J|A|C|S
COMMUNICATIONS

Iridium-Catalyzed [3 + 2] Annulation of 1,3-Dienes with *ortho*-Carbonylated Phenylboronic Acids. A Catalytic Process Involving Regioselective 1,2-Addition

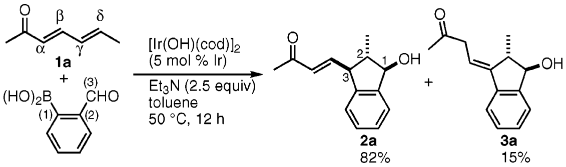
Takahiro Nishimura,* Yuichi Yasuhara, and Tamio Hayashi*

Department of Chemistry, Graduate School of Science, Kyoto University, Kyoto 606-8502, Japan

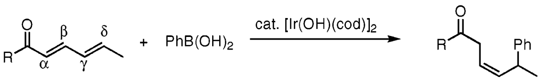
Received April 12, 2007; E-mail: tnishi@kuchem.kyoto-u.ac.jp; thayashi@kuchem.kyoto-u.ac.jp

Use of iridium complexes as catalysts for carbon−carbon bond forming reactions has recently attracted increasing attention because they are capable of providing synthetically useful transformations characteristic to the iridium catalysis.[1] Here we wish to report a new type of annulation reaction where an iridium(I) complex catalyzes the reaction of 1,3-dienes with *ortho*-carbonylated phenylboronic acids giving indanol derivatives with high regioselectivity. Although several addition−cyclization reactions using *ortho*-functionalized arylboronic acids have been reported under rhodium catalysis,[2,3] the present iridium-catalyzed reaction is substantially different from these rhodium-catalyzed reactions in the reaction pathway.

The new type of annulation reaction was found to take place with $[Ir(OH)(cod)]_2$[4] as a catalyst. Thus, 3,5-heptadien-2-one (**1a**) was allowed to react with 2-formylphenylboronic acid (2 equiv) in the presence of 5 mol % (Ir) of $[Ir(OH)(cod)]_2$ and triethylamine (2.5 equiv) in toluene at 50 °C for 12 h to give 82% yield of 2,3-disubstituted 1-indanol **2a** together with 15% yield of its olefinic double bond isomer **3a** (eq 1). An X-ray crystallographic analysis determined the structure of **2a** to be as shown in eq 1, indicating that two carbon−carbon bonds were formed between C(γ) of dienone **1a** and C(1) of 2-formylphenylboronic acid and between C(δ) and formyl carbon C(3). The relative stereochemistry in indanol **2a** is 1,2-*trans* and 1,3-*cis*. Considering that the iridium-catalyzed reaction of dienone **1a** with phenylboronic acid forms the carbon−carbon bond at the C(δ) position (eq 2),[5] the regiochemistry forming C(γ)−C(1) bond observed in the present iridium-catalyzed cyclization is very unique, suggesting that the present reaction does not involve the conjugate addition (1,4- or 1,6-addition) of an aryl−iridium intermediate to **1a** in the catalytic cycle (vide infra).



(1)

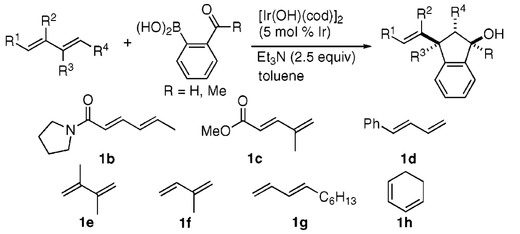


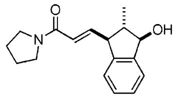
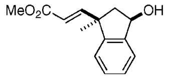
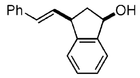
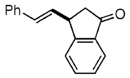
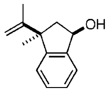
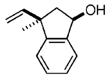
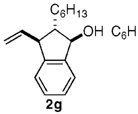
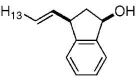
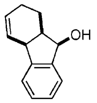
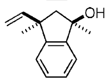
(2)

The annulation forming indanol was also catalyzed by $[IrCl(cod)]_2$, whereas $[IrCl(coe)_2]_2$ or $[IrCl(coe)_2]_2$/binap did not catalyze the reaction. It is likely that 1,5-cyclooctadiene (cod) works as an effective ligand throughout the reaction. The reaction was not catalyzed by rhodium complex $[Rh(OH)(cod)]_2$ under the same reaction conditions.

The results obtained for the iridium-catalyzed annulation with various types of 1,3-dienes are summarized in Table 1, which contains three characteristic features (i)−(iii) on the reactivity and the regioselectivity. (i) The scope of 1,3-diene is broad, both substituted with electron-donating alkyl groups and with electron-withdrawing groups being good substrates to produce indanols in high yields. (ii) Of the two double bonds constituting 1,3-diene substrates, the more electron-rich one participates in the reaction. (iii) Of the two carbons of the reacting double bond in 1,3-diene, the terminal carbon forms a bond with the carbonyl carbon of 2-formylphenylboronic acid.[6] In entries 1 and 2, dienamide **1b** and dienoate **1c** underwent the reaction at the double bond far away from the carbonyl group with the perfect regioselectivity, as shown

Table 1. Iridium-Catalyzed Annulation of 1,3-Dienes with 2-Formylphenylboronic Acid[a]

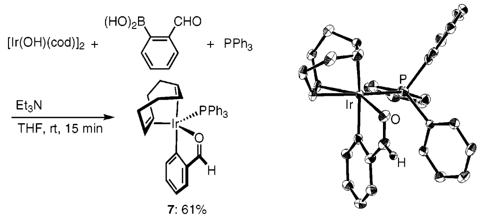


entry	diene	product	conditions	isolated yield (%)
1	**1b**	 **2b**	80 °C/6 h	92
2	**1c**	 **2c**	80 °C/3 h	97
3[b]	**1d**	 **2d**  **4d**	80 °C/12 h	**2d**: 65 **4d**: 11
4	**1e**	 **2e**	50 °C/24 h	53
5	**1f**	 **2f**	80 °C/3 h	89
6	**1g**	 **2g**  **5g**	50 °C/12 h	92 (**2g**/**5g** = 82/18)
7	**1h**	 **2h**	50 °C/3 h	29
8[c]	**1f**	 **6f**	80 °C/24 h	73

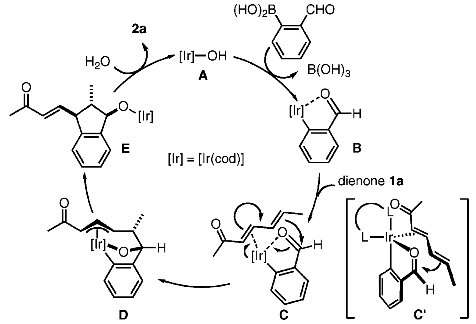
[a] Reaction conditions: 1,3-diene **1** (0.30 mmol), 2-formylphenylboronic acid (0.60 mmol), $[Ir(OH)(cod)]_2$ (5 mol % Ir), toluene (0.9 mL). [b] 2-Formylphenylboronic acid (1.20 mmol) and Et_3N (1.35 mmol) were used. [c] 2-Acetylphenylboronic acid was used.

10.1021/ja072369v CCC: $37.00

Scheme 1. Structure of Iridium(I) Complex **7**



Scheme 2. Proposed Catalytic Cycle



in the features (ii) and (iii), irrespective of the position of the methyl substituent. The same regioselectivity was observed for 1-phenyl-1,3-butadiene (**1d**) where the phenyl group works as an electron-withdrawing group, the reaction being accompanied by formation of a minor amount of indanone **4d** (entry 3). Entries 4−6 demonstrate that electron-rich dienes substituted with alkyl groups, 2,3-dimethyl-1,3-butadiene (**1e**), isoprene (**1f**), and 1,3-decadiene (**1g**), are also reactive toward the present annulation. The regiochemistry observed for the electron-rich unsymmetrical dienes **1f** and **1g** is consistent with that for electron-deficient dienes **1a**−**1d**. Thus, the reaction took place preferentially at the more electron-rich double bond due to the alkyl substitution, although the regioselectivity was not perfect for **1g** (82/18). The reaction of 1,3-cyclohexadiene (**1h**) gave a modest yield of tricyclic alcohol **2h** where the indanol skeleton has a 1,2,3-*cis* structure (entry 7). The cyclization was also successful using 2-acetylphenylboronic acid giving 73% yield of *tert*-alcohol **6f** in the reaction with isoprene (**1f**) (entry 8). It should be noted that the annulation reaction did not take place with monoenes such as styrene or 1-octene.[7]

We succeeded in isolating and characterizing an iridium complex containing 2-formylphenyl group and cod ligand, which gave us significant information on the mechanism of the present iridium-catalyzed reaction. Thus, treatment of $[\mathrm{Ir(OH)(cod)}]_2$ with 2-formylphenylboronic acid and triphenylphosphine in the presence of triethylamine at room temperature brought about a selective formation of aryliridium(I) complex **7**, which was isolated in 61% yield (Scheme 1). As shown in its X-ray crystal structure, a central iridium(I) has a distorted trigonal bipyramid orientation with a carbon atom of the aryl group on the apical site, and the other apical site is occupied by an alkene part of the chelating cod. A carbonyl oxygen in the equatorial site coordinates to the iridium center intramolecularly, creating a planer metallacyclic structure. The other equatorial sites are occupied by the remaining alkenic linkage and a phosphorus atom.[8] This complex **7** must be formed by transmetalation of the 2-formylphenyl group from boron to iridium and is stabilized by coordination of triphenylphosphine. The intermediacy of the 2-formylphenyliridium complex in the catalytic cycle was supported by stoichiometric reactions of the complex **7** with an excess amount of dienes **1a** and **1f**, which gave high yields of the cyclization products **2a** and **2f**, respectively, with the same regioselectivity as that in the catalytic reactions (eq 3).

$$\text{complex }\mathbf{7} \;+\; \begin{matrix}\mathbf{1a}\\ (10\text{ equiv})\\ \text{or}\\ \mathbf{1f}\\ (10\text{ equiv})\end{matrix} \xrightarrow[\substack{\text{dioxane/H}_2\text{O (5/1)}\\ 80\ ^\circ\text{C, 1 h}}]{\text{B(OH)}_3\text{ (20 equiv)}} \begin{matrix}\mathbf{2a}\text{: 96\%}\\ \text{or}\\ \mathbf{2f}\text{: 88\%}\end{matrix} \qquad (3)$$

On the basis of the regiochemistry observed in the annulation reactions and the structure of the complex **7**, the catalytic cycle of the present reaction is proposed as illustrated in Scheme 2. Transmetalation of a 2-formylphenyl group to the iridium center forms a 2-formylphenyliridium(I) species **B**. Nucleophilic attack of the electron-rich terminal carbon of diene on the formyl carbon in intermediate **C**, where the other double bond of diene is coordinated to iridium, forms a π-allyliridium(III) **D** via the oxidative cyclization.[9] In this step, the formyl group is activated by coordination to the iridium center to facilitate the attack of a relatively electron-rich alkene. Meanwhile, the iridium center becomes more electron-rich, resulting in increase of back-donation of the electron to a relatively electron-poor double bond. The complex **D** undergoes reductive elimination forming a carbon−carbon bond to give an alkoxoiridium(I) **E**, and subsequent hydrolysis gives the indanol and regenerates the hydroxoiridium **A**. The stereoselectivity of the product **2a** may be derived from the formation of the π-allyliridium **D** via the five-coordinate intermediate **C′** analogous to the complex **7**.

In summary, we have found a new type of annulation reaction of 1,3-dienes with 2-carbonylated phenylboronic acids giving indanol derivatives with high regio- and stereoselectivity by use of an iridium catalyst.

Acknowledgment. This work has been supported in part by a Grant-in-Aid for Scientific Research, the Ministry of Education, Culture, Sports, Science and Technology, Japan (Priority Areas “Advanced Molecular Transformations of Carbon Resources”). Y.Y. thanks the Japan Society for the Promotion of Science for Young Scientists for a research fellowship.

Supporting Information Available: Experimental procedures and spectroscopic and analytical data for the substrates and products (pdf) and X-ray data (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) For recent reviews, see: (a) Takeuchi, R.; Kezuka, S. *Synthesis* **2006**, 3349. (b) Ishii, Y.; Sakaguchi, S. *Bull. Chem. Soc. Jpn.* **2004**, *77*, 909.

(2) For the use of *ortho*-carbonylated arylboron reagents in the rhodium-catalyzed addition−cyclization reactions, see: (a) Shintani, R.; Okamoto, K.; Hayashi, T. *Chem. Lett.* **2005**, *34*, 1294. (b) Matsuda, T.; Makino, M.; Murakami, M. *Chem. Lett.* **2005**, *34*, 1416. For the use of 2-cyanophenylboronic acid, see: (c) Miura, T.; Murakami, M. *Org. Lett.* **2005**, *7*, 3339.

(3) For examples of the use of *ortho*-functionalized arylboron reagents in the rhodium-catalyzed reactions, see: (a) Lautens, M.; Mancuso, J. *Org. Lett.* **2002**, *4*, 2105. (b) Lautens, M.; Mancuso, J. *J. Org. Chem.* **2004**, *69*, 3478. (c) Lautens, M.; Marquardt, T. *J. Org. Chem.* **2004**, *69*, 4607. (d) Tseng, N.-W.; Mancuso, J.; Lautens, M. *J. Am. Chem. Soc.* **2006**, *128*, 5338.

(4) Green, L. M.; Meek, D. W. *Organometallics* **1989**, *8*, 659.

(5) Nishimura, T.; Yasuhara, Y.; Hayashi, T. *Angew. Chem., Int. Ed.* **2006**, *45*, 5164.

(6) In the nickel-catalyzed homoallylation of aldehydes, similar selectivity of dienes has been reported: (a) Kimura, M.; Ezoe, A.; Shibata, K.; Tamaru, Y. *J. Am. Chem. Soc.* **1998**, *120*, 4033. (b) Kimura, M.; Ezoe, A.; Mori, M.; Iwata, K.; Tamaru, Y. *J. Am. Chem. Soc.* **2006**, *128*, 8559 and references therein.

(7) The use of benzaldehyde in place of *ortho*-formylphenylboronic acid for the reaction with **1a** did not give the indanol.

(8) For five-coordinate methyliridium(I) complexes bearing two tertiary phosphines and 1,5-cyclooctadiene as ligands, see: (a) Shapley, J. R.; Osborn, J. A. *Acc. Chem. Res.* **1973**, *6*, 305. (b) Churchill, M. R.; Bezman, S. A. *Inorg. Chem.* **1972**, *11*, 2243. (c) Shapley, J. R.; Osborn, J. A. *J. Am. Chem. Soc.* **1970**, *92*, 6976.

(9) In the rhodium-catalyzed annulation of *ortho*-formylphenylboronic acid with alkynes, the first carbon−carbon bond formation takes place by the insertion of an alkyne into a rhodium−carbon bond; see ref 2.

JA072369V