JOC The Journal of Organic Chemistry

Note

pubs.acs.org/joc

Palladium-Catalyzed Cross-Coupling Reaction of Diazo Compounds and Vinyl Boronic Acids: An Approach to 1,3-Diene Compounds

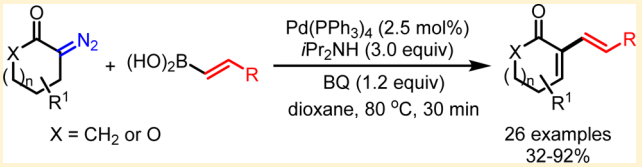
Yamu Xia,[†,‡] Ying Xia,[‡] Zhen Liu,[‡] Yan Zhang,[‡] and Jianbo Wang*[,‡]

[†]College of Chemical Engineering, Qingdao University of Science & Technology, Qingdao 266042, China

[‡]Beijing National Laboratory of Molecular Sciences (BNLMS), Key Laboratory of Bioorganic Chemistry and Molecular Engineering of Ministry of Education, College of Chemistry, Peking University, Beijing 100871, China

Supporting Information

ABSTRACT: A palladium-catalyzed oxidative cross-coupling of vinyl boronic acids and cyclic α-diazocarbonyl compounds has been reported. The reaction constitutes an efficient method for the synthesis of 1,3-diene compounds bearing a ring structure. Mechanistically, the reaction involves migratory insertion of palladium carbene as the key step.

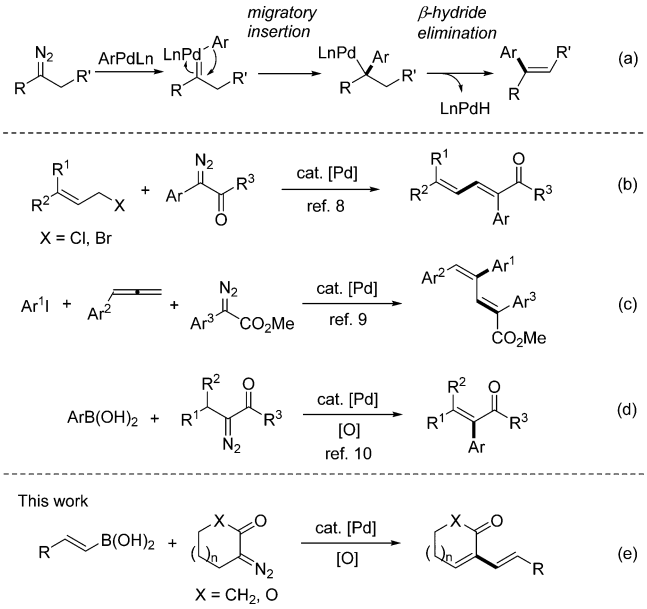


1,3-Diene structures widely exist in natural products and biologically active pharmaceutical and medicinal agents.[1] Moreover, 1,3-dienes play important roles in the field of organic synthesis and materials chemistry.[2] Owing to the importance of 1,3-dienes, their efficient synthesis has attracted much attention over the years, and a variety of synthetic methodologies were explored. In particular, the methods based on transition-metal-catalyzed coupling reactions provide highly efficient and versatile synthesis of 1,3-diene compounds.[3] Although many efforts have been devoted to this area, it is still highly desirable to develop novel and efficient cross-coupling reactions for the synthesis of 1,3-dienes.

In recent years, Pd-catalyzed cross-coupling reactions involving carbene migratory insertion have rapidly evolved into a new type of coupling reactions since the pioneering work by Van Vranken and co-workers.[4,5] This type of reaction uses diazo compounds or *N*-tosylhydrazones (for the generation of nonstabilized diazo substrates *in situ*)[6] as the cross-coupling partners to form the Pd carbene intermediate, which undergoes migratory insertion and leads to the formation of the carbon−carbon bond. Typically, regeneration of the Pd catalyst is achieved via β-hydrogen elimination of palladium species, leading to the formation of C═C double bond (Scheme 1a). Therefore, this type of reaction has become an efficient method for the synthesis of vinyl compounds.[5,7]

Based on these novel cross-coupling reactions, 1,3-diene compounds could also be synthesized. We have previously reported the Pd-catalyzed reaction of allyl halides and diazo compounds to afford 1,3-diene products (Scheme 1b).[8] Subsequently, the three-component reaction of allenes, aryl iodides, and diazo compounds was developed in our group and applied to the synthesis of 1,3-dienes (Scheme 1c).[9] In addition, we have also reported the Pd-catalyzed oxidative coupling of boronic acids with α-diazocarbonyl compounds to form α,β-aryl unsaturated carbonyl compounds (Scheme 1d).[10] As a continuation of our interest in this field, herein we further extend the scope of this reaction using vinyl boronic acids and

Scheme 1. Pd-Catalyzed Cross-Coupling Reactions Involving Carbene Migratory Insertion



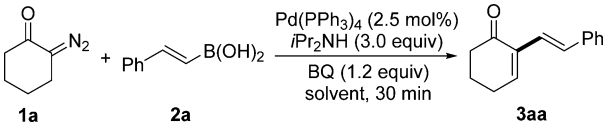
cyclic diazo compounds as the substrates (Scheme 1e). This reaction provides a new methodology for the synthesis of 1,3-diene compounds bearing cyclic moiety.

At the outset of the investigation, we employed the 2-diazocyclohexanone **1a** and (*E*)-styrylboronic acid **2a** as the substrates to examine the reaction (Table 1). Initially, the cross-coupling reaction with **1a** (0.2 mmol) and **2a** (0.2 mmol) afforded the desired 1,3-diene **3aa** in 62% yield (entry 1), under the similar reaction conditions that we have previously used for oxidative coupling with aryl boronic acids [$Pd(PPh_3)_4$ (2.5 mol

Received: June 6, 2014
Published: July 14, 2014

   dx.doi.org/10.1021/jo5012703 | J. Org. Chem. 2014, 79, 7711−7717

Table 1. Optimization of the Reaction Conditions[a]



entry	solvent	temp (°C)	1a/2a	3aa, %[b]
1	dioxane	80	1:1	62
2	dioxane	80	1:1.5	66
3	dioxane	80	1:2	67
4	dioxane	80	1.5:1	76
5	dioxane	80	1.5:1	84[c]
6	dioxane	90	1.5:1	74[c]
7	dioxane	60	1.5:1	65[c]
8	PhMe	80	1.5:1	75[c]
9	MeCN	80	1.5:1	47[c]

[a]All the reactions of **1a** and **2a** were carried out in the presence of $Pd(PPh_3)_4$ (0.005 mmol), iPr_2NH (0.60 mmol), BQ (0.24 mmol), and dioxane (2 mL). [b]Yields refer to the isolated products. [c]**1a** was dropped into the reaction system in 5 min.

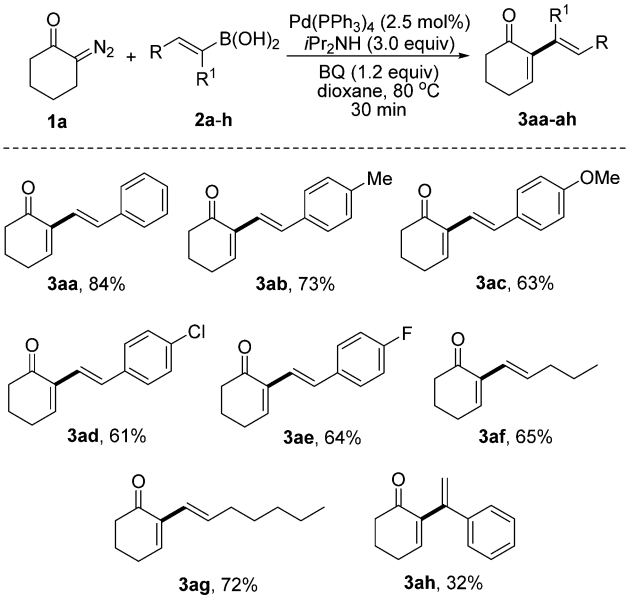
%) as catalyst, iPr_2NH (0.6 mmol), BQ (0.24 mmol) as oxidant, dioxane (2 mL) as solvent, 80 °C, 30 min].[10] To further optimize the reaction conditions, the ratio of **1a** and **1b** was adjusted. We found that the yields could not be increased by using an excess amount of **2a** (entry 2, 3). On the contrary, increase of **1a** led to the improvement of yield, affording **3aa** in 76% yield with **1a**/**2b** = 1.5:1 (entry 4). The reaction could be further improved by dropping **1a** into the reaction system in 5 min (entry 5). Thereafter, we examined the reaction temperature and solvent and observed diminished yields at higher and lower temperature or with PhMe and MeCN as the solvents (entries 6−9).

With the optimized conditions in hand, the scope of the reaction was first explored with various vinyl boronic acids and 2-diazocyclohexanone. As shown in Scheme 2, the coupling reaction with β-substituted vinyl boronic acids proceeded smoothly, affording the corresponding 1,3-diene products **3aa**−**ag** in moderate yields. However, the reaction with α-aryl vinyl boronic acid gave the coupling products in noticeably diminished yields (**3ah**).

Next, a series of cyclic diazo compounds **1b**−**h** were employed as substrates to react with (*E*)-styrylboronic acid **2a** and (*E*)-hept-1-en-1-ylboronic acid **2g**. As shown in Scheme 3, the alkyl substituents in 2-diazocyclohexanone had essentially no effect on the reaction, in all cases the 1,3-dienes were obtained in over 80% yields (**3ba**−**3da**). However, the reaction was drastically affected by the size of the ring of the diazo substrates. The diazo compound with a five-membered ring afforded the 1,3-diene product in 32% yields (**3ea**), while the reactions of the cyclic diazo substrates bearing the rings larger than a five-membered ring all afforded the products in good yields. Notably, for the reaction with 2-diazocyclododecan-1-one **1h**, the corresponding 1,3-diene products **3ha** or **3hg** were obtained as single products in each case; however, their configuration was not determined.

Furthermore, examinations of the scope of diazo compounds with lactone structure were carried out (Scheme 4). In these cases, optimal results could be obtained under similar reaction conditions except with the revised ratio of diazo substrates to vinyl boronic acids (1:1.5). Under such conditions, the 1,3-diene products could be obtained in moderately good yields.

Scheme 2. Substrate Scope of Vinyl Boronic Acids[a]



[a]All the reactions were carried out with **1a** (0.30 mmol), **2a**−**h** (0.20 mmol), $Pd(PPh_3)_4$ (0.005 mmol), BQ (0.24 mmol), and iPr_2NH (0.6 mmol) in dioxane (2 mL), 80 °C for 30 min. **1a** was added dropwise to the reaction system in 5 min. Yields refer to the isolated products with silica gel column chromatography.

Finally, for comparison, the Pd-catalyzed reaction was explored with methyl 2-diazo-3-phenylpropanoate **6a** as the substrate. As shown in Scheme 5, the reaction also gave the corresponding 1,3-dienes in good yields. However, stereoisomeric mixtures were obtained with essentially no selectivity (Scheme 5).

Based on the previous studies,[5] we proposed a possible mechanism as shown in Scheme 6. First, $Pd(0)L_n$ is oxidized to Pd(II) species **A** by benzoquinone (BQ). Then intermediate **B** is formed through transmetalation with vinyl boronic acid. The reaction of the diazo compound with the intermediate **B** generates the Pd carbene intermediate **C**, followed by migratory insertion of the vinyl group to give Pd species **D**. Finally, the 1,3-diene product **E** is produced through β-hydride elimination of the intermediate **D**.

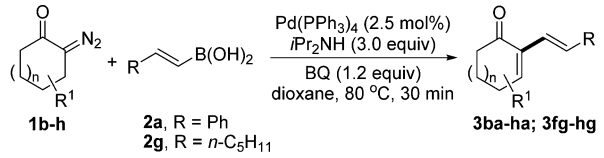
In summary, we have developed a new synthetic approach toward 1,3-diene compounds bearing ring structure through Pd-catalyzed oxidative cross-coupling of diazo compounds with vinyl boronic acids. The reaction is under mild conditions and is operationally simple. This reaction further demonstrates the generality of the diazo compounds as a new type of reaction partners in Pd-catalyzed cross-coupling reactions.

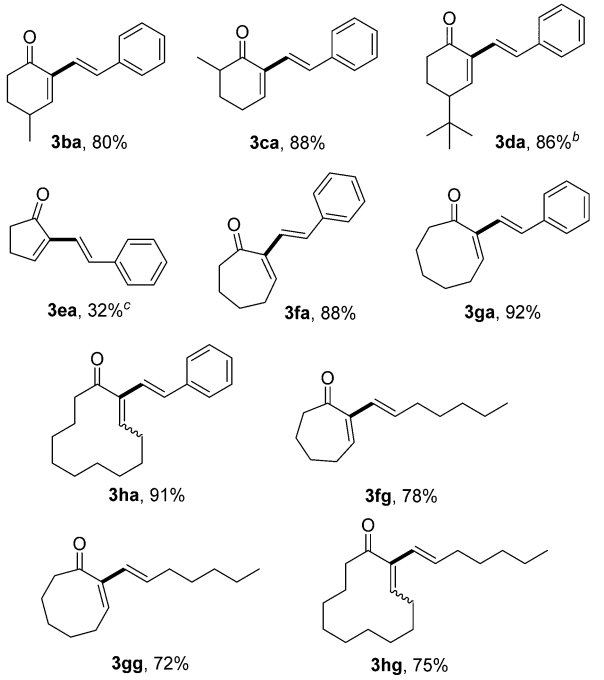
EXPERIMENTAL SECTION

General Experimental Methods. All the palladium-catalyzed reactions were performed under argon atmosphere in a flame-dried reaction flask. All solvents were distilled under nitrogen atmosphere prior to use. Dioxane and toluene were dried over Na with benzophenone−ketyl intermediate as indicator, and acetonitrile was dried over CaH_2. Diazo compounds were prepared according to the literature procedure.[11,12] Unless otherwise noted, chemicals were used as received without further purification. For chromatography, 200−300 mesh silica gel was used. ^1H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively. Chemical

dx.doi.org/10.1021/jo5012703 | J. Org. Chem. 2014, 79, 7711−7717

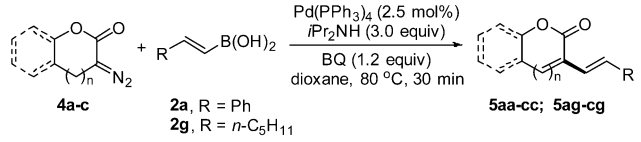
Scheme 3. Substrate Scope of Diazo Compounds[a]

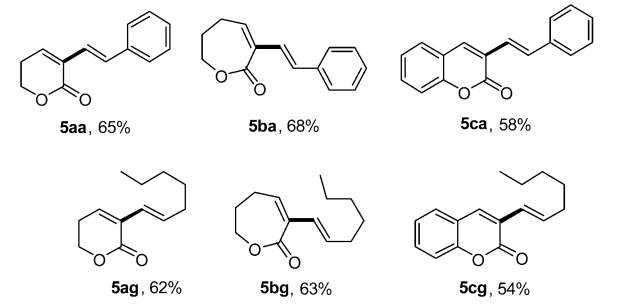




[a]The reactions were carried out with **1b**, **1c**, or **1f**–**h** (0.30 mmol), **2a** or **2g** (0.20 mmol), $Pd(PPh_3)_4$ (0.005 mmol), BQ (0.24 mmol), and iPr_2NH (0.6 mmol) in dioxane (2 mL), 80 °C for 30 min. The yields refer to the isolated products with silica gel column chromatography. [b]**1d** was dissolved in 0.2 mL of dioxane and was added dropwise to the reaction system within 5 min. [c]The reactions were carried out with **1e** (0.20 mmol) and **2a** (0.30 mmol); **1e** was dissolved in 0.2 mL of dioxane, and the solution was added dropwise to the reaction system in 5 min.

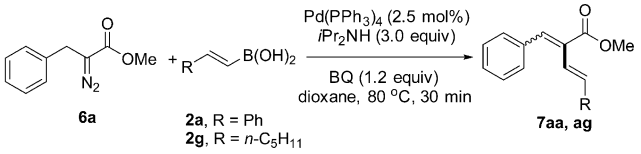
Scheme 4. Substrate Scope of Diazo Compounds with Lactone[a]

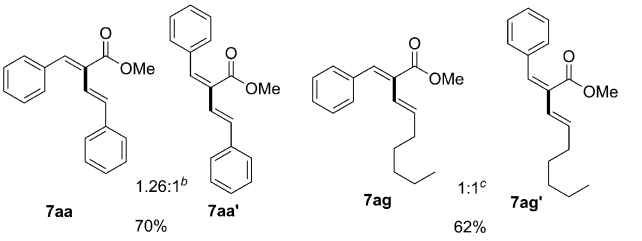




[a]All the reactions were carried out with **4a**–**c** (0.20 mmol), **2a** or **2g** (0.30 mmol), $Pd(PPh_3)_4$ (0.005 mmol), BQ (0.24 mmol), and iPr_2NH (0.6 mmol) in dioxane (2 mL), 80 °C for 30 min. **4a**–**c** was dissolved in 0.2 mL of dioxane; the solution was then added dropwise to the reaction system in 5 min. Yields refer to the isolated products with silica gel column chromatography.

Scheme 5. Substrate Scope of Methyl 2-Diazo-3-phenylpropanoate[a]





[a]All the reactions were carried out with **6a** (0.20 mmol), **2a** or **2g** (0.30 mmol), $Pd(PPh_3)_4$ (0.005 mmol), BQ (0.24 mmol), and iPr_2NH (0.6 mmol) in dioxane (2 mL), 80 °C for 30 min. **6a** was added dropwise to the reaction system in 5 min. Yields refer to the isolated products with silica gel column chromatography. [b]The ratio was determined by isolated products. [c]The ratio was determined by ^1H NMR.

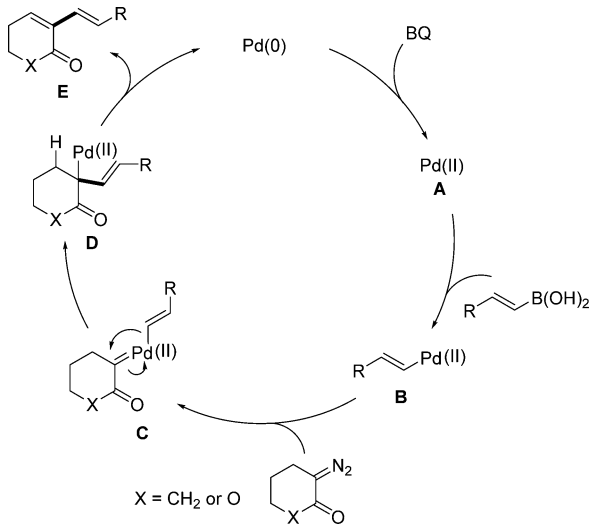
shifts are reported in ppm using tetramethylsilane as internal standard. IR spectra were recorded in wavenumbers (cm^{-1}). For HRMS measurements, the mass analyzer is FT-ICR. Melting points are reported as uncorrected.

General Procedure I: Pd-Catalyzed Cross-Coupling of Diazo Compounds 1a–h and Vinyl Boronic Acid Derivatives (Schemes 2, 3). Under an argon atmosphere, $Pd(PPh_3)_4$ (5.5 mg, 0.005 mmol, 2.5 mol%), BQ (25.9 mg, 0.24 mmol), and *trans*-2-phenylvinylboronic acid (29.6 mg, 0.2 mmol) were successively added to a flame-dried 25 mL Schlenk flask. The reaction flask was degassed three times with argon and dry dioxane (2.0 mL), and diisopropylamine (60.6 mg, 0.6 mmol) was added using a syringe and the reaction solution was heated to 80 °C. Then 2-diazocyclohexanone (37.2 mg, 0.3 mmol) was added dropwise to the reaction system in 5 min (alternatively, 2-diazocyclohexanone could be dissolved in 0.2 mL of dioxane and dropped into the reaction solution of 1.8 mL of dioxane). The reaction was stirred for 30 min, then cooled to room temperature, and filtered through a short path of neutral alumina with ethyl acetate (30 mL) as eluent. Solvent was then removed *in vacuo* to leave a crude mixture, which was purified by silica gel column chromatography (PE/EA = 30:1, PE = petroleum ether, ethyl acetate = EA) to afford the pure 1,3-diene product **3aa**.

*(E)-2-Styrylcyclohex-2-enone (**3aa**).* A yellow solid (33.3 mg, 84%); mp 61–63 °C. IR (film): 1674, 1448, 1249, 1175, 1103, 970, 750, 692 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 7.2 Hz, 2H), 7.34–7.20 (m, 3H), 7.13 (t, J = 4.8 Hz, 1H), 7.06 (d, J = 16.8 Hz, 1H), 6.95 (d, J = 16.8 Hz, 1H), 2.53–2.42 (m, 4H), 2.06–2.00 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.4, 144.9, 137.4, 136.1, 130.1, 128.5, 127.5, 126.5, 122.8, 38.8, 26.4, 22.5. LRMS (EI, m/z): 198 (M^+, 37), 169 (25), 154 (46), 141 (100), 115 (43). HRMS (ESI, m/z): calcd for $C_{14}H_{15}O$ $[M + H]^+$ 199.1117, found 199.1113.

dx.doi.org/10.1021/jo5012703 | J. Org. Chem. 2014, 79, 7711–7717

Scheme 6. Proposed Reaction Mechanism



(E)-2-(4-Methylstyryl)cyclohex-2-enone (**3ab**). The crude compound was prepared through the general procedure. After purification by silica gel column chromatography (PE/EA = 30:1), compound **3ab** was isolated as a yellow solid (30.9 mg, 73%); mp 59−61 °C. IR (film): 1665, 1512, 1370, 1257, 1138, 816 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, J = 8.0 Hz, 2H), 7.13−7.09 (m, 3H), 7.02 (d, J = 16.4 Hz, 1H), 6.91 (d, J = 16.4 Hz, 1H), 2.52−2.46 (m, 4H), 2.33 (s, 3H), 2.04−2.00 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.4, 144.4, 137.4, 136.1, 134.6, 129.9, 129.2, 126.4, 121.7, 38.8, 26.4, 22.5, 21.1. LRMS (EI, m/z): 212 (M^+, 54), 197 (12), 184 (13), 155 (100), 141 (72). HRMS (ESI, m/z): calcd for $C_{15}H_{17}O$ $[M + H]^+$ 213.1274, found 213.1270.

(E)-2-(4-Methoxystyryl)cyclohex-2-enone (**3ac**). The crude compound was prepared through the general procedure. After purification by silica gel column chromatography (PE/EA = 15:1), compound **3ac** was isolated as a yellow solid (28.7 mg, 63%); mp 70−72 °C. IR (film): 1664, 1510, 1252, 1174, 1029, 970, 732 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 8.8 Hz, 2H), 7.08 (t, J = 4.4 Hz, 1H), 7.00 (d, J = 16.4 Hz, 1H), 6.87−6.80 (m, 3H), 3.80 (s, 3H), 2.52−2.46 (m, 4H), 2.04−2.00 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.5, 159.2, 144.0, 136.2, 130.2, 129.5, 127.7, 120.6, 113.9, 55.2, 38.8, 26.4, 22.5. LRMS (EI, m/z): 228 (M^+, 100), 213 (15), 199 (17), 185 (21), 171 (98). HRMS (ESI, m/z): calcd for $C_{15}H_{17}O_2$ $[M + H]^+$ 229.1223, found 229.1219.

(E)-2-(4-Chlorostyryl)cyclohex-2-enone (**3ad**). The crude compound was prepared through the general procedure. After purification by silica gel column chromatography (PE/EA = 30:1), compound **3ad** was isolated as a yellow solid (28.3 mg, 61%); mp 163−165 °C. IR (film): 1675, 1490, 1090, 970, 822 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 8.4 Hz, 2H), 7.12 (t, J = 4.4 Hz, 1H), 7.03 (d, J = 16.4 Hz, 1H), 6.90 (d, J = 16.4 Hz, 1H), 2.54−2.48 (m, 4H), 2.07−1.99 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.3, 145.5, 135.9, 135.8, 133.1, 128.8, 128.6, 127.7, 123.5, 38.8, 26.4, 22.5. LRMS (EI, m/z): 232 (M^+, 63), 207 (13), 175 (82), 141 (100). HRMS (ESI, m/z): calcd for $C_{14}H_{14}ClO$ $[M + H]^+$ 233.0728, found 233.0728.

(E)-2-(4-Fluorostyryl)cyclohex-2-enone (**3ae**). The crude compound was prepared through the general procedure. After purification by silica gel column chromatography (PE/EA = 30:1), compound **3ae** was isolated as a yellow solid (27.7 mg, 64%); mp 168−170 °C. IR (film): 1674, 1507, 1225, 1157, 970, 828 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.43−7.39 (m, 2H), 7.12 (t, J = 4.4 Hz, 1H), 7.06−6.98 (m, 3H), 6.86 (d, J = 16.4 Hz, 1H), 2.54−2.48 (m, 4H), 2.07−2.01 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.4, 162.3 (d, J = 245.7 Hz), 145.0, 135.9, 133.6 (d, J = 3.2 Hz), 128.9, 128.0 (d, J = 7.9 Hz), 122.6, 115.4 (d, J = 21.4 Hz), 38.8, 26.4, 22.5. LRMS (EI, m/z): 216 (M^+, 72), 187 (13), 172 (28), 159 (100), 146 (32). HRMS (ESI, m/z): calcd for $C_{14}H_{14}FO$ $[M + H]^+$ 217.1023, found 217.1018.

(E)-2-(Pent-1-en-1-yl)cyclohex-2-enone (**3af**). The crude compound was prepared through the general procedure. After purification by silica gel column chromatography (PE/EA = 30:1), compound **3af** was isolated as a yellow oil (21.3 mg, 65%). IR (film): 1677, 1376, 1175, 1106, 971 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 6.93 (t, J = 4.8 Hz, 1H), 6.22 (d, J = 15.6 Hz, 1H), 6.11 (dt, J = 15.6 Hz, 6.8 Hz, 1H), 2.48−2.40 (m, 4H), 2.12−1.95 (m, 4H), 1.48−1.38 (m, 2H), 0.91 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.7, 143.5, 136.5, 132.5, 123.9, 38.7, 35.2, 26.2, 22.6, 22.4, 13.7. LRMS (EI, m/z): 164 (M^+, 40), 149 (16), 135 (100), 121 (18). HRMS (ESI, m/z): calcd for $C_{11}H_{17}O$ $[M + H]^+$ 165.1274, found 165.1289.

(E)-2-(Hept-1-en-1-yl)cyclohex-2-enone (**3ag**). The crude compound was prepared through the general procedure. After purification by silica gel column chromatography (PE/EA = 30:1), compound **3ag** was isolated as a yellow oil (27.7 mg, 72%). IR (film): 1678, 1456, 1375, 1176, 1105, 972 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 6.92 (t, J = 4.4 Hz, 1H), 6.21 (d, J = 16.0 Hz, 1H), 6.11 (dt, J = 16.0 Hz, 6.4 Hz, 1H), 2.48−2.39 (m, 4H), 2.14−1.95 (m, 4H), 1.43−1.25 (m, 6H), 0.88 (t, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.7, 143.4, 136.5, 132.8, 123.7, 38.7, 33.1, 31.4, 28.9, 26.2, 22.6, 22.5, 13.9. LRMS (EI, m/z): 192 (M^+, 36), 149 (18), 135 (100), 121 (12). HRMS (ESI, m/z): calcd for $C_{13}H_{21}O$ $[M + H]^+$ 193.1587, found 193.1583.

2-(1-Phenylvinyl)cyclohex-2-enone (**3ah**).[12] The crude compound was prepared through the general procedure. After purification by silica gel column chromatography (PE/EA = 30:1), compound **3ah** was isolated as a yellow oil (12.7 mg, 32%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.30−7.23 (m, 5H), 6.95 (t, J = 4.4 Hz, 1H), 5.52 (d, J = 0.8 Hz, 1H), 5.27 (s, 1H), 2.54−2.47 (m, 4H), 2.13−2.07 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.8, 148.6, 145.7, 141.3, 140.3, 128.2, 127.5, 126.3, 115.8, 38.9, 26.3, 22.9.

(E)-4-Methyl-2-styrylcyclohex-2-enone (**3ba**). The crude compound was prepared through the general procedure. After purification by silica gel column chromatography (PE/EA = 30:1), compound **3ba** was isolated as a yellow oil (33.9 mg, 80%). IR (film): 1676, 1448, 1372, 1178, 1016, 970, 752, 692 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 7.6 Hz, 2H), 7.34−7.20 (m, 3H), 7.07 (d, J = 16.4 Hz, 1H), 6.96−6.91 (m, 2H), 2.69−2.67 (m, 1H), 2.62−2.55 (m, 1H), 2.48−2.39 (m, 1H), 2.14−2.07 (m, 1H), 1.72−1.61 (m, 1H), 1.21 (d, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.4, 150.6, 137.3, 134.7, 130.2, 128.5, 127.5, 126.5, 122.6, 37.6, 31.8, 30.5, 20.5. LRMS (EI, m/z): 212 (M^+, 85), 197 (24), 179 (23), 169 (44), 155 (100), 141 (73). HRMS (ESI, m/z): calcd for $C_{15}H_{17}O$ $[M + H]^+$ 213.1274, found 213.1270.

(E)-6-Methyl-2-styrylcyclohex-2-enone (**3ca**). The crude compound was prepared through the general procedure. After purification by silica gel column chromatography (PE/EA = 30:1), compound **3ca** was isolated as a yellow oil (37.3 mg,

dx.doi.org/10.1021/jo5012703 | J. Org. Chem. 2014, 79, 7711−7717

88%). IR (film): 1674, 1448, 1375, 1003, 968, 741 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, J = 7.6 Hz, 2H), 7.33−7.20 (m, 3H), 7.09−7.04 (m, 2H), 6.94 (d, J = 16.8 Hz, 1H), 2.53−2.44 (m, 3H), 2.11−2.04 (m, 1H), 1.82−1.71 (m, 1H), 1.18 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.1, 144.1, 137.4, 135.4, 130.0, 128.4, 127.5, 126.5, 123.1, 42.0, 30.5, 25.7, 15.1. LRMS (EI, m/z): 212 (M^+, 32), 169 (41), 154 (46), 141 (100). HRMS (ESI, m/z): calcd for $C_{15}H_{17}O$ $[M + H]^+$ 213.1274, found 213.1269.

*(E)-4-(tert-Butyl)-2-styrylcyclohex-2-enone (**3da**).* The crude compound was prepared through the general procedure. After purification by silica gel column chromatography (PE/EA = 30:1), compound **3da** was isolated as a yellow oil (43.7 mg, 86%). IR (film): 1678, 1366, 1227, 970, 945, 692 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 7.2 Hz, 2H), 7.40−7.20 (m, 3H), 7.14−7.08 (m, 2H), 6.94 (d, J = 16.4 Hz, 1H), 2.64−2.58 (m, 1H), 2.45−2.30 (m, 2H), 2.13−2.07 (m, 1H), 1.79−1.67 (m, 1H), 1.01 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.7, 147.6, 137.4, 136.0, 130.2, 128.4, 127.5, 126.5, 123.3, 47.5, 38.5, 33.3, 27.4, 24.0. LRMS (EI, m/z): 254 (M^+, 23), 198 (100), 180 (22), 165 (17). HRMS (ESI, m/z): calcd for $C_{18}H_{23}O$ $[M + H]^+$ 255.1743, found 255.1742.

*(E)-2-Styrylcyclohept-2-enone (**3fa**).* The crude compound was prepared through the general procedure. After purification by silica gel column chromatography (PE/EA = 30:1), compound **3fa** was isolated as a yellow oil (37.3 mg, 88%). IR (film): 1680, 1448, 1245, 965, 744, 693 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 8.0 Hz, 2H), 7.32−7.18 (m, 3H), 6.82 (d, J = 16.4 Hz, 1H), 6.76 (d, J = 16.4 Hz, 1H), 6.66 (t, J = 6.4 Hz, 1H), 2.67−2.63 (m, 2H), 2.49−2.44 (m, 2H), 1.86−1.73 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.4, 141.5, 139.7, 137.3, 129.3, 128.4, 127.4, 126.4, 126.0, 42.8, 27.9, 24.8, 22.3. LRMS (EI, m/z): 212 (M^+, 52), 183 (20), 155 (45), 141 (100). HRMS (ESI, m/z): calcd for $C_{15}H_{17}O$ $[M + H]^+$ 213.1274, found 213.1269.

*(E)-2-(Hept-1-en-1-yl)cyclohept-2-enone (**3fg**).* The crude compound was prepared through the general procedure. After purification by silica gel column chromatography (PE/EA = 30:1), compound **3fg** was isolated as a yellow oil (32.1 mg, 78%). IR (film): 1683, 1455, 1378, 966 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 6.46 (t, J = 6.4 Hz, 1H), 6.04 (d, J = 16.0 Hz, 1H), 6.11 (dt, J = 16.0 Hz, 6.8 Hz, 1H), 2.60 (t, J = 6.8 Hz, 2H), 2.42−2.37 (m, 2H), 2.11−2.05 (m, 2H), 1.83−1.68 (m, 4H), 1.43−1.25 (m, 6H), 0.88 (t, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.8, 141.7, 137.8, 132.1, 126.8, 42.8, 33.0, 31.4, 28.9, 27.7, 24.9, 22.5, 22.3, 14.0. LRMS (EI, m/z): 206 (M^+, 28), 177 (8), 163 (12), 149 (100), 135 (26). HRMS (ESI, m/z): calcd for $C_{14}H_{23}O$ $[M + H]^+$ 207.1743, found 207.1739.

*2-[(E)-Styryl]cyclooct-2-enone (**3ga**).* The crude compound was prepared through the general procedure. After purification by silica gel column chromatography (PE/EA = 30:1), compound **3ga** was isolated as a yellow oil (41.6 mg, 92%). IR (film): 1690, 1448, 959, 692 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, J = 7.6 Hz, 2H), 7.31−7.18 (m, 3H), 6.66 (d, J = 16.4 Hz, 1H), 6.25 (d, J = 16.4 Hz, 1H), 6.02 (t, J = 5.6 Hz, 1H), 2.58−2.54 (m, 2H), 2.35−2.32 (m, 2H), 1.94−1.89 (m, 2H), 1.68−1.66 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.6, 138.9, 136.9, 134.3, 128.4, 127.9, 127.7, 127.4, 126.2, 45.1, 29.7, 29.1, 22.9, 22.4. LRMS (EI, m/z): 226 (M^+, 67), 211 (12), 197 (16), 183 (25), 157 (92), 141 (100). HRMS (ESI, m/z): calcd for $C_{16}H_{19}O$ $[M + H]^+$ 227.1430, found 227.1427.

*2-[(E)-Hept-1-en-1-yl]cyclooct-2-enone (**3gg**).* The crude compound was prepared through the general procedure. After purification by silica gel column chromatography (PE/EA = 30:1), compound **3gg** was isolated as a yellow oil (31.7 mg, 72%). IR (film): 1693, 1454, 1382, 962 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 5.93 (d, J = 16.0 Hz, 1H), 5.75 (t, J = 5.6 Hz, 1H), 5.38 (dt, J = 16.0 Hz, 6.8 Hz, 1H), 2.50−2.46 (m, 2H), 2.30−2.21 (m, 2H), 2.07−2.01 (m, 2H), 1.95−1.86 (m, 2H), 1.65−1.62 (m, 4H), 1.40−1.23 (m, 6H), 0.87 (t, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.2, 139.0, 130.9, 130.7, 128.8, 45.0, 32.7, 31.3, 29.3, 29.1, 28.8, 23.0, 22.5, 22.4, 13.9. LRMS (EI, m/z): 220 (M^+, 29), 191 (8), 177 (22), 163 (43), 149 (100). HRMS (ESI, m/z): calcd for $C_{15}H_{25}O$ $[M + H]^+$ 221.1900, found 221.1895.

*2-[(E)-Styryl]cyclododec-2-enone (**3ha**).* The crude compound was prepared through the general procedure. After purification by silica gel column chromatography (PE/EA = 30:1), compound 2-[(*E*)-styryl]cyclododec-2-enone **3ha** was isolated as a yellow oil (51.3 mg, 91%). IR (film): 1692, 1465, 1446, 1076, 981, 748, 692 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, J = 7.2 Hz, 2H), 7.34−7.21 (m, 3H), 6.74 (d, J = 16.4 Hz, 1H), 6.34 (d, J = 16.4 Hz, 1H), 5.67 (t, J = 8.0 Hz, 1H), 2.79 (t, J = 6.4 Hz, 2H), 2.28−2.22 (m, 2H), 1.80−1.73 (m, 2H), 1.53−1.47 (m, 2H), 1.39−1.25 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.0, 143.8, 136.8, 136.4, 129.7, 128.6, 127.6, 127.2, 126.2, 40.9, 27.4, 26.6, 25.4, 23.9, 23.8, 23.7, 22.7, 22.7. LRMS (EI, m/z): 282 (M^+, 69), 254 (11), 225 (31), 183 (38), 155 (58), 141 (100). HRMS (ESI, m/z): calcd for $C_{20}H_{27}O$ $[M + H]^+$ 283.2056, found 283.2057.

*2-[(E)-Hept-1-en-1-yl]cyclododec-2-enone (**3hg**).* The crude compound was prepared through the general procedure. After purification by silica gel column chromatography (PE/EA = 30:1), compound **3hg** was isolated as a yellow oil (41.4 mg, 75%). IR (film): 1694, 1465, 1442, 963 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 6.02 (d, J = 16.0 Hz, 1H), 5.47 (dt, J = 16.0 Hz, 7.2 Hz, 1H), 5.40 (t, J = 8.0 Hz, 1H), 2.69 (t, J = 6.0 Hz, 2H), 2.20−2.05 (m, 4H), 1.74−1.70 (m, 2H), 1.48−1.20 (m, 18H), 0.88 (t, J = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.5, 143.9, 133.6, 132.5, 128.3, 40.6, 32.9, 31.3, 28.8, 27.5, 26.2, 25.4, 23.7, 23.7, 23.6, 22.7, 22.7, 22.4, 13.9. LRMS (EI, m/z): 276 (M^+, 17), 233 (12), 219 (24), 205 (100). HRMS (ESI, m/z): calcd for $C_{19}H_{33}O$ $[M + H]^+$ 277.2526, found 277.2527.

General Procedure II: Pd-Catalyzed Cross-Coupling of Diazo Compounds 4a−c and Vinyl Boronic Acid Derivatives (Scheme 4). Under an argon atmosphere, $Pd(PPh_3)_4$ (5.5 mg, 0.005 mmol, 2.5 mol%), BQ (25.9 mg, 0.24 mmol), and *trans*-2-phenylvinylboronic acid (44.4 mg, 0.3 mmol) were successively added to a flame-dried 25 mL Schlenk flask. The reaction flask was degassed three times with argon. Dry dioxane (1.8 mL) and diisopropylamine (60.6 mg, 0.6 mmol) were added using a syringe, and the solution was heated to 80 °C. Then 2-diazocyclopentanone (22.0 mg, 0.2 mmol) was dissolved in 0.2 mL of dioxane, and this solution was added dropwise to the reaction system. The reaction was stirred for 30 min, then cooled to room temperature, and filtered through a short path of neutral alumina with ethyl acetate (30 mL) as eluent. Solvent was then removed in *vacuo* to leave a crude mixture, which was purified by silica gel column chromatography (PE/EA = 30:1) to afford the pure (*E*)-2-styrylcyclopent-2-enone **3ea** as a yellow solid (11.8 mg, 32%);[13] mp 94−96 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.60−7.53 (m, 2H), 7.47 (d, J = 7.2 Hz, 2H), 7.36−7.23 (m, 3H), 6.81 (d, J = 16.4 Hz, 1H), 2.69−2.66 (m, 2H), 2.55−2.51 (m, 2H). ^{13}C NMR (100 MHz,

dx.doi.org/10.1021/jo5012703 | J. Org. Chem. 2014, 79, 7711−7717

$CDCl_3$) δ 208.0, 158.3, 140.9, 137.1, 132.5, 128.5, 127.9, 126.6, 118.1, 35.7, 26.5.

*(E)-3-Styryl-5,6-dihydro-2H-pyran-2-one (**5aa**).* The crude compound was prepared through the general procedure. After purification by silica gel column chromatography (PE/EA = 5:1), compound (*E*)-3-styryl-5,6-dihydro-2*H*-pyran-2-one **5aa** was isolated as a yellow solid (26.0 mg, 65%); mp 218−220 °C. IR (film): 1719, 1400, 1277, 1122, 969, 745, 693 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 7.6 Hz, 1H), 7.36−7.24 (m, 4H), 7.19 (d, J = 16.4 Hz, 1H), 6.99 (t, J = 4.8 Hz, 1H), 6.90 (d, J = 16.4 Hz, 1H), 4.41 (t, J = 6.0 Hz, 2H), 2.61−2.56 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6, 138.4, 136.8, 131.8, 129.9, 128.6, 128.0, 126.7, 122.6, 66.0, 24.7. LRMS (EI, m/z): 200 (M^+, 25), 169 (11), 155 (22), 141 (100). HRMS (ESI, m/z): calcd for $C_{13}H_{13}O_2$ $[M + H]^+$ 201.0910, found 201.0905.

*(E)-3-(Hept-1-en-1-yl)-5,6-dihydro-2H-pyran-2-one (**5ag**).* The crude compound was prepared through the general procedure. After purification by silica gel column chromatography (PE/EA = 5:1), compound (*E*)-3-(hept-1-en-1-yl)-5,6-dihydro-2*H*-pyran-2-one **5ag** was isolated as a yellow oil (24.1 mg, 62%). IR (film): 1722, 1398, 1274, 1121, 981 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 6.78 (t, J = 4.8 Hz, 1H), 6.26 (dt, J = 16.0 Hz, 6.4 Hz, 1H) 6.17 (d, J = 16.0 Hz, 1H), 4.35 (t, J = 6.4 Hz, 2H), 2.52−2.47 (m, 2H), 2.16−2.10 (m, 2H), 1.44−1.25 (m, 6H), 0.88 (t, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 136.8, 134.6, 130.1, 123.8, 66.0, 33.0, 31.4, 28.7, 24.5, 22.5, 14.0. LRMS (EI, m/z): 194 (M^+, 4), 151 (15), 137 (76), 124 (72), 77 (100). HRMS (ESI, m/z): calcd for $C_{12}H_{19}O_2$ $[M + H]^+$ 195.1380, found 195.1375.

*(E)-3-Styryl-6,7-dihydrooxepin-2(5H)-one (**5ba**).* The crude compound was prepared through the general procedure. After purification by silica gel column chromatography (PE/EA = 5:1), compound (*E*)-3-styryl-6,7-dihydrooxepin-2(5*H*)-one **5ba** was isolated as a yellow solid (29.1 mg, 68%); mp 67−69 °C. IR (film): 1722, 1350, 1233, 1121, 1039, 963, 748, 693 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, J = 7.2 Hz, 2H), 7.34−7.22 (m, 3H), 6.92 (d, J = 16.4 Hz, 1H), 6.73 (d, J = 16.4 Hz, 1H), 6.41 (t, J = 7.2 Hz, 1H), 4.25 (t, J = 6.4 Hz, 2H), 2.45−2.39 (m, 2H), 2.03−1.99 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 136.7, 134.6, 133.4, 131.0, 128.5, 127.8, 126.5, 124.7, 66.0, 26.2, 23.0. LRMS (EI, m/z): 214 (M^+, 78), 183 (13), 169 (18), 155 (38), 141 (100). HRMS (ESI, m/z): calcd for $C_{14}H_{15}O_2$ $[M + H]^+$ 215.1067, found 215.1062.

*(E)-3-(Hept-1-en-1-yl)-6,7-dihydrooxepin-2(5H)-one (**5bg**).* The crude compound was prepared through the general procedure. After purification by silica gel column chromatography (PE/EA = 5:1), compound (*E*)-3-(hept-1-en-1-yl)-6,7-dihydrooxepin-2(5*H*)-one **5bg** was isolated as a yellow oil (26.2 mg, 63%). IR (film): 1727, 1466, 1349, 1116, 1040, 965 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 6.18 (t, J = 7.2 Hz, 1H), 6.08−5.98 (m, 2H), 4.21 (t, J = 6.4 Hz, 2H), 2.37−2.31 (m, 2H), 2.13−2.07 (m, 2H), 2.01−1.95 (m, 2H), 1.43−1.25 (m, 6H), 0.88 (t, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 134.6, 134.0, 130.8, 125.8, 65.9, 32.9, 31.3, 28.6, 26.2, 22.7, 22.4, 13.9. LRMS (EI, m/z): 208 (M^+, 52), 180 (6), 165 (8), 151 (100), 137 (27). HRMS (ESI, m/z): calcd for $C_{13}H_{21}O_2$ $[M + H]^+$ 209.1536, found 209.1532.

*(E)-3-Styryl-2H-chromen-2-one (**5ca**).* The crude compound was prepared through the general procedure. After purification by silica gel column chromatography (PE/EA = 3:1), compound (*E*)-3-styryl-2*H*-chromen-2-one **5ca** was isolated as yellow solid (28.8 mg, 58%); mp 159−161 °C. IR (film): 1713, 1457, 1179, 1112, 974, 747 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.61 (d, J = 16.0 Hz, 1H), 7.56−7.47 (m, 4H), 7.40−7.25 (m, 5H), 7.14 (d, J = 16.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 152.8, 136.8, 136.7, 133.6, 131.0, 128.7, 128.4, 127.6, 126.9, 124.9, 124.5, 122.0, 119.6, 116.4. LRMS (EI, m/z): 248 (M^+, 100), 231 (24), 219 (41), 189 (27). HRMS (ESI, m/z): calcd for $C_{17}H_{13}O_2$ $[M + H]^+$ 249.0910, found 249.0911.

*(E)-3-(Hept-1-en-1-yl)-2H-chromen-2-one (**5cg**).* The crude compound was prepared through the general procedure. After purification by silica gel column chromatography (PE/EA = 3:1), compound (*E*)-3-(hept-1-en-1-yl)-2*H*-chromen-2-one **5cg** was isolated as a yellow oil (26.1 mg, 54%). IR (film): 1724, 1455, 1179, 1062, 973, 753 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.61 (s, 1H), 7.47−7.43 (m, 2H), 7.31−7.22 (m, 2H), 7.68 (dt, J = 16.0 Hz, 7.2 Hz, 1H), 6.42 (d, J = 16.0 Hz, 1H), 2.27−2.21 (m, 2H), 1.53−1.31 (m, 6H), 0.90 (t, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 152.6, 137.2, 135.6, 130.5, 127.3, 125.3, 124.3, 123.3, 119.7, 116.2, 33.5, 31.4, 28.6, 22.4, 13.9. LRMS (EI, m/z): 242 (M^+, 69), 213 (13), 199 (32), 185 (38), 172 (100). HRMS (ESI, m/z): calcd for $C_{16}H_{19}O_2$ $[M + H]^+$ 243.1380, found 243.1379.

*Methyl (E)-2-((E)-Benzylidene)-4-phenylbut-3-enoate (**7aa**) and Methyl (E)-2-((Z)-Benzylidene)-4-phenylbut-3-enoate (**7aa′**).*[14,15] The crude compound was prepared through the general procedure. After purification by silica gel column chromatography (PE/EA = 30:1), compound **7aa** was isolated as a yellow oil (20.6 mg, 39%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (s, 1H), 7.47−7.24 (m, 11H), 7.05 (d, J = 16.4 Hz, 1H), 3.89 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 139.0, 137.4, 135.5, 134.8, 130.1, 128.7, 128.6, 128.4, 127.9, 126.7, 121.5, 52.1. Compound **7aa′** was isolated as a yellow solid (16.4 mg, 31%). mp 65−67 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, J = 7.2 Hz, 2H), 7.36−7.24 (m, 8H), 6.87 (d, J = 16.4 Hz, 1H), 6.75 (s, 1H), 6.62 (d, J = 16.4 Hz, 1H), 3.83 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 136.6, 135.4, 133.8, 132.8, 131.1, 128.6, 128.5, 128.3, 128.1, 128.0, 127.2, 126.6, 52.2.

*Methyl (E)-2-((E)-benzylidene)non-3-enoate (**7ag**) and methyl (E)-2-((Z)-benzylidene)non-3-enoate (**7ag′**).* The crude compound was prepared through the general procedure. After purification by silica gel column chromatography (PE/EA = 30:1), the inseparable mixture of **7ag** and **7ag′** (ratio about 1:1, according to ^1H NMR) was isolated as a yellow oil (30.9 mg, 60%). IR (film): 1723, 1434, 1242, 1147, 961, 693 cm^{-1}. HRMS (ESI, m/z): calcd for $C_{17}H_{23}O_2$ $[M + H]^+$ 259.1693, found 259.1694. (2E,3E)-Methyl 2-benzylidenenon-3-enoate **7ag**: ^1H NMR (400 MHz, $CDCl_3$) δ 7.44−7.34 (m, 5H), 6.53 (s, 1H), 6.15 (d, J = 16.0 Hz, 1H), 5.77 (dt, J = 16.0 Hz, 7.2 Hz, 1H), 3.82 (s, 3H), 2.18−2.12 (m, 2H), 1.45−1.41 (m, 2H), 1.32−1.28 (m, 4H), 0.89 (t, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 138.2, 136.8, 134.3, 129.9, 128.4, 128.2, 127.9, 122.5, 51.9, 33.5, 31.4, 28.6, 22.4, 14.0. LRMS (EI, m/z): 258 (M^+, 31), 227 (14), 201 (27), 187 (55), 155 (43), 141 (100). (2*Z*,3*E*)-Methyl 2-benzylidene-4-phenylbut-3-enoate (**7ag′**): ^1H NMR (400 MHz, $CDCl_3$) δ 7.32−7.21(m, 6H), 6.34−6.23 (m, 2H), 3.78 (s, 3H), 2.18−2.12 (m, 2H), 1.45−1.41 (m, 2H), 1.32−1.28 (m, 4H), 0.89 (t, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 135.7, 135.6, 134.0, 130.2, 128.5, 128.3, 127.9, 122.5, 52.0, 32.9, 31.4, 28.5, 22.4, 13.9. LRMS (EI, m/z): 258 (M^+, 45), 227 (9), 201 (23), 187 (46), 155 (41), 141 (100).

dx.doi.org/10.1021/jo5012703 | *J. Org. Chem.* 2014, 79, 7711−7717

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C spectra for all products. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: wangjb@pku.edu.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This project was supported by 973 Program (Grant 2012CB821600) and NSFC (Grants 21272010 and 21332002).

■ REFERENCES

(1) For selected leading references, see: (a) Peters, L.; König, G. M.; Terlau, H.; Wright, A. D. *J. Nat. Prod.* **2002**, *65*, 1633. (b) Wnuk, S. F.; Ro, B.-O.; Valdez, C. A.; Lewandowska, E.; Valdez, N. X.; Sacasa, P. R.; Yin, D. Y.; Zhang, J.; Borchardt, R. T.; Clercq, E. D. *J. Med. Chem.* **2002**, *45*, 2651. (c) Begemann, P.; Christova-Georgieva, N. I.; Sangaiah, R.; Koc, H.; Zhang, D.; Golding, B. T.; Gold, A.; Swenberg, J. A. *Chem. Res. Toxicol.* **2004**, *17*, 929. (d) Mandal, A. K.; Schneekloth, J. S., Jr.; Crews, C. M. *Org. Lett.* **2005**, *7*, 3645. (e) Li, C.; La, M.-P.; Li, L.; Li, X.-B.; Tang, H.; Liu, B.-S.; Krohn, K.; Sun, P.; Yi, Y.-H.; Zhang, W. *J. Nat. Prod.* **2011**, *74*, 1658. (f) Ponnapakam, A. P.; Liu, J.; Bhinge, K. N.; Drew, B. A.; Wang, T. L.; Antoon, J. W.; Nguyen, T. T.; Dupart, P. S.; Wang, Y.; Zhao, M.; Liu, Y. Y.; Foroozesh, M.; Beckman, B. S. *Bioorg. Med. Chem.* **2014**, *22*, 1412.

(2) For selected leading references, see: (a) Takimoto, M.; Mori, M. *J. Am. Chem. Soc.* **2001**, *123*, 2895. (b) Tobisch, A. *Acc. Chem. Res.* **2002**, *35*, 96. (c) Ohmura, T.; Masuda, K.; Takase, I.; Suginome, M. *J. Am. Chem. Soc.* **2009**, *131*, 16624. (d) Jiménez, M. V.; Pérez-Torrente, J. J.; Bartolomé, M. I.; Vispe, E.; Lahoz, F. J.; Oro, L. A. *Macromolecules* **2009**, *42*, 8146. (e) Kitamura, T.; Tanaka, N.; Mihashi, A.; Matsumoto, A. *Macromolecules* **2010**, *43*, 1800. (f) Tanaka, N.; Sato, E.; Matsumoto, A. *Macromolecules* **2011**, *44*, 9125. (g) Pham, H. V.; Paton, R. S.; Ross, A. G.; Danishefsky, S. J.; Houk, K. N. *J. Am. Chem. Soc.* **2014**, *136*, 2397. (h) Parker, S. E.; Börgel, J.; Ritter, T. *J. Am. Chem. Soc.* **2014**, *136*, 4857.

(3) For selected examples, see: (a) Luken, C.; Moberg, C. *Org. Lett.* **2008**, *10*, 2505. (b) Lindhardt, A. T.; Mantel, M. L. H.; Skrydstrup, T. *Angew. Chem., Int. Ed.* **2008**, *47*, 2668. (c) Negishi, E.; Huang, Z.; Wang, G.; Mohan, S.; Wang, C.; Hattori, H. *Acc. Chem. Res.* **2008**, *41*, 1474. (d) Ogata, K.; Murayama, H.; Sugasawa, J.; Suzuki, N.; Fukuzawa, S.-I. *J. Am. Chem. Soc.* **2009**, *131*, 3176. (e) Huang, J.; Dong, Y.; Wang, X. X.; Luo, H. C. *Chem. Commun.* **2010**, *46*, 1035. (f) Billard, F.; Robiette, R.; Pospíšil, J. *J. Org. Chem.* **2012**, *77*, 6358. (g) Li, W.; Zhang, J. *Org. Lett.* **2014**, *16*, 162.

(4) Greenman, K. L.; Carter, D. S.; Van Vranken, D. L. *Tetrahedron* **2001**, *57*, 5219.

(5) For reviews on Pd-catalyzed cross-coupling reactions involving carbene migratory insertion, see: (a) Zhang, Y.; Wang, J. *Eur. J. Org. Chem.* **2011**, 1015. (b) Barluenga, J.; Valdés, C. *Angew. Chem., Int. Ed.* **2011**, *50*, 7486. (c) Shao, Z.; Zhang, H. *Chem. Soc. Rev.* **2012**, *41*, 560. (d) Xia, Y.; Zhang, Y.; Wang, J. *ACS Catal.* **2013**, *3*, 2586−2598. (e) Xiao, Q.; Zhang, Y.; Wang, J. *Acc. Chem. Res.* **2013**, *46*, 236. (f) Liu, Z.; Wang, J. *J. Org. Chem.* **2013**, *78*, 10024.

(6) Barluenga, J.; Moriel, P.; Valdés, C.; Aznar, F. *Angew. Chem., Int. Ed.* **2007**, *46*, 5587.

(7) For selected examples, see: (a) Devine, S. K. J.; Van Vranken, D. L. *Org. Lett.* **2007**, *9*, 2047. (b) Kudirka, R.; Devine, S. K. J.; Adams, C. S.; Van Vranken, D. L. *Angew. Chem., Int. Ed.* **2009**, *48*, 3677. (c) Chen, Z.-S.; Duan, X.-H.; Zhou, P.-X.; Ali, S.; Luo, J.-Y.; Liang, Y.-M. *Angew. Chem., Int. Ed.* **2012**, *51*, 1370. (d) Zhou, P.-X.; Zhou, Z.-Z.; Chen, Z.-S.; Ye, Y.-Y.; Zhao, L.-B.; Yang, Y.-F.; Xia, X.-F.; Luo, J.-Y.; Liang, Y.-M. *Chem. Commun.* **2013**, *49*, 561. (e) Yang, K.; Zhang, J.; Li, Y.; Cheng, B.; Zhao, L.; Zhai, H. *Org. Lett.* **2013**, *15*, 808. (f) Zhou, P.-X.; Luo, J.-Y.; Zhao, L.-B.; Ye, Y.-Y.; Liang, Y.-M. *Chem. Commun.* **2013**, *49*, 3254.

(8) Chen, S.; Wang, J. *Chem. Commun.* **2008**, 4198.

(9) Xiao, Q.; Wang, B.; Tian, L.; Yang, Y.; Ma, J.; Zhang, Y.; Chen, S.; Wang, J. *Angew. Chem., Int. Ed.* **2013**, *52*, 9305.

(10) Peng, C.; Wang, Y.; Wang, J. *J. Am. Chem. Soc.* **2008**, *130*, 1566.

(11) DeAngelis, A.; Dmitrenko, O.; Fox, J. M. *J. Am. Chem. Soc.* **2012**, *134*, 11035.

(12) Rossi, R.; Bellina, F.; Ciucci, D. *J. Organomet. Chem.* **1997**, *542*, 113.

(13) Rossi, R.; Bellina, F.; Ciucci, D.; Carpita, A.; Fanelli, C. *Tetrahedron* **1998**, *54*, 7595.

(14) Crist, R. M.; Reddy, P. V.; Borhan, B. *Tetrahedron Lett.* **2001**, *42*, 619.

(15) Lim, C. H.; Kim, S. H.; Park, K. H.; Lee, J.; Kim, J. N. *Tetrahedron Lett.* **2013**, *54*, 387.