### Accepted Manuscript

Cobalt-catalyzed regioselective [3+2] annulation of *ortho*-formyl and acetyl substituted phenylboronic acids with alkynes

Mitsuhiro Ueda, Tamami Ueno, Yuki Suyama, Ilhyong Ryu

PII:	\$0040-4039(17)30780-3
DOI:	http://dx.doi.org/10.1016/j.tetlet.2017.06.049
Reference:	TETL 49041
To appear in:	Tetrahedron Letters
Received Date:	26 May 2017
Revised Date:	13 June 2017
Accepted Date:	16 June 2017



Please cite this article as: Ueda, M., Ueno, T., Suyama, Y., Ryu, I., Cobalt-catalyzed regioselective [3+2] annulation of *ortho*-formyl and acetyl substituted phenylboronic acids with alkynes, *Tetrahedron Letters* (2017), doi: http://dx.doi.org/10.1016/j.tetlet.2017.06.049

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

### **Graphical Abstract**

To create your abstract, type over the instructions in the template box below. Fonts or abstract dimensions should not be changed or altered.





Tetrahedron Letters journal homepage: www.elsevier.com

journal nomepage. www.ersevier.com

# Cobalt-catalyzed regioselective [3+2] annulation of *ortho*-formyl and acetyl substituted phenylboronic acids with alkynes

Mitsuhiro Ueda,\*<sup>1</sup> Tamami Ueno,<sup>1</sup> Yuki Suyama,<sup>1</sup> and Ilhyong Ryu<sup>1,2</sup>

<sup>1</sup>Department of Chemistry, Graduate School of Science, Osaka Prefecture University, Sakai, Osaka 599-8531, Japan <sup>2</sup>Department of Applied Chemistry, National Chiao Tung University, Hsinchu 30010, Taiwan, R.O.C.

### ARTICLE INFO

### ABSTRACT

Article history: Received Received in revised form Accepted Available online Treatment of alkynes with *ortho*-formyl and acetyl phenylboronic acids in the presence of a cobalt catalyst resulted in the formation of 2,3-disubstituted indenols in good yields. When aryl silyl alkynes were used, 2-aryl-3-silyl indenols were obtained regioselectively in good yields.

2009 Elsevier Ltd. All rights reserved.

2,3-disubstituted indenol silyl aryl alkyne cobalt [3+2] annulation Ortho-carbonylated phenylboronic acid

### Introduction

2.3-Disubstituted indenols are an important class of organic molecules, since they serve as synthetic intermediates of biological active compounds useful in pharmaceutical and agricultural chemistry.<sup>1,2,3</sup> In 2005, Rh-catalyzed [3+2] annulation reactions of ortho-carbonylated phenylboronic acids with alkynes were studied for the synthesis of 2,3-disubstituted indenols by Hayashi and Murakami, independently.4a,4b These previous studies exhibited variable regioselectivities when unsymmetrical as 1-phenyl-1-propyne alkynes, such and 1-(trimethylsilyl)propyne, were used. In 2007, Lu and co-workers reported a Pd-catalyzed reaction of ortho-formylphenylboronic acids with alkynoate esters, which gave the corresponding 2methoxycarbonyl-3-substituted indenols regioselectively.<sup>4c</sup> We recently reported the synthesis of 2,3-disubstituted indenones by a Co-catalyzed regioselective [3+2] annulation of orthomethoxycarbonylphenylboronic acid with alkynes, which gave the corresponding indenones in good yields.<sup>5,6</sup> In this study we extended the Co-catalyzed [3+2] annulation method to the synthesis of 2,3-disubstituted indenols, in which ortho-formyl and acetyl phenylboronic acids were reacted with alkynes.

### **Results and discussion**

In our previous work, the Co-catalyzed [3+2] annulation of *ortho*-methoxycarbonylphenylboronic acid with 1-phenyl-2-trimethylsilylacetylene (**2a**) produced 2-phenyl-3-silyl indenone as a single regioisomer (1st equation, Scheme 1). This led us to investigate the reaction of *ortho*-formylphenylboronic acid with **2a** (2nd equation, Scheme 1). In the presence of 10 mol % of



**Scheme 1.** Cobalt-catalyzed [3+2] annulation of *ortho*-carbonylated phenylboronic acids with silyl aryl acetylenes

DPPE,<sup>7</sup>  $Co(acac)_2$ and the reaction of orthoformylphenylboronic acid (1a) with 1-phenyl-2-trimethylsilyl acetylene (2a) in acetonitrile was carried out at 80 °C for 12 h, which gave 2-phenyl-3-silyl indenol 3a as a single regioisomer in 84% yield (Table 1). The reaction of [4-(methoxyphenyl)ethynyl]trimethylsilane (2b) with 1a also proceeded regioselectively to form the corresponding 3-silyl-substituted indenol 3b in 95% yield. 4-[(Trimethylsilyl)ethynyl]phenol (2c) was also applicable albeit in modest yield due to the desilylation of 2c. Methyl 4-[(trimethylsilyl)ethynyl]benzoate (2d) gave 3d in 72% yield.<sup>8</sup> 3-(Trimethylsilylethynyl)benzonitrile (2e) tolerated the reaction conditions and formed the corresponding indenol 3e in 53% yield as a single regioisomer. The modest yield of 3e was mainly attributed to the slow reaction. When 1-(trimethylsilyl)propyne (2f) was reacted with 1a, 2-methyl-3-silyl indenol 3f was obtained in 70% yield with a regioselectivity of 95:5. In a similar protocol, ortho-acetylphenylboronic acid (1b)

<sup>\*</sup> Corresponding author. Tel.: +81-72-254-9670; fax: +81-72-254-9670; e-mail: ueda@c.s.osakafu-u.ac.jp (M. Ueda)

Tetrahedron

reacted with silyl alkynes **2a–2d** to give the corresponding indenols **3g–3j** in good to excellent yields.

 Table 2. Co-catalyzed [3+2] annulation of 1 with internal alkynes 2g-2j<sup>a</sup>







<sup>a</sup> Reaction conditions: **1** (1.5 equiv), **2** (0.5 mmol), Co(acac)<sub>2</sub> (10 mol %), DPPE (10 mol %) in MeCN (2 mL) at 80 °C for 12 h. <sup>b</sup> Determined by NMR analysis.

<sup>a</sup> Reaction conditions: **1** (1.5 equiv), **2** (0.5 mmol), Co(acac)<sub>2</sub> (10 mol %), DPPE (10 mol %) in MeCN (2 mL) at 80 °C for 12 h. <sup>b</sup> Determined by NMR analysis.

In contrast to the regioselective [3+2] annulation with silyl-substituted alkynes, other unsymmetrical alkynes 2g-2i gave regioisomeric mixtures of the corresponding 2,3disubstituted indenols (Table 2). For example, the reaction of methyl phenyl acetylene 2g with 1a gave 3k in good yield with 81:19 selectivity in favor of the 2-phenyl orientation. 1-Phenylpentyne (2h) and ethyl 2-butynoate (2i) gave 3l and 3m in 68% and 71% yields, respectively, with similar regioselectivities. Diphenylacetylene (2j) reacted with 1a to give 2,3-diphenyl indenol 3n in 89% yield. Similarly, 4octyne (2k) gave the corresponding product 30 in 98% yield. We also examined the reaction of 2-formyl-3-thienylboronic acid with 2j. As a result, the corresponding product 3p was obtained, albeit in moderate yield due to the slow reaction. The reaction of *ortho*-acetylphenylboronic acid (1b) with 2j also proceeded to form the corresponding 2,3-disubstituted indenol **3q** in 90% yield.

In our previous work, the [3+2] annulation of orthomethoxycarbonylphenylboronic acid with 4-[(trimethylsilyl)ethynyl]benzoate (2d) gave the desired indenone 4 in very low yield due to the sluggish reaction (Scheme 2). In contrast, 2-(4-methoxycarbonylphenyl)-3-silyl indenol 3d was obtained in good yield by the reaction of 1a and 2d. Indenol successfully 3d was converted 2-(4to methoxycarbonylphenyl)-3-silyl indenone 4 by PCC oxidation in 90% yield (Scheme 2).



Scheme 2. Synthesis of indenone 4 from indenol 3d

A proposed mechanism for the Co-catalyzed annulation process is shown in Scheme 3. Arylcobalt complex I would be generated via the transmetalation of [Co]-X (X = OH or acac) with *ortho*-formylphenylboronic acid (1a).<sup>9</sup> The regioselective insertion of silyl alkyne 2a forms vinylcobalt complex II. The [Co]-carbon bond of complex II undergoes migratory insertion into the aldehyde to form alkoxycobalt complex III, which undergoes protonation to give indenol 3a and regenerates the [Co]-X catalyst.

2



Scheme 3. Proposed reaction mechanism

#### Conclusion

In summary, we have demonstrated that the Co-catalyzed [3+2] annulation of *ortho*-formyl and acyl-substituted phenylboronic acids with alkynes led to 2,3-disubstituted indenols. When silyl alkynes were used, regioselective annulation took place to give 3-silyl-substituted indenols. Further studies regarding the synthesis of biological active compounds are currently underway in our laboratory.

### Acknowledgments

This work was supported by a Grant-in-Aid for Scientific Research from the MEXT (25810024 for MU) and the JSPS (26248031 for IR)

### **Supplementary Material**

Supplementary data associated with this article can be found, in the online version, at http://

#### **References and notes**

- (a) Clive, D. L. J.; Yu, M.; Sannigrah, M. J. Org. Chem. 2004, 69, 4116-4125. (b) Clive, D. L. J.; Yu, M. Chem. Commun. 2002, 2380-2381. (c) Clark, W. M.; Tickner-Eldridge, A. M.; Huang, G. K.; Pridgen, L. M.; Olsen, M. A.; Mills, R. J.; Lantos, I.; Braine, N. H. J. Am. Chem. Soc. 1998, 120, 4550-4551. (d) Ishiguro, Y.; Okamoto, K.; Ojima, F.; Sonoda, Y. Chem. Lett. 1993, 1139-1140. (e) Myers, A. G.; Proteau, P. J.; Handel, T. M. J. Am. Chem. Soc. 1988, 110, 7212-7214.
- Transition-metal-catalyzed [3+2] annulation of ortho-halobenzoyl compounds with alkynes. (a) Chang, K.-J.; Rayabarapu, D. K.; Cheng, C.-H. J. Org. Chem. 2004, 69, 47814787. (b) Rayabarapu, D. K.; Yang, C.-H.; Cheng, C.-H. J. Org. Chem. 2003, 68, 6726-6731. (c) Chang, K.-J.; Rayabarapu, D. K.; Cheng, C.-H. Org. Lett. 2003, 5, 3963-3966. (d) Rayabarapu, D. K.; Cheng, C.-H. Org. Lett. 2003, 5, 3963-3966. (d) Rayabarapu, D. K.; Cheng, C.-H. Org. Lett. 2003, 5, 3963-3966. (e) Gevorgyan, V.; Quan, L. G.; Yamamoto, Y. Tetrahedron Lett. 1999, 40, 4089-4092. (f) Quan, L. G.; Gevorgyan, V.; Yamamoto, Y. J. Am. Chem. Soc. 1999, 121, 3545-3546. (g) Vicente, J.; Abad, J.-A.; Gil-Rubio, J. Organometallics 1996, 15, 3509-3519. (h) Vicente, J; Abad, J.-A.; Gil-Rubio, J. J. Organomet. Chem. 1992, 436, C9-C12.
- Other synthetic methods of indenols. (a) Chinnagolla, R. K.; Jeganmohan, M. Eur. J. Org. Chem. 2012, 417-423. (b) Muralirajan, K.; Parthasarathy, K.; Cheng, C.-H. Angew. Chem. Int. Ed. 2011, 50, 4169-4172. (c) Yu, X.; Lu, X. Org. Lett. 2009, 11, 4366-4369. (d) Vicente, J.; Abad, J.-A.; López-Peláez, B.; Martínez-Viviente, E. Organometallics 2002, 21, 58-67. (e)

Cambie, R. C.; Metzler, M. R.; Rutledge, P. S.; Woodgate, P. D. J. Organomet. Chem. 1990, 398, C22-C24. (f) Cambie, R. C.;
Metzler, M. R.; Rutledge, P. S.; Woodgate, P. D. J. Organomet. Chem. 1990, 381, C26-C30. (g) Liebeskind, L. S.; Gasdaska, J. R.;
MaCallum, J. S.; Tremont, S. J. J. Org. Chem. 1989, 54, 669-677. (h) Robinson, N. P.; Main, L.; Nicholson, B. K. J. Organomet. Chem. 1989, 364, C37-C39.

- (a) Matsuda, T.; Makino, M.; Murakami, M. Chem. Lett. 2005, 34, 1416-1417. (b) Shintani, R.; Okamoto, K.; Hayashi, T. Chem. Lett. 2005, 34, 1294-1295. (c) Yang, M.; Zhang, X.; Lu, X. Org. Lett. 2007, 9, 5131-5133.
- Ueda, M.; Ueno, T.; Suyama, Y.; Ryu, I. Chem. Commun. 2016, 52, 13237-13240.
- For selected examples of Co-catalyzed [3+2] annulation based on C-H activation, see: (a) Kong, L.; Yang, X.; Zhou, X.; Yu, S.; Li, X. Org. Chem. Front. 2016, 3, 813-816. (b) Yu, W.; Zhang, W.; Liu, Z.; Zhang, Y. Chem. Commun. 2016, 52, 6837-6840. (c) Lu, Q.; Vásquez-Céspedes, S.; Gensch, T.; Glorius, F. ACS Catal. 2016, 6, 2352-2356. (d) Ikemoto, H.; Yoshino, T.; Sakata, K.; Matsunaga, S.; Kanai, M. J. Am. Chem. Soc. 2014, 136, 5424-5431.
- A survey of cobalt catalysts, ligands, and solvents revealed that the optimal reaction conditions were as follows: 10 mol % Co(acac)<sub>2</sub>, 10 mol % DPPE, MeCN, 80 °C, 12 h.
- 8. Typical Procedure for a Cobalt-Catalyzed [3+2] Regioselective Annulation of Ortho-Formyl and Acetyl Phenylboronic Acids with Alkynes: A 25 mL sealed tube equipped with a magnetic stirring bar was charged with Co(acac)<sub>2</sub> (0.05 mmol, 10 mol %), DPPE (0.05 mmol, 10 mol %), ortho-formylphenylboronic acid 1a (0.75 mmol, 1.5 equiv), an alkyne 2d (0.50 mmol, 1.0 equiv), and MeCN (2 mL). The reaction mixture was stirred at 80 °C for 12 h. The mixture was then filtered through silica gel pad. The filtrate was concentrated, and the residue was purified by column chromatography on silica gel to yield the desired product 3d as a yellow solid in 72% yield (121.6 mg, 0.359 mmol);

**3d**: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.12 (s, 9H), 1.62 (d, J = 8.8 Hz, 1H), 3.94 (s, 3H), 5.39 (d, J = 8.0 Hz, 1H), 7.24 (dt, J = 7.2 Hz, 0.8 Hz, 2H), 7.33 (dt, J = 7.2 Hz, 1.2 Hz, 1H), 7.39-7.45 (m, 2H), 7.56 (d, J = 7.2 Hz, 1H), 8.07 (d, J = 8.0 Hz, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  0.42, 52.3, 80.9, 123.0, 123.8, 125.9, 128.8, 129.4, 129.5 (two peaks overlap), 140.9, 142.5, 144.9, 146.3, 160.0, 167.1; IR (neat) 3466, 2952, 1724, 1608 cm<sup>-1</sup>; EI-MS m/z (relative intensity) 338 ([M<sup>+</sup>], 40), 279 (20), 235 (19), 12 (100), 206 (93), 178 (16), 73 (87); HRMS (EI) m/z calcd for C<sub>20</sub>H<sub>22</sub>O<sub>3</sub>Si ([M]<sup>+</sup>) 338.1338, found: 338.1346.

**3j**: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.04 (s, 9H), 1.42 (s, 3H), 1.86 (s, 1H), 3.94 (s, 3H), 7.23 (dt, *J* = 7.6 Hz, 1.2 Hz, 1H), 7.30 (dt, *J* = 7.2 Hz, 1.6 Hz, 1H), 7.35 (d, *J* = 6.8 Hz, 2H), 7.40 (d, *J* = 7.2 Hz, 1H), 7.46 (d, *J* = 7.2 Hz, 1H), 8.01 (d, *J* = 8.0 Hz, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  0.2 23.8, 52.3, 84.3, 122.3, 123.0, 126.1, 128.7, 129.2, 129.4, 129.7, 138.8, 142.5, 145.0, 149.0, 162.4, 167.2; IR (neat) 3466, 3066, 1776 cm<sup>-1</sup>; El-MS *m/z* (relative intensity) 352 (59), 337 (43), 279 (100), 277 (47), 248 (78), 220 (64), 73 (59); HRMS (EI) *m/z* calcd for C<sub>21</sub>H<sub>24</sub>O<sub>3</sub>Si ([M]<sup>+</sup>) 352.1495, found: 352.1489.

**3p**: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  1.78 (d, *J* = 8.4 Hz, 1H), 5.56 (d, *J* = 8.0 Hz, 1H), 7.25-7.31 (m, 5H), 7.34-7.37 (m, 5H), 7.50 (dd, *J* = 7.8 Hz, 1.8 Hz, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  74.7, 122.6, 126.4, 127.5, 128.4, 128.5, 128.7, 128.9, 129.2, 134.4, 134.5, 135.1, 144.4, 147.3, 147.6; IR (neat) 3408, 3060 cm<sup>-1</sup>; EI-MS *m/z* (relative intensity) 290 (100), 288 (57), 212 (43), 189 (35), 149 (38), 105 (76), 77 (33); HRMS (EI) *m/z* calcd for C<sub>19</sub>H<sub>14</sub>OS ([M]<sup>+</sup>) 290.0764.

 (a) Chen, M.-H.; Mannathan, S.; Lin, P.-S.; Cheng, C.-H. Chem. Eur. J. 2012, 18, 14918-14922. (b) Kobayashi, T.; Yorimitsu, H.; Oshima, K. Chem. Asian J. 2011, 6, 669-673. (c) Karthikeyan, J.; Jeganmohan, M.; Cheng, C.-H. Chem. Eur. J. 2010, 16, 8989-8992.

### JUSCRIPT ACCEPTED

Tetrahedron

4

Acceler

Highlights:

Co-catalyzed regioselective [3+2] annulation

The formation of 2,3-disubstituted indenols

Accepter

### **IUSCRIPT** ACCEPTED

Tetrahedron

Accepter

6