Tetrahedron Letters 51 (2010) 4648–4652

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Synthesis of dihydroindenofuran scaffold via a Pd-catalyzed 5-*endo-trig* cyclization/enolate O-alkylation cascade

Eun Sun Kim [a], Ko Hoon Kim [a], Sunhong Park [b], Jae Nyoung Kim [a,*]

[a] Department of Chemistry and Institute of Basic Science, Chonnam National University, Gwangju 500-757, Republic of Korea
[b] Department of Chemistry and Research Institute of Natural Science, Gyeongsang National University, Jinju 660-701, Republic of Korea

ARTICLE INFO

Article history:
Received 26 May 2010
Revised 23 June 2010
Accepted 28 June 2010
Available online 3 July 2010

Keywords:
Palladium
Enolate O-alkylation
Dihydroindenofurans
Baylis–Hillman adducts

ABSTRACT

An efficient synthesis of dihydroindenofurans was carried out starting from the Baylis–Hillman adducts via a Pd-catalyzed 5-*endo-trig*-carbopalladation and enolate O-alkylation cascade as a key step. This is the first example of enolate O-alkylation with a C(sp^3)-bound palladium intermediate.

The palladium-catalyzed C-arylation reaction of a ketone enolate with haloarenes is a powerful method for the construction of α-aryl ketones that has demonstrated excellent substrate scope.[1] The reactions with the enolates of ester and malonate have also been reported.[2] However, all the reactions provided C-arylated products. Intramolecular O-arylation could be realized when the enolate and aryl halide are present together in the same molecule and when the competitive C-arylation is difficult at the same time. Recently, a Pd-catalyzed intramolecular O-arylation has been applied for the synthesis of many interesting compounds including benzofurans and isocoumarins.[3]

The Baylis–Hillman reaction, which involves the coupling of activated vinylic compounds with electrophiles under the catalytic influence of a tertiary amine, gives rise to adducts, so called Baylis–Hillman adducts, with a new stereocenter and has proven to be a very useful carbon–carbon bond-forming method in the synthesis of highly functionalized molecules.[4] The chemical transformations of Baylis–Hillman adducts provided many interesting compounds and are well documented in many review articles.[4] The Baylis–Hillman adducts could also supply various substrates that can be used in the Pd-catalyzed reaction to furnish valuable compounds.[4g,5] As an example, a Pd-catalyzed domino reaction with modified Baylis–Hillman adducts has been used for the synthesis of tetracyclic butterfly-like scaffold.[5a]

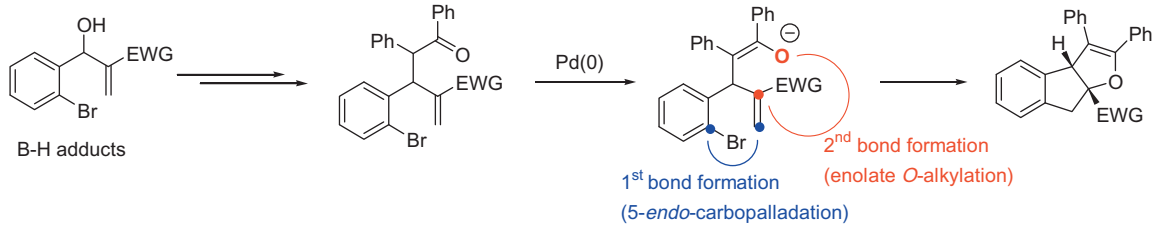
During the studies[5] we reasoned out that dihydroindenofuran scaffold could be constructed in a one-pot via the intramolecular 5-*endo-trig*-carbopalladation and enolate O-alkylation cascade, as shown in Scheme 1. Numerous dihydrofuran moiety-containing tri- and[6] polycyclic[7] compounds were found in biologically important natural products, and the construction of these scaffolds has received much attention.[6,7] Pd-catalyzed O-arylations between arylpalladium intermediates and enolates have been reported as described above;[3] however, an intramolecular O-alkylation between alkylpalladium intermediate and an enolate has not been reported, to the best of our knowledge.[3h,i]

Two cinnamyl bromides, **1a** and **1b**, were prepared from the corresponding Baylis–Hillman adducts with HBr according to the reported method.[8,9] The starting materials **3a–j** were prepared by the reactions of **1a** and **1b** with active methylene compounds **2a–f**, as shown in Table 1. Introduction of **2a–f** at the secondary position of the cinnamyl bromides was carried out in CH_3CN in the presence of DABCO and additional base such as NaOH or K_2CO_3 depending on the substrates, as reported.[9,10] When we used **2a** and **2c–e**, the corresponding products were formed as a *syn*/*anti* mixture, and the separation was somewhat difficult. However, the stereochemistry of **3** would not affect the Pd-catalyzed cyclization because the reaction would involve an enolate intermediate as shown in Scheme 1, thus we used a *syn*/*anti* mixture for the Pd-catalyzed reaction without separation.[11]

Initially, we examined the Pd-catalyzed reaction of **3a**, as a representative example, under various conditions, as shown in Table 2. The use of Et_3N in DMF was totally ineffective either at 70–80 °C or at higher temperature (entries 1 and 2). The use of Cs_2CO_3 in toluene afforded **4a** in 57% isolated yield (entry 3).[10] The use of TBAB/K_2CO_3 both in DMF and CH_3CN produced **4a** in

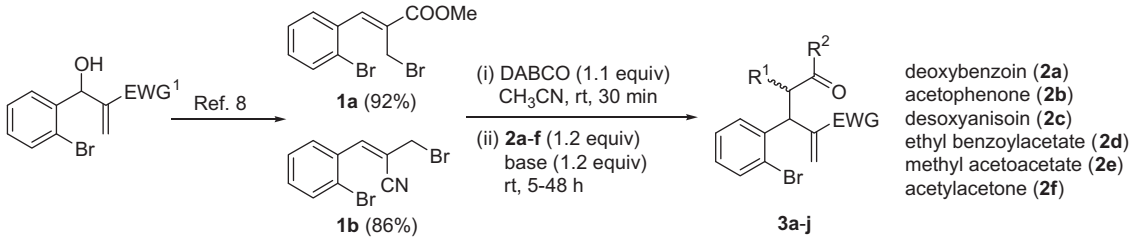
* Corresponding author. Tel.: +82 62 530 3381; fax: +82 62 530 3389.
E-mail address: kimjn@chonnam.ac.kr (J.N. Kim).

0040-4039/$ - see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2010.06.127



Scheme 1.

Table 1
Preparation of starting materials **3a–j**



Entry	Substrates	R^1/R^2/EWG	Base/Time (h)	Products[a] (%)
1	**1a** + **2a**	Ph/Ph/COOMe	NaOH/48	**3a** (85, 2/1)
2	**1a** + **2b**[b]	H/Ph/COOMe	NaOH/48	**3b** (56)
3	**1b** + **2a**	Ph/Ph/CN	NaOH/48	**3c** (89, 3/2)
4	**1b** + **2c**	*p*-MeOPh/*p*-MeOPh/CN	NaOH/24	**3d** (83, 3/2)
5	**1a** + **2d**	COOEt/Ph/COOMe	K_2CO_3/5	**3e** (83, 3/2)
6	**1b** + **2d**	COOEt/Ph/CN	K_2CO_3/24	**3f** (90, 3/2)
7	**1a** + **2e**	COOMe/Me/COOMe	K_2CO_3/24	**3g** (68, 1/1)
8	**1b** + **2e**	COOMe/Me/CN	K_2CO_3/24	**3h** (85, 1/1)
9	**1a** + **2f**	COOMe/Me/COOMe	K_2CO_3/24	**3i** (83)
10	**1b** + **2f**	COOMe/Me/CN	K_2CO_3/24	**3j** (88)

[a] Isolated yield and the ratio of *syn*/*anti* in the parenthesis was based on ^{1}H NMR.
[b] Excess amounts (3.0 equiv) of **2b** was used. Otherwise the yield of a bis alkylation product was increased.

Table 2
Optimization of reaction conditions for the synthesis of **4a**

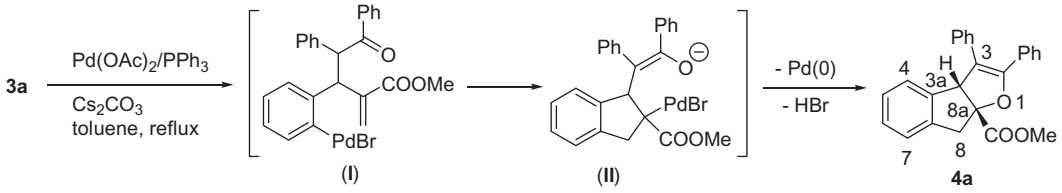
Entry	Conditions[a]	Yield (%)
1	PPh_3 (20 mol %), Et_3N (2.0 equiv), DMF, 70–80 °C, 2 h	Sluggish
2	PPh_3 (20 mol %), Et_3N (2.0 equiv), DMF, 110–120 °C, 30 min	Decompose
3	PPh_3 (20 mol %), Cs_2CO_3 (2.0 equiv), toluene, reflux, 1 h	57
4	TBAB (1.0 equiv), K_2CO_3 (2.0 equiv), DMF, 70–80 °C, 2 h	27
5	TBAB (1.0 equiv), K_2CO_3 (2.0 equiv), CH_3CN, reflux, 18 h	20

[a] $Pd(OAc)_2$ (10 mol %) is common.

low yield (20–27%) along with many intractable side products (entries 4 and 5). As is often the case in the Pd-catalyzed coupling reactions of aryl bromide and a ketone enolate,[3a–d] the use of Cs_2CO_3 in toluene showed the best results.

The mechanism for the formation of **4a** could be postulated as shown in Scheme 2. Oxidative addition of Pd(0) to form (**I**), 5-*endo*-*trig*-carbopalladation[12] to form the palladium intermediate (**II**), and the following coupling with enolate to produce dihydroindenofuran **4a**. The structure of **4a** was confirmed to be dihydroindenofuran (exactly, 3a,8-dihydro-1-oxacyclopenta[*a*] indene) by its HMBC and NOE data, as shown in Figure 1. The structure of dihydroindenofuran and the *cis*-ring junction (*cis* around 3a- and 8a-positions) was confirmed unequivocally by the X-ray crystal structure of **4g** (vide infra),[13] as shown in Figure 2.

Encouraged by the results, we carried out the synthesis of various dihydroindenofurans with **3b–j** under the optimized conditions (entry 3 in Table 2), and the results are summarized in Table 3. As shown in Table 3, the yields of products were highly dependent on the substrates. The reaction of deoxybenzoin derivative **3c** (entry 3) showed a similar result with that of **3a**, while the reaction of acetophenone derivative **3b** produced **4b** in low yield (entry 2) presumably due to low enolate content of the acetophenone moiety. Desoxyanisoin derivative **3d** also showed a low yield of **4d** due to a similar reason, and the reaction required a long reaction time (entry 4). As expected from the results of entries 1–4,



Scheme 2.

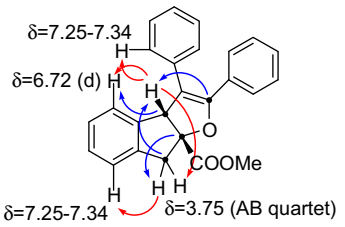


Figure 1. Selected HMBC (C→H) and NOE (H→H) correlations for **4a**.

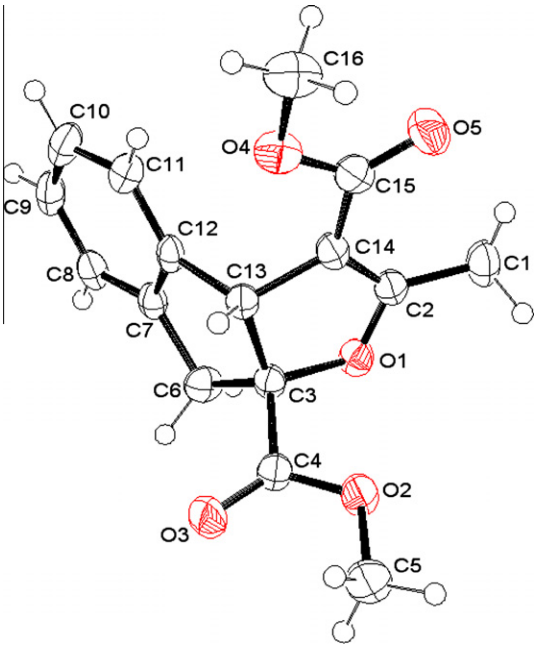


Figure 2. ORTEP drawing of compound **4g**.

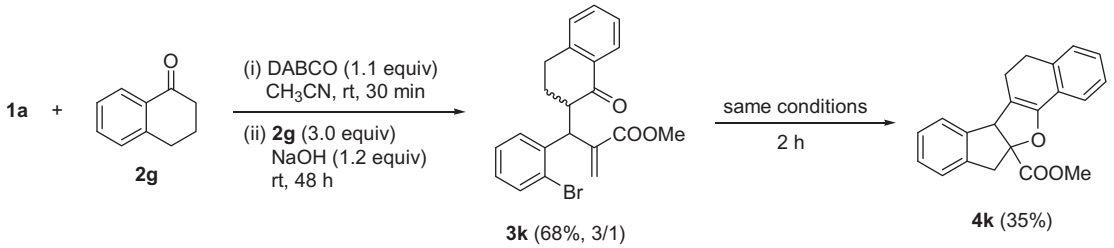
higher yields of dihydroindenofurans were expected for the substrates **3e–j** that has higher enol contents. The expectation was found to be correct, and the yields of dihydroindenofurans were good (74–81%) for the ester derivatives **3e**, **3g,** and **3i** (entries 5, 7 and 9); however, the yields of dihydroindenofurans having a nitrile group (**4f**, **4h** and **4j**) were very low (26–41%), as shown in entries 6, 8, and 10. The formation of many intractable side products was observed, but the reason is not clear at this stage.

As a next entry, we examined the synthesis of a dihydrofuran moiety-containing pentacyclic compound **4k** using **1a** and α-tetralone (**2g**), as shown in Scheme 3. The starting material **3k** was prepared in 68% yield using the procedure in Table 1. The next Pd-catalyzed cyclization of **3k** under the same conditions afforded **4k** in a reasonable yield (35%).

Table 3
Pd-catalyzed synthesis of dihydroindenofurans **4**[a]

Entry	3	Time (h)	Product 4 (%)
1	**3a**	1	**4a** (57)
2	**3b**	12	**4b** (42)
3	**3c**	22	**4c** (62)
4[b]	**3d**	22	**4d** (31)
5	**3e**	1	**4e** (80)
6	**3f**	12	**4f** (41)
7	**3g**	1	**4g** (74)
8	**3h**	2	**4h** (28)
9	**3i**	1	**4i** (81)
10	**3j**	1	**4j** (26)

[a] Conditions: compound **3** (1.0 mmol), $Pd(OAc)_2$ (10 mol %), PPh_3 (20 mol %), Cs_2CO_3 (2.0 equiv), toluene, reflux, 22 h.
[b] Ar is *p*-methoxyphenyl.



Scheme 3.

In summary, we disclosed an efficient synthesis of dihydroindenofu rans starting from the Baylis–Hillman adducts via the Pd-catalyzed 5-*endo*-*trig*-carbopalladation and enolate O-alkylation cascade as a key step. This is the first example of enolate O-alkylation with a C(sp^3)-bound palladium intermediate.

Acknowledgments

This work was supported by the National Research Foundation of Korea Grant funded by the Korean Government (2010-0015675). Spectroscopic data were obtained from the Korea Basic Science Institute, Gwangju branch.

References and notes

1. For the Pd-catalyzed intermolecular C-arylation of ketone enolate, see: (a) Hamann, B. C.; Hartwig, J. F. *J. Am. Chem. Soc.* **1997**, *119*, 12382–12383; (b) Kawatsura, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **1999**, *121*, 1473–1478; (c) Fox, J. M.; Huang, X.; Chieffi, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2000**, *122*, 1360–1370; (d) Culkin, D. A.; Hartwig, J. F. *Organometallics* **2004**, *23*, 3398–3416.
2. For the Pd-catalyzed intermolecular C-arylation of ester enolate or malonate, see: (a) Moradi, W. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2001**, *123*, 7996–8002; (b) Lee, S.; Beare, N. A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2001**, *123*, 8410–8411; (c) Aramendia, M. A.; Borau, V.; Jimenez, C.; Marinas, J. M.; Ruiz, J. R.; Urbano, F. J. *Tetrahedron Lett.* **2002**, *43*, 2847–2849.
3. For the Pd-catalyzed intramolecular O-arylation of enolate, see: (a) Willis, M. C.; Taylor, D.; Gillmore, A. T. *Org. Lett.* **2004**, *6*, 4755–4757; (b) Willis, M. C.; Taylor, D.; Gillmore, A. T. *Tetrahedron* **2006**, *62*, 11513–11520; (c) Churruca, F.; SanMartin, R.; Tellitu, I.; Dominguez, E. *Eur. J. Org. Chem.* **2005**, 2481–2490; (d) Terao, Y.; Satoh, T.; Miura, M.; Nomura, M. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 2345–2350; (e) Eidamshaus, C.; Burch, J. D. *Org. Lett.* **2008**, *10*, 4211–4214; (f) Tenaglia, A.; Kammerer, F. *Synlett* **1996**, 576–578; (g) Millemaggi, A.; Perry, A.; Whitwood, A. C.; Taylor, R. J. K. *Eur. J. Org. Chem.* **2009**, 2947–2952; Intermolecular trapping of an acylpalladium intermediate with an *O*-enolate has been reported, see: (h) Tadd, A. C.; Fielding, M. R.; Willis, M. C. *Chem. Commun.* **2009**, 6744–6746; (i) Negishi, E.-I.; Liou, S.-Y.; Xu, C.; Shimoyama, I.; Makabe, H. *J. Mol. Catal. A: Chem.* **1999**, *143*, 279–286.
4. For the general review on Baylis–Hillman reaction, see: (a) Basavaiah, D.; Rao, A. J.; Satyanarayana, T. *Chem. Rev.* **2003**, *103*, 811–891; (b) Singh, V.; Batra, S. *Tetrahedron* **2008**, *64*, 4511–4574; (c) Kim, J. N.; Lee, K. Y. *Curr. Org. Chem.* **2002**, *6*, 627–645; (d) Lee, K. Y.; Gowrisankar, S.; Kim, J. N. *Bull. Korean Chem. Soc.* **2005**, *26*, 1481–1490; (e) Radha Krishna, P.; Sachwani, R.; Reddy, P. S. *Synlett* **2008**, 2897–2912; (f) Declerck, V.; Martinez, J.; Lamaty, F. *Chem. Rev.* **2009**, *109*, 1–48; (g) Gowrisankar, S.; Lee, H. S.; Kim, S. H.; Lee, K. Y.; Kim, J. N. *Tetrahedron* **2009**, *65*, 8769–8780.
5. For our recent contributions on Pd-catalyzed reactions of modified Baylis–Hillman adducts, see: (a) Kim, K. H.; Lee, H. S.; Kim, S. H.; Kim, S. H.; Kim, J. N. *Chem. Eur. J.* **2010**, *16*, 2375–2380; (b) Lee, H. S.; Kim, S. H.; Kim, T. H.; Kim, J. N. *Tetrahedron Lett.* **2008**, *49*, 1773–1776; (c) Gowrisankar, S.; Lee, H. S.; Kim, J. M.; Kim, J. N. *Tetrahedron Lett.* **2008**, *49*, 1670–1673; (d) Gowrisankar, S.; Lee, H. S.; Lee, K. Y.; Lee, J.-E.; Kim, J. N. *Tetrahedron Lett.* **2007**, *48*, 8619–8622; (e) Lee, H. S.; Kim, S. H.; Gowrisankar, S.; Kim, J. N. *Tetrahedron* **2008**, *64*, 7183–7190; (f) Kim, H. S.; Gowrisankar, S.; Kim, S. H.; Kim, J. N. *Tetrahedron Lett.* **2008**, *49*, 3858–3861; (g) Kim, H. S.; Lee, H. S.; Kim, S. H.; Kim, J. N. *Tetrahedron Lett.* **2009**, *50*, 3154–3157.
6. For the synthesis of dihydrofuran moiety-containing tricyclic natural products, see: (a) Malona, J. A.; Cariou, K.; Frontier, A. J. *J. Am. Chem. Soc.* **2009**, *131*, 7560–7561; (b) Giese, M. W.; Moser, W. H. *Org. Lett.* **2008**, *10*, 4215–4218; (c) Li, H.; Fu, B.; Wang, M. A.; Li, N.; Liu, W. J.; Xie, Z. Q.; Ma, Y. Q.; Qin, Z. *Eur. J. Org. Chem.* **2008**, 1753–1758; (d) Sous, M. E.; Khoo, M. L.; Holloway, G.; Owen, D.; Scammells, P. J.; Rizzacasa, M. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 7835–7838; (e) Adams, T. E.; Sous, M. E.; Hawkins, B. C.; Himer, S.; Holloway, G.; Khoo, M. L.; Owen, D. J.; Savage, G. P.; Scammells, P. J.; Rizzacasa, M. A. *J. Am. Chem. Soc.* **2009**, *131*, 1607–1616; (f) Gerard, B.; Cencic, R.; Pelletier, J.; Porco, J. A., Jr. *Angew. Chem., Int. Ed.* **2007**, *46*, 7831–7834.
7. For the examples of dihydrofuran moiety-containing polycyclic compounds, see: (a) Lee, Y. R.; Kim, B. S.; Kim, D. H. *Tetrahedron* **2000**, *56*, 8845–8853; (b) Sajimon, M. C.; Ramaiah, D.; Thomas, K. G.; George, M. V. *J. Org. Chem.* **2001**, *66*, 3182–3187; (c) Venkata, N.; Mudiganti, S.; Claessens, S.; De Kimpe, N. *Tetrahedron* **2009**, *65*, 1716–1723; (d) Azuma, T.; Tanaka, Y.; Kikuzaki, H. *Phytochemistry* **2008**, *69*, 2743–2748; (e) Na, J. E.; Lee, K. Y.; Seo, J.; Kim, J. N. *Tetrahedron Lett.* **2005**, *46*, 4505–4508; (f) Almog, J.; Rozin, R.; Klein, A.; Shamuilov-Levinton, G.; Cohen, S. *Tetrahedron* **2009**, *65*, 7954–7962.
8. The cinnamyl bromides were prepared by treatment of the Baylis–Hillman alcohols with aqueous HBr according to the literature procedure, see: (a) Buchholz, R.; Hoffmann, H. M. R. *Helv. Chim. Acta* **1991**, *74*, 1213–1220; (b) Ameer, F.; Drewes, S. E.; Emslie, N. D.; Kaye, P. T.; Mann, R. L. *J. Chem. Soc., Perkin Trans. 1* **1983**, 2293–2295; (c) Gowrisankar, S.; Kim, S. H.; Kim, J. N. *Bull. Korean Chem. Soc.* **2009**, *30*, 726–728. and further references cited therein; (d) Basavaiah, D.; Reddy, K. R.; Kumaragurubaran, N. *Nat. Protocols* **2007**, *2*, 2665–2676.
9. For the introduction of nucleophiles at the secondary position of Baylis–Hillman adducts, see Kim, E. S.; Kim, K. H.; Kim, S. H.; Kim, J. N. *Tetrahedron Lett.* **2009**, *50*, 5098–5101. and further references cited therein.
10. *Typical procedure for the synthesis of* **3a**: To a solution of **1a** (668 mg, 2.0 mmol) in CH_3CN (5 mL) was added DABCO (246 mg, 2.2 mmol) and the reaction mixture was stirred at room temperature for 30 min. Deoxybenzoin (**2a**, 470 mg, 2.4 mmol) and NaOH (96 mg, 2.4 mmol) were added to the solution and the reaction mixture was stirred at room temperature for 48 h. After the usual aqueous workup and column chromatographic purification process (hexanes/CH_2Cl_2/diethyl ether, 15:1:1) **3a** was isolated as a *syn*/*anti* (2:1) mixture, 763 mg, (85%). Other starting materials **3b**–**k** were prepared similarly, and compounds **3c**–**h** and **3k** were isolated as *syn*/*anti* mixtures. Selected spectroscopic data of **3a**, **3b,** and **3i** are as follows. Analytically pure samples of major-**3a** and minor-**3a** were obtained by careful column chromatography, and the stereochemistry was not confirmed.
Compound **3a** (major): white solid, mp 157–159 °C; IR (KBr) 1722, 1680, 1268 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.64 (s, 3H), 5.40–5.49 (m, 2H), 5.78 (s, 1H), 6.28 (s, 1H), 6.91 (t, J = 7.8 Hz, 1H), 7.04–7.09 (m, 3H), 7.11–7.21 (m, 3H), 7.28 (d, J = 7.8 Hz, 1H), 7.37–7.43 (m, 3H), 7.47–7.52 (m, 1H), 7.98–8.01 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 48.16, 51.77, 57.11, 125.44, 126.02, 126.94, 127.22, 127.93, 128.23, 128.49, 128.58, 129.23, 129.56, 132.93, 133.01, 135.12, 136.64, 138.84, 141.43, 166.63, 197.81; ESIMS m/z 449 (M^++1), 451 (M^++3). Anal. Calcd for $C_{25}H_{21}BrO_3$: C, 66.82; H, 4.71. Found: C, 67.03; H, 4.82.
Compound **3a** (minor): white solid, mp 127–129 °C; IR (KBr) 1717, 1682, 1438 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.55 (s, 3H), 5.18 (d, J = 11.7 Hz, 1H), 5.61 (s, 1H), 5.91 (d, J = 11.7 Hz, 1H), 6.03 (s, 1H), 6.98 (t, J = 7.8 Hz, 1H), 7.11 (t, J = 7.8 Hz, 1H), 7.16–7.22 (m, 1H), 7.25–7.48 (m, 7H), 7.52–7.60 (m, 2H), 7.92–7.95 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 51.06, 51.51, 55.72, 125.91, 127.17, 127.49, 128.04, 128.50 (2C), 128.55, 128.83, 129.16, 129.74, 132.90, 133.48, 136.65, 136.73, 138.77, 139.67, 166.67, 197.71; ESIMS m/z 449 (M^++1), 451 (M^++3).
Compound **3b**: 56%; colorless oil; IR (film) 1720, 1686, 1438 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.43 (dd, J = 17.4 and 7.5 Hz, 1H), 3.60 (dd, J = 17.4 and 7.5 Hz, 1H), 3.70 (s, 3H), 5.12 (t, J = 7.5 Hz, 1H), 5.51 (s, 1H), 6.39 (s, 1H), 7.05–7.10 (m, 1H), 7.21–7.27 (m, 2H), 7.42–7.48 (m, 2H), 7.53–7.59 (m, 2H), 7.93–7.99 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 41.41, 42.35, 51.99, 124.93, 126.06, 127.43, 128.06, 128.22, 128.34, 128.61, 133.19, 133.39, 136.57, 140.83, 141.18, 166.75, 197.03; ESIMS m/z 373 (M^++1), 375 (M^++3).
Compound **3i**: 83%; colorless oil; IR (film) 1723, 1700, 1437 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.95 (s, 3H), 2.24 (s, 3H), 3.68 (s, 3H), 4.92 (d, J = 12.3 Hz, 1H), 5.17 (d, J = 12.3 Hz, 1H), 5.93 (s, 1H), 6.30 (s, 1H), 7.07 (t, J = 7.8 Hz, 1H), 7.25 (t, J = 7.8 Hz, 1H), 7.39 (d, J = 7.8 Hz, 1H), 7.55 (d, J = 7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 29.35, 29.76, 46.19, 51.96, 71.92, 125.35, 127.69, 128.80, 128.88, 129.65, 133.76, 137.25, 138.25, 166.28, 202.11, 202.54; ESIMS m/z 353 (M^++1), 355 (M^++3).
Typical procedure for the synthesis of **4a**: A mixture of **3a** (450 mg, 1.0 mmol), $Pd(OAc)_2$ (22 mg, 10 mol %), PPh_3 (52 mg, 20 mol %), and Cs_2CO_3 (652 mg, 2.0 mmol) in toluene (3 mL) was heated to reflux for 1 h. After the usual aqueous workup and column chromatographic purification process (hexanes/CH_2Cl_2/diethyl ether, 5:1:1), **4a** was isolated as a white solid, 210 mg (57%). Other compounds **4b**–**k** were prepared similarly, and the selected spectroscopic data of **4a**–**c**, **4g**, **4i,** and **4k** are as follows.
Compound **4a**: 57%; pale yellow solid, mp 116–118 °C; IR (KBr) 1755, 1737, 1237 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.64 (d, J = 17.4 Hz, 1H), 3.85 (s, 3H), 3.86 (d, J = 17.4 Hz, 1H), 5.21 (s, 1H), 6.72 (d, J = 7.2 Hz, 1H), 7.02 (t, J = 7.2 Hz, 1H), 7.17–7.24 (m, 4H), 7.25–7.34 (m, 6H), 7.37–7.42 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 44.52, 52.87, 63.72, 92.24, 112.77, 124.19, 124.85, 126.88, 126.97, 127.62, 127.67, 127.99, 128.53, 128.57, 129.36, 130.89, 134.09, 139.48, 141.89, 149.42, 173.66; ESIMS m/z 391 (M^++Na). Anal. Calcd for $C_{25}H_{20}O_3$: C, 81.50; H, 5.47. Found: C, 81.29; H, 5.61.
Compound **4b**: 42%; colorless oil; IR (film) 1735, 1244, 1207 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.56 (d, J = 17.7 Hz, 1H), 3.82 (s, 3H), 3.86 (d, J = 17.7 Hz, 1H), 4.85 (d, J = 3.3 Hz, 1H), 5.57 (d, J = 3.3 Hz, 1H), 7.20–7.34 (m, 7H), 7.56–7.59 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 44.56, 52.76, 60.14, 94.06, 97.38, 123.88, 125.14, 125.48, 127.46, 127.50, 128.20, 128.69, 130.24, 139.35, 143.02, 155.98, 173.66; ESIMS m/z 293 (M^++1). Anal. Calcd for $C_{19}H_{16}O_3$: C, 78.06; H, 5.52. Found: C, 78.33; H, 5.49.
Compound **4c**: 62%; colorless oil; IR (firm) 2239, 1655, 1261 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.87 (d, J = 17.7 Hz, 1H), 3.94 (d, J = 17.7 Hz, 1H), 5.32 (s, 1H), 6.72 (d, J = 7.8 Hz, 1H), 7.10 (t, J = 7.8 Hz, 1H), 7.21–7.28 (m, 4H), 7.30–7.42 (m, 8H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 45.70, 65.47, 82.29, 113.05, 119.94, 124.19, 124.96, 127.41, 127.58, 127.68, 128.08, 128.29, 128.84, 129.03, 129.45, 129.80, 133.00, 137.53, 140.05, 148.91; ESIMS m/z 336 (M^++1). Anal. Calcd for $C_{24}H_{17}NO$: C, 85.94; H, 5.11; N, 4.18. Found: C, 85.67; H, 5.35; N, 4.08.
Compound **4g**: 74%; white solid, mp 57–59 °C; IR (KBr) 1742, 1705, 1648 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.22 (s, 3H), 3.47 (d, J = 17.7 Hz, 1H), 3.77 (d, J = 17.7 Hz, 1H), 3.81 (s, 3H), 3.82 (s, 3H), 4.92 (s, 1H), 7.22–7.26 (m, 3H), 7.52–7.56 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.33, 43.52, 50.96, 52.89, 58.55, 94.47, 105.65, 124.66, 125.26, 127.56, 127.84, 138.70, 142.46, 165.69, 168.33, 172.26; ESIMS m/z 289 (M^++1). Anal. Calcd for $C_{16}H_{16}O_5$: C, 66.66; H, 5.59. Found: C, 66.95; H, 5.77.
Compound **4i**: 81%; colorless oil; IR (film) 1751, 1625, 1385 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.26 (s, 3H), 2.35 (s, 3H), 3.47 (d, J = 17.7 Hz, 1H), 3.77 (d, J = 17.7 Hz, 1H), 3.80 (s, 3H), 5.03 (s, 1H), 7.18–7.24 (m, 3H), 7.51–7.54 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 15.59, 29.44, 43.29, 52.87, 59.21, 93.91, 118.06, 124.49, 125.82, 127.65, 127.75, 138.48, 142.74, 166.87, 172.14, 193.07; ESIMS m/z 273

(M^++1). Anal. Calcd for $C_{16}H_{16}O_4$: C, 70.57; H, 5.92. Found: C, 70.50; H, 6.13. *Compound* **4k**: 35%; pale yellow oil; IR (film) 1737, 1437, 1260 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.49–2.57 (m, 2H), 2.79–3.01 (m, 2H), 3.55 (d, J = 17.7 Hz, 1H), 3.82 (s, 3H), 3.87 (d, J = 17.7 Hz, 1H), 4.76 (s, 1H), 7.06–7.29 (m, 7H), 7.32–7.34 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.04, 28.44, 44.86, 52.76, 62.11, 94.32, 110.20, 120.85, 123.44, 125.08, 126.27, 127.14, 127.17, 127.49, 127.51, 127.80, 135.89, 139.53, 141.78, 149.35, 173.55; ESIMS m/z 319 (M^++1). Anal. Calcd for $C_{21}H_{18}O_3$: C, 79.22; H, 5.70. Found: C, 79.56; H, 5.55.

11. We separated the two isomers in the case of **3a**,[10] and carried out the Pd-catalyzed cyclization reactions separately. Both isomers produced **4a** as the major product, although the yield with minor isomer was slightly lower (37%) than the cases of major isomer (59%) and the mixture (57%, entry 1 in Table 2).
12. For the examples of Pd-catalyzed cyclizations involving 5-*endo*-carbopalladation in Baylis–Hillman chemistry, see: (a) Vasudevan, A.; Tseng, P.-S.; Djuric, S. W. *Tetrahedron Lett.* **2006**, *47*, 8591–8593; (b) Park, J. B.; Ko, S. H.; Hong, W. P.; Lee, K.-J. *Bull. Korean Chem. Soc.* **2004**, *25*, 927–930.
13. *Crystal data of compound* **4g**: solvent of crystal growth (hexane); empirical formula $C_{16}H_{16}O_5$, Fw = 288.29, crystal dimensions 0.34 × 0.20 × 0.09 mm^3, monoclinic, space group $P2(1)/n$, a = 10.3057(19) Å, b = 10.362(2) Å, c = 13.347(3) Å, α = 90°, β = 104.855(10)°, γ = 90°, V = 1377.6(5) $Å^3$, Z = 4, D_{calcd} = 1.390 mg/m^3, F_{000} = 608, MoKα (λ = 0.71073 Å), R_1 = 0.0898, wR_2 = 0.2598 ($I>2\sigma(I)$). The X-ray data has been deposited in CCDC with number 777033.