of alkyne **2a** were used. [e]The reaction conversion was 83%, determined by crude ^{1}H NMR.

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.

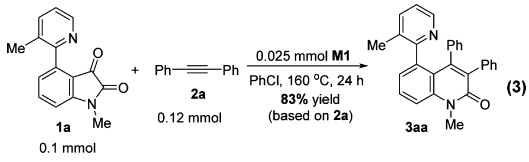
Regarding the mechanistic features, a key question is why the reaction requires a relatively high temperature to take place? Consequently, it is natural to be concerned about the ease of oxidative addition of Rh into the isatin C−C bonds. To probe the mechanism, reaction of isatin **1a** with stoichiometric $[Rh(C_2H_4)_2Cl]_2$ was investigated (Scheme 3). Interestingly, the C−C

Scheme 3. Mechanistic Exploration



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 for 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).



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 is 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 2π-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.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures and spectral data. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*gbdong@cm.utexas.edu

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank UT Austin and CPRIT for a startup fund, NIGMS (R01GM109054-01) and the Welch Foundation (F 1781) for research grants. G.D. 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 salts.

■ REFERENCES

(1) For selected books on cycloadditions: (a) *Cycloaddition Reactions in Organic Synthesis*; Kobayashi, S., Jørgensen, K. A., Eds; Wiley-VCH Verlag GmbH: Weinheim, 2001. (b) *Advances in Cycloaddition*; Curran, D. P., Lautens, M., Harmata, M., Eds.; JAI, Press Inc: Stamford, CT, 1988−1999; Vol. *1*−*6*. For selected reviews on cycloadditions: (c) Yu,

DOI: 10.1021/ja512306a
J. Am. Chem. Soc. 2015, 137, 1408−1411

Z.-X.; Wang, Y.; Wang, Y. *Chem.—Asian J.* **2010**, *5*, 1072. (d) Schore, N. E. *Chem. Rev.* **1988**, *88*, 1081. (e) Murakami, M. *Angew. Chem., Int. Ed.* **2003**, *42*, 718. (f) Perreault, S.; Rovis, T. *Chem. Soc. Rev.* **2009**, *38*, 3149. (g) Varela, J. A.; Saá, C. *Chem. Rev.* **2003**, *103*, 3787. (h) Ylijoki, K. E. O.; Stryker, J. M. *Chem. Rev.* **2012**, *113*, 2244. (i) Heller, B.; Hapke, M. *Chem. Soc. Rev.* **2007**, *36*, 1085.

(2) For selected reviews on transition-metal-mediated C−C bond activations: (a) Jones, W. D. *Nature* **1993**, *364*, 676. (b) Murakami, M.; Ito, Y. *Top. Organomet. Chem.* **1999**, *3*, 97. (c) Rybtchinski, B.; Milstein, D. *Angew. Chem., Int. Ed.* **1999**, *38*, 870. (d) Perthuisot, C.; Edelbach, B. L.; Zubris, D. L.; Simhai, N.; Iverson, C. N.; Müller, C.; Satoh, T.; Jones, W. D. *J. Mol. Catal. A* **2002**, *189*, 157. (e) van der Boom, M. E.; Milstein, D. *Chem. Rev.* **2003**, *103*, 1759. (f) Jun, C.-H. *Chem. Soc. Rev.* **2004**, *33*, 610. (g) Satoh, T.; Miura, M. *Top. Organomet. Chem.* **2005**, *14*, 1. (h) Jun, C.-H.; Park, J. W. *Top. Organomet. Chem.* **2007**, *24*, 117. (i) Necas, D.; Kotora, M. *Curr. Org. Chem.* **2007**, *11*, 1566. (j) Crabtree, R. H. *Chem. Rev.* **1985**, *85*, 245. (k) Kondo, T.; Mitsudo, T. A. *Chem. Lett.* **2005**, *34*, 1462. (l) Ruhland, K. *Eur. J. Org. Chem.* **2012**, 2683. (m) Korotvicka, A.; Necas, D.; Kotora, M. *Curr. Org. Chem.* **2012**, *16*, 1170. (n) Seiser, T.; Saget, T.; Tran, D. N.; Cramer, N. *Angew. Chem., Int. Ed.* **2011**, *50*, 7740. (o) Murakami, M.; Matsuda, T. *Chem. Commun.* **2011**, *47*, 1100. (p) Dermenci, A.; Coe, P. W.; Dong, G. *Org. Chem. Front.* **2014**, *1*, 567. (q) *C−C bond activation*. In *Topics in Current Chemistry*; Dong, G., Ed.; Springer-Verlag: Berlin, 2014; Vol. *346*.

(3) For a recent review of decarbonylative C−C bond formation: 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; for biphenylenes: (a) Edelbach, B. L.; Lachicotte, R. J.; Jones, W. D. *Organometallics* **1999**, *18*, 4040. For cyclobutenones: (b) Huffman, M. A.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1990**, *112*, 8617. For cyclobutenediones: (c) South, M. S.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1984**, *106*, 4181. For cyclobutanones: (d) Murakami, M.; Itahashi, T.; Ito, Y. *J. Am. Chem. Soc.* **2002**, *124*, 13976. For linear ketones: (e) Wentzel, M. T.; Reddy, V. J.; Hyster, T. K.; Douglas, C. J. *Angew. Chem., Int. Ed.* **2009**, *48*, 6121. (f) Dreis, A. M.; Douglas, C. J. *J. Am. Chem. Soc.* **2009**, *131*, 412. For cyclopropanes: (g) Narasaka, K.; Koga, Y. *Chem. Lett.* **1999**, *28*, 705. For cyclopropenes: (h) Li, C.; Zhang, H.; Feng, J.; Zhang, Y.; Wang, J. *Org. Lett.* **2010**, *12*, 3082. For vinylcyclopropanes: (i) Jiao, L.; Lin, M.; Zhuo, L.-G.; Yu, Z.-X. *Org. Lett.* **2010**, *12*, 2528. (j) Wender, P. A.; Takahashi, H.; Witulski, B. *J. Am. Chem. Soc.* **1995**, *117*, 4720. For amino cyclopropanes: (k) Shaw, M. H.; Melikhova, E. Y.; Kloer, D. P.; Whittingham, W. G.; Bower, J. F. *J. Am. Chem. Soc.* **2013**, *135*, 4992. For cyclobutenols: (l) Ishida, N.; Sawano, S.; Masuda, Y.; Murakami, M. *J. Am. Chem. Soc.* **2012**, *134*, 17502. For methylenecyclopropanes: (m) Weintz, H.-J.; Binger, P. *Tetrahedron Lett.* **1985**, *26*, 4075. For C−CN bond cleavage: (n) Nakao, Y.; Oda, S.; Hiyama, T. *J. Am. Chem. Soc.* **2004**, *126*, 13904.

(5) (a) Murakami, M.; Amii, H.; Ito, Y. *Nature* **1994**, *370*, 540. (b) Murakami, M.; Amii, H.; Shigeto, K.; Ito, Y. *J. Am. Chem. Soc.* **1996**, *118*, 8285. (c) Matsuda, T.; Shigeno, M.; Murakami, M. *Chem. Lett.* **2006**, *35*, 288. For a seminal example of decarbonylation of linear diketones: (d) Kaneda, K.; Azuma, H.; Wayaku, M.; Tehanishi, S. *Chem. Lett.* **1974**, *3*, 215.

(6) (a) Kondo, T.; Nakamura, A.; Okada, T.; Suzuki, N.; Wada, K.; Mitsudo, T. A. *J. Am. Chem. Soc.* **2000**, *122*, 6319. (b) Kondo, T.; Taguchi, Y.; Kaneko, Y.; Niimi, M.; Mitsudo, T.-A. *Angew. Chem., Int. Ed.* **2004**, *43*, 5369. (c) Yamamoto, Y.; Kuwabara, S.; Hayashi, H.; Nishiyama, H. *Adv. Synth. Catal.* **2006**, *348*, 2493. A related decarbonylative ring expansion of cyclobutanones: (d) Wender, P. A.; Carrea, A. G.; Sato, Y.; Sun, R. *J. Am. Chem. Soc.* **2000**, *122*, 7815.

(7) Chen, P.-H.; 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: (a) Kajita, Y.; Kurahashi, T.; Matsubara, S. *J. Am. Chem. Soc.* **2008**, *130*, 17226. (b) Kajita, Y.; Matsubara, S.; Kurahashi, T. *J. Am. Chem. Soc.* **2008**, *130*, 6058. (c) Fujiwara, K.; Kurahashi, T.; Matsubara, S. *Org. Lett.* **2010**, *12*, 4548. (d) Fujiwara, K.; Kurahashi, T.; Matsubara, S. *Chem. Lett.* **2011**, *40*, 322. (e) Inami, T.; Baba, Y.; Kurahashi, T.; Matsubara, S. *Org. Lett.* **2011**, *13*, 1912. (f) Inami, T.; Kurahashi, T.; Matsubara, S. *Chem. Commun.* **2011**, *47*, 9711. (g) Ochi, Y.; Kurahashi, T.; Matsubara, S. *Org. Lett.* **2011**, *13*, 1374. (h) Inami, T.; Kurahashi, T.; Matsubara, S. *Org. Lett.* **2014**, *16*, 5660. For the Ni-catalyzed [6 + 2 − 2] transformations through denitrogenation: (i) Miura, T.; Yamauchi, M.; Murakami, M. *Org. Lett.* **2008**, *10*, 3085. (j) Yamauchi, M.; Morimoto, M.; Miura, T.; Murakami, M. *J. Am. Chem. Soc.* **2009**, *132*, 54. (k) Miura, T.; Morimoto, M.; Yamauchi, M.; Murakami, M. *J. Org. Chem.* **2010**, *75*, 5359. (l) 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: (a) Periana, R. A.; Bergman, R. G. *J. Am. Chem. Soc.* **1986**, *108*, 7346. (b) Gozin, M.; Weisman, A.; Ben-David, Y.; Milstein, D. *Nature* **1993**, *364*, 699.

(11) For selected reviews: (a) Kakiuchi, F.; Murai, S. *Acc. Chem. Res.* **2002**, *35*, 826. (b) Ritleng, V.; Sirlin, C.; Pfeffer, M. *Chem. Rev.* **2002**, *102*, 1731. (c) Kakiuchi, F.; Kochi, T. *Synthesis* **2008**, 3013. (d) Foley, N. A.; Lee, J. P.; Ke, Z.; Gunnoe, T. B.; Cundari, T. R. *Acc. Chem. Res.* **2009**, *42*, 585. (e) Kitamura, T. *Eur. J. Org. Chem.* **2009**, 1111. (f) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624. (g) Yoshikai, N. *Synlett* **2011**, 1047. (h) Colby, D. A.; Tsai, A. S.; Bergman, R. G.; Ellman, J. A. *Acc. Chem. Res.* **2012**, *45*, 814.

(12) For a Rh(III)-catalyzed selective C−C cleavage vs C−H activation via β-C elimination followed by Heck coupling: Li, H.; Li, Y.; Zhang, X.-S.; Chen, K.; Wang, X.; Shi, Z.-J. *J. Am. Chem. Soc.* **2011**, *133*, 15244.

(13) Shi et al. reported the first pyridine-directed decarbonylation of aryl ketones: Lei, Z.-Q.; Li, H.; Li, Y.; Zhang, X.-S.; Chen, K.; Wang, X.; Sun, J.; Shi, Z.-J. *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: (a) Kalyani, D.; Deprez, N. R.; Desai, L. V.; Sanford, M. S. *J. Am. Chem. Soc.* **2005**, *127*, 7330. (b) Hull, K. L.; Lanni, E. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2006**, *128*, 14047. (c) Kalyani, D.; Dick, A. R.; Anani, W. Q.; Sanford, M. S. *Org. Lett.* **2006**, *8*, 2523. (d) Chen, X.; Goodhue, C. E.; Yu, J.-Q. *J. Am. Chem. Soc.* **2006**, *128*, 12634. (e) Chen, X.; Hao, X.-S.; Goodhue, C. E.; Yu, J.-Q. *J. Am. Chem. Soc.* **2006**, *128*, 6790. (f) Deprez, N. R.; Sanford, M. S. *J. Am. Chem. Soc.* **2009**, *131*, 11234. (g) Guo, X.; Deng, G.; Li, C.-J. *Adv. Synth. Catal.* **2009**, *351*, 2071. (h) Zhao, X.; Dimitrijević, E.; Dong, V. M. *J. Am. Chem. Soc.* **2009**, *131*, 3466. (i) Li, Y.; Li, B.-J.; Wang, W.-H.; Huang, W.-P.; Zhang, X.-S.; Chen, K.; Shi, Z.-J. *Angew. Chem., Int. Ed.* **2011**, *50*, 2115. (j) Feng, C.-G.; Ye, M.; Xiao, K.-J.; Li, S.; Yu, J.-Q. *J. Am. Chem. Soc.* **2013**, *135*, 9322.

(15) Their presence was confirmed by crude ^{1}H NMR and LC-MS.

(16) Phenyl acetylene was found not stable under the reaction conditions only leading to a complex mixture. Nevertheless, still ∼20% of the desired product was observed by crude ^{1}H 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: (a) Suggs, J. W.; Cox, S. D. *J. Organomet. Chem.* **1981**, *221*, 199. (b) Suggs, J. W.; Jun, C.-H. *J. Am. Chem. Soc.* **1984**, *106*, 3054. (c) Suggs, J. W.; Jun, C.-H. *J. Am. Chem. Soc.* **1986**, *108*, 4679. (d) Suggs, J. W.; Jun, C.-H. *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** (oxazolinyl), the C−C activation also proceeded at rt within 16 h; 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; details in Supporting Information.

DOI: 10.1021/ja512306a
J. Am. Chem. Soc. 2015, 137, 1408−1411