

## Iridium-Catalyzed Formal [4 + 1] Cycloaddition of Biphenylenes with Alkenes Initiated by C–C Bond Cleavage for the Synthesis of 9,9-Disubstituted Fluorenes

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## Supporting Information

**ABSTRACT:** An Ir-catalyzed intermolecular reaction of biphenylenes as a C4 unit with various alkenes as a C1 unit gave 9,9-disubstituted fluorenes in moderate to high yields. Preliminary mechanistic studies revealed that this formal [4 + 1] cycloaddition probably proceeds via C–C bond cleavage, alkene insertion,  $\beta$ -hydrogen elimination, intramolecular alkene insertion, and then reductive elimination. An example of enantioselective reaction was also disclosed.

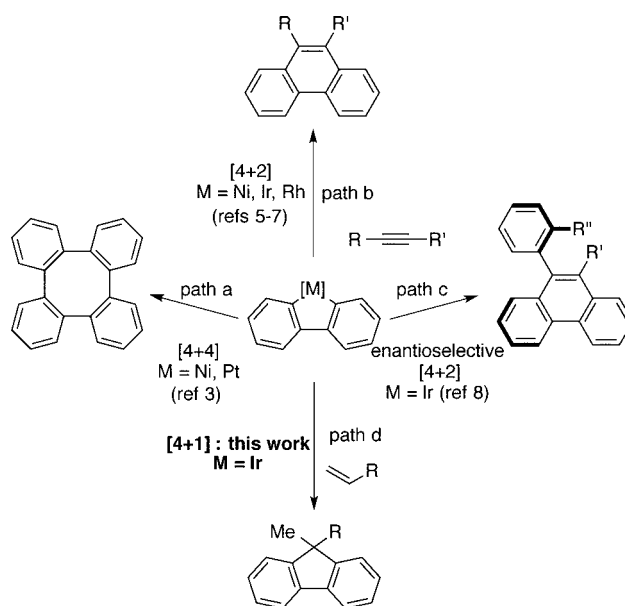


Generally, a carbon–carbon (C–C) single bond is inactive and cannot be directly used in organic synthesis. However, C–C bonds found in small ring compounds such as cyclopropane and cyclobutane can be cleaved due to their ring strain. In particular, transition metal complexes can realize oxidative cleavage of such C–C single bonds under relatively mild reaction conditions to give metallacycles. Therefore, various types of transition-metal-catalyzed synthetic transformations of small ring compounds initiated by C–C bond activation have been reported.<sup>1,2</sup> Biphenylene is a typical substrate that reacts with transition metal complexes to form dibenzometallacyclopentadiene and, thus, often used as a C4 unit (Scheme 1). For example, nickel- or platinum-catalyzed homocoupling of biphenylene gives *o,o,o,o*-tetraphenylene as a formal [4 + 4] cycloadduct (path a).<sup>3,4</sup> The iridium- or rhodium-catalyzed reaction of biphenylene with alkynes and nitriles affords phenanthrenes and phenanthridines, respectively (path b).<sup>5–7</sup> We reported asymmetric variants, where an iridium-catalyzed enantioselective formal [4 + 2] cycloaddition of biphenylene with *ortho*-substituted arylalkynes gave axially chiral phenanthrene derivatives (path c).<sup>8</sup>

Herein we report a new pattern of formal [4 + 1] cycloaddition (path d):<sup>9–11</sup> Ir-catalyzed reaction of biphenylenes with alkenes as a C1 unit provides a variety of 9,9-disubstituted fluorenes in moderate to high yields. The reaction mechanism involving inter- and intramolecular alkene insertions is also discussed.

We first examined the reaction of biphenylene (1a) with styrene (2a) in the presence of an Ir catalyst prepared *in situ* from  $[\text{Ir}(\text{cod})\text{Cl}]_2$  and 2,2'-bis(diphenylphosphino)-1,1'-biphenyl (BIPHEP) in xylene at 135 °C (Scheme 2). While the expected [4 + 2] cycloadduct could not be detected at all,

**Scheme 1.** Formal Cycloadditions of Dibenzometallacyclopentadiene as a C4 Unit Derived from Biphenylene

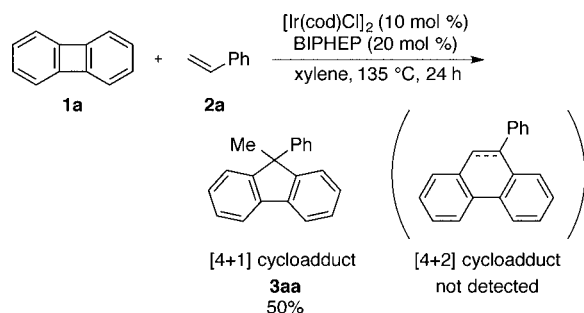


fluorene derivative 3aa was obtained in moderate yield, where styrene was incorporated as a C1 unit to construct a cyclopentadiene ring.<sup>12</sup>

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Scheme 2. Reaction of Biphenylene (1a) with Styrene (2a)



To improve the yield of the formal [4 + 1] cycloadduct 3aa, we screened several reaction conditions (Table 1). When

Table 1. Screening of Reaction Conditions<sup>a</sup>

entry <sup>a</sup>	ligand	solvent	yield (%)
1	BINAP	xylene	83
2	DPPF	xylene	NR
3	PPh <sub>3</sub> <sup>b</sup>	xylene	NR
4	BINAP	1,4-dioxane	44
5	BINAP	PhCl	5
6 <sup>c</sup>	BINAP	xylene	ND
7 <sup>d</sup>	BINAP	xylene	71

<sup>a</sup>Conditions: 1a (0.10 mmol), 2a (0.40 mmol),  $[\text{Ir}(\text{cod})\text{Cl}]_2$  (0.010 mmol), ligand (0.020 mmol). <sup>b</sup>Triphenylphosphine (40 mol %) was used. <sup>c</sup> $[\text{Rh}(\text{cod})\text{Cl}]_2$  was used in place of  $[\text{Ir}(\text{cod})\text{Cl}]_2$ . <sup>d</sup>Conditions:  $[\text{Ir}(\text{cod})\text{Cl}]_2$  (2.5 mol %), BINAP (5.0 mol %), 4 days.

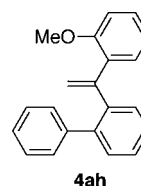
racemic-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP) was used as a ligand, most of the biphenylene (1a) was consumed and a higher yield was achieved (entry 1). In contrast, no reaction proceeded when using other ligands such as 1,1'-bis(diphenylphosphino)ferrocene (DPPF) and triphenylphosphine (entries 2 and 3). The solvent effect was very large, and xylene was the best among three solvents (entries 1, 4, and 5). In the present reaction, the Rh counterpart was ineffective (entry 6). The amount of the catalyst could be reduced to 5 mol %, but a longer reaction time was required (entry 7).

Under the optimum conditions indicated in entry 1 of Table 1, various alkenes were subjected to the formal [4 + 1] cycloaddition (Table 2). We first examined styrene derivatives 2b–f possessing various substituents at the para position (entries 1 and 2). Although 4-chlorostyrene (2b) gave the corresponding product 3ab in moderate yield because of low conversion of 1a, 4-fluorostyrene (2c) gave 3ac in high yield. In addition to phenyl and methyl groups, a methoxy group was also tolerated, and the corresponding products 3ad–3af were obtained in moderate to high yields. 3-Methoxystyrene (2g) was also a good coupling partner, but 2-methoxystyrene (2h) was not, and the yield of cycloadduct 3ah was low along with the formation of uncyclized product 4ah having an exo olefin moiety, which is possibly derived from a reaction intermediate as we discuss later (entry 2). Vinylsilanes 2i and 2j and allylsilane 2k also reacted with biphenylene (1a) to give 9-silylated and 9-silylmethylated fluorenes 3ai–3ak (entries 3 and 4). Finally, 1-nonene (2l) as a simple alkene was examined, and

Table 2. Formal [4 + 1] Cycloaddition of Biphenylene (1a) with Various Alkenes 2<sup>a</sup>

entry	alkene	product
1	2b (R' = Cl) 2c (R' = F) 2d (R' = Ph) 2e (R' = Me)	3ab, 42% 3ac, 88% 3ad, 66% 3ae, 88%
2	2f (R' = 4-MeO) 2g (R' = 3-MeO) 2h (R' = 2-MeO)	3af, 70% 3ag, 70% 3ah, 17% <sup>b</sup>
3	2i (R = SiMe <sub>3</sub> ) 2j (R = SiEt <sub>3</sub> )	3ai, 44% 3aj, 51%
4	2k	3ak, 70%
5	2l	3al, 63%

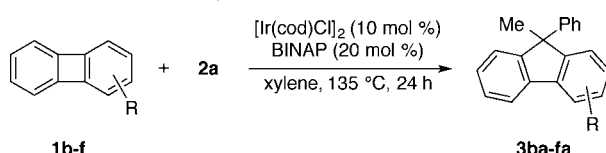
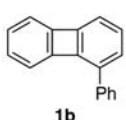
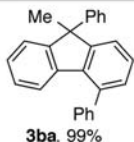
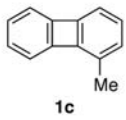
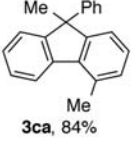
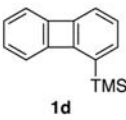
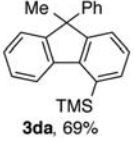
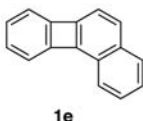
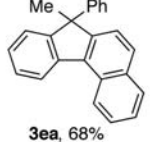
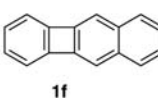
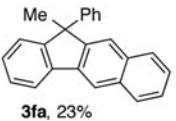
<sup>a</sup>Condition: 1a (0.10 mmol), 2 (0.40 mmol),  $[\text{Ir}(\text{cod})\text{Cl}]_2$  (0.010 mmol), BINAP (0.020 mmol). <sup>b</sup>Byproduct 4ah was obtained in 27% yield.



9,9-dialkylated fluorene 3al was obtained in 63% yield (entry 5).<sup>13</sup>

Next, we examined the scope of biphenylene derivatives 1b–1f using styrene (2a) as a standard alkene (Table 3). The formal [4 + 1] cycloaddition of 1-phenylbiphenylene (1b) proceeded to give 3ba quantitatively (entry 1). Methyl and trimethylsilyl substituents were tolerable, and 4-substituted fluorenes 3ca and 3da were obtained (entries 2 and 3). The reaction of benzo[a]biphenylene (1e) with styrene also proceeded smoothly to afford 7,7-disubstituted benzo[c]-fluorene 3ea<sup>14</sup> in 68% yield (entry 4). Notably, the sterically less hindered single bond of biphenylenes was selectively cleaved, and regioisomeric fluorenes could not be detected in all entries. The reaction of benzo[b]biphenylene (1f) proceeded to give 3fa, but in low yield probably because of instability of 1f under the reaction conditions (entry 5).

Table 3. Formal [4 + 1] Cycloaddition of Biphenylene Derivatives **1** with Styrene (**2a**)<sup>a</sup>

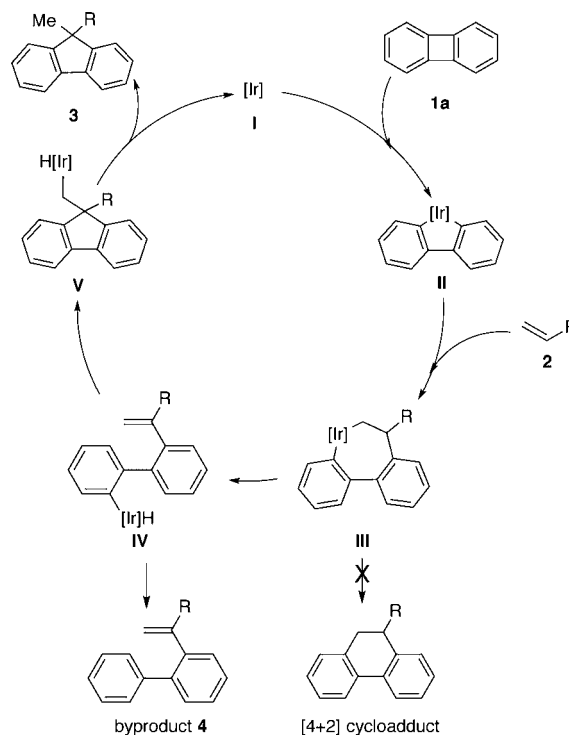
		
entry	biphenylene	product
1		
2		
3		
4 <sup>b</sup>		
5		

<sup>a</sup>Condition: **1** (0.10 mmol), **2a** (0.40 mmol), [Ir(cod)Cl]<sub>2</sub> (0.010 mmol), BINAP (0.020 mmol). <sup>b</sup>The reaction time was 4 h.

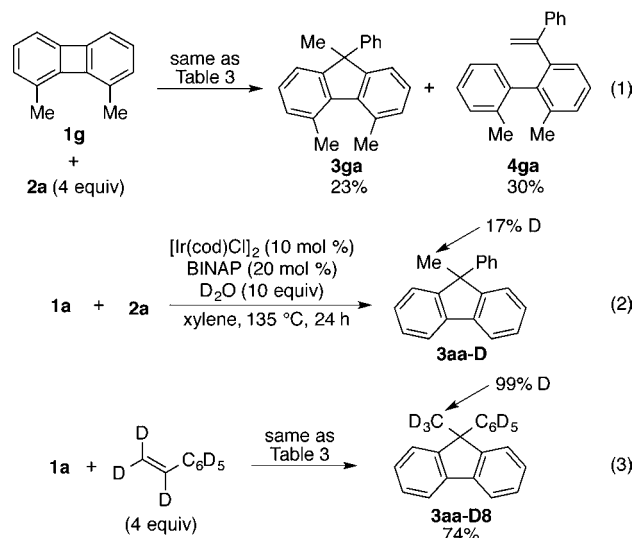
We propose the reaction mechanism of this formal [4 + 1] cycloaddition in Scheme 3. The reaction is initiated by oxidative addition of the Ir(I) catalyst to the C–C single bond of biphenylene (**1a**) to give iridacyclopentadiene **II**. The insertion of alkene **2** leads to seven-membered metallacycle **III**. Next,  $\beta$ -hydrogen elimination proceeds prior to reductive elimination, which affords a [4 + 2] cycloadduct, and iridium hydride species **IV** is formed. Intramolecular alkene insertion along with the formation of a five-membered ring and subsequent reductive elimination afford 9,9-disubstituted fluorene **3** and regenerates the Ir catalyst. The existence of intermediate **IV** was supported by the formation of byproduct **4ah** in entry 2 of Table 2.

To reinforce our speculation, we investigated the reaction of 1,8-dimethylbiphenylene (**1g**) with styrene (**2a**), where two methyl groups can facilitate the reductive elimination from intermediate **IV** due to their bulkiness (eq 1 in Scheme 4). As a result, a significant amount of exo olefin compound **4ga** was obtained as we expected, in addition to [4 + 1] cycloadduct **3ga**.<sup>15</sup> When the reaction was conducted in the presence of excess amounts of deuterated water, deuteration of the methyl proton was observed (eq 2). When styrene-*d*<sub>8</sub> was used, almost perfect transfer of the vinylic protons to the methyl group in the product was observed (eq 3).

Scheme 3. Proposed Mechanism

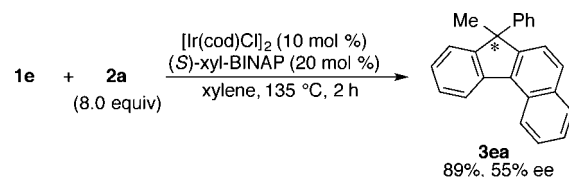


Scheme 4. Mechanism Studies



As a preliminary application of this protocol, we examined an enantioselective reaction of benzo[*a*]biphenylene (**1e**) with styrene (**2a**) (Scheme 5). Among several chiral ligands,<sup>16</sup> xyl-BINAP could induce moderate enantioselectivity, and benzo-

Scheme 5. Enantioselective Reaction



[c]fluorene **3ea** with an all-carbon quaternary stereogenic center was obtained in high yield.

In summary, we developed an Ir-catalyzed formal [4 + 1] cycloaddition initiated by C–C bond cleavage of biphenylenes. Various alkenes could be used as a C1 unit, and 9,9-disubstituted fluorenes were obtained.<sup>17</sup> This unprecedented transformation probably includes  $\beta$ -hydrogen elimination between intermolecular and intramolecular alkene insertion. Synthetic applications including asymmetric synthesis are to be studied in due course in our laboratory.

## ■ ASSOCIATED CONTENT

### ■ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b00619.

Experimental procedure, characterization, and NMR copies of all new compounds (PDF)

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### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

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(13) The reaction of **1a** with disubstituted alkenes, such as *cis*-stilbene and norbornene, did not give [4 + 1] cycloadducts.

(14) The structure of **3ea** was determined by NOESY analyses (see Supporting Information).

(15) The obtained **4ga** was subjected to the reaction, but the formation of **3ga** could not be detected.

(16) Table S1 in Supporting Information.

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