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Stereoselective Synthesis of 3-Alkylideneoxindoles via Palladium-Catalyzed Domino Reactions†

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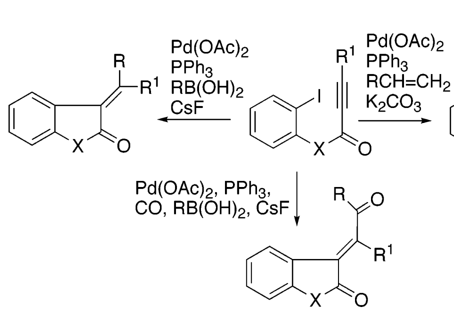

We have developed efficient catalytic methods for the stereoselective and diversity synthesis of various (*E*)-, (*Z*)-, and disubstituted 3-alkylideneoxindoles and 3-alkylidenebenzofuran-2-ones via palladium-catalyzed Heck/Suzuki–Miyaura, Heck/Heck, and Heck/carbonylation/Suzuki–Miyaura domino reactions.

Oxindoles are important compounds of natural indole alkaloids,[1] drug candidates,[2] and metabolic intermediates. Among them, 3-alkylideneoxindoles are well-known to be versatile compounds in terms of biological activity and synthetic applicability. For example, the (*E*)-3-alkylideneoxindoles are important synthetic intermediates of TMC-95A,[3] and the (*E*)- and (*Z*)-3-alkylideneoxindoles are involved in drug candidates of tyrosine kinase inhibitors,[4] cyclin-dependent protein kinase inhibitors,[5] antirheumatic compounds,[6] and analogues of the anti-breast cancer drug tamoxifen. However, despite their importance, stereoselective synthesis of these 3-alkylideneoxindoles had remained a difficult problem.[3,7] Recently, we have reported the first efficient method for stereoselective synthesis of (*E*)-, (*Z*)-, and disubstituted-3-alkylideneoxindoles **A** using reductive radical cyclization reactions of compound **B** with a typical metal indium (path a). The key step of this reaction is the strong coordination of the indium cation to the amide carbonyl oxygen (Scheme 1).[8] However, different starting materials should be prepared to synthesize both (*E*)- and (*Z*)-isomers. On the other hand, domino reactions initiated by intramolecular Heck reactions[9] have been developed and advanced to prepare polycyclic compounds in a single operation.[10] In contrast to these facts, oxindole synthesis via a domino Pd-catalyzed reaction has seldom been examined until now. Recently, Cossy reported an elegant synthesis of (*E*)-3-alkylideneoxyisoindoles via a Heck/Suzuki–Miyaura domino reaction,[11] and very recently, Müller applied a Heck/Sonogashira domino reaction to synthesize 3-alkylideneoxindole derivatives.[12] The key step of these reactions is the syn addition of arylpalladium halide to the triple bond. If the same palladium-

† This paper is dedicated to the memory of the late Professor Kiyoshi Tanaka.

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(1) (a) Kam, T.-S.; Choo, Y.-M. *Tetrahedron* **2000**, *56*, 6143. (b) Cane, A.; Tournaire, M.-C.; Barritault, D.; Crumeyrolle-Arias, M. *Biochem. Biophys. Res. Commun.* **2000**, *276*, 379. (c) Tsuda, M.; Mugishima, T.; Komatsu, K.; Sone, T.; Tanaka, M.; Mikami, Y.; Shiro, M.; Hirai, M.; Ohizumi, Y.; Kobayashi, J. *Tetrahedron* **2003**, *59*, 3227. (d) Marti, C.; E. Carreira, M. *Eur. J. Org. Chem.* **2003**, 2209. (e) Akai, S.; Tsujino, T.; Akiyama, E.; Tanimoto, K.; Naka, T.; Kita, Y. *J. Org. Chem.* **2004**, *69*, 2478.

(2) Zhang, T. Y.; Zhang, H. *Tetrahedron Lett.* **2002**, *43*, 193 and references therein.

(3) (a) Ma, D.; Wu, Q. *Tetrahedron Lett.* **2000**, *41*, 9089. (b) Lin, S.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 1967. (c) Inoue, M.; Furuyama, H.; Sakazaki, H.; Hirama, M. *Org. Lett.* **2001**, *3*, 2863. (d) Lin, S.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2002**, *41*, 512. (e) Kaiser, M.; Groll, M.; Renner, C.; Huber, R.; Moroder, L. *Angew. Chem., Int. Ed.* **2002**, *41*, 780. (f) Albrecht, B. K.; Williams, R. M. *Org. Lett.* **2003**, *5*, 197. (g) Lin, S.; Yang, Z.-Q.; Kwok, B. H. B.; Koldobskiy, M.; Crews, C. M.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2004**, *126*, 6347.

(4) (a) Mohammadi, M.; McMahon, G.; Sun, L.; Tang, C.; Hirth, P.; Yeh, B. K.; Hubbard, S. R.; Schlessinger, J. *Science* **1997**, *276*, 955. (b) Sun, L.; Tran, N.; Tang, F.; App, H.; Hirth, P.; McMahon, G.; Tang, C. *J. Med. Chem.* **1998**, *41*, 2588. (c) Sun, L.; Tran, N.; Liang, C.; Hubbard, S.; Tang, F.; Lipson, K.; Schreck, R.; Zhou, Y.; McMahon, G.; Tang, C. *J. Med. Chem.* **2000**, *43*, 2655. (d) Vieth, M.; Cummins, D. J. *J. Med. Chem.* **2000**, *43*, 3020. (e) Bramson, H. N.; Corona, J.; Davis, S. T.; Dickerson, S. H.; Edelstein, M.; Frye, S. V.; Gampe, R. T., Jr.; Harris, P. A.; Hassell, A.; Holmes, W. D.; Hunter, R. N.; Lackey, K. E.; Lovejoy, B.; Luzzio, M. J.; Montana, V.; Rocque, W. J.; Rusnak, D.; Schewchuk, L.; Veal, J. M.; Walker, D. H.; Kuyper, L. F. *J. Med. Chem.* **2001**, *44*, 4339. (f) Sun, L.; Liang, C.; Shirazian, S.; Zhou, Y.; Miller, T.; Cui, J.; Fukuda, J. Y.; Chu, J.-Y.; Nematalla, A.; Wang, X.; Chen, H.; Sistla, A.; Luu, T. C.; Tang, F.; Wei, J.; Tang, C. *J. Med. Chem.* **2003**, *46*, 1116.

(5) Woodard, C. L.; Li, Z.; Kathcart, A. K.; Terrell, J.; Gerena, L.; Sanchez, M. L.; Kyle, D. E.; Bhattacharjee, A. K.; Nichols, D. A.; Ellis, W.; Prigge, S. T.; Geyer, J. A.; Waters, N. C. *J. Med. Chem.* **2003**, *46*, 3877.

(6) Robinson, R. P.; Reiter, L. A.; Barth, W. E.; Campeta, A. M.; Cooper, K.; Cronin, B. J.; Destito, R.; Donahue, K. M.; Falkner, F. C.; Fiese, E. F.; Johnson, D. L.; Kuperman, A. V.; Liston, T. E.; Malloy, D.; Martin, J. J.; Mitchell, D. Y.; Rusek, F. W.; Shamblin, S. L.; Wright, C. F. *J. Med. Chem.* **1996**, *39*, 10.

(7) *E*:*Z* = 5:1–1:5, for example: (a) Mori, M.; Ban, Y. *Tetrahedron Lett.* **1979**, *20*, 1133. (b) Fielding, M. R.; Grigg, R.; Urch, C. J. *Chem. Commun.* **2000**, 2239. (c) Teichert, A.; Jantos, K.; Harms, K.; Studer, A. *Org. Lett.* **2004**, *6*, 3477.

(8) Yanada, R.; Obika, S.; Oyama, M.; Takemoto, Y. *Org. Lett.* **2004**, *6*, 2825.

(9) Lautens, M.; Tayama, E.; Herse, C. *J. Am. Chem. Soc.* **2005**, *127*, 72.

(10) For an excellent review on cyclic carbopalladations: Negishi, E.-I.; Cöperet, C.; Ma, S.; Liou, S.-Y.; Liu, F. *Chem. Rev.* **1996**, *96*, 365.

(11) Couty, S.; Liégault, B.; Meyer, C.; Cossy, J. *Org. Lett.* **2004**, *6*, 2511.

(12) D'Souza, D. M.; Rominger, F.; Müller, T. J. J. *Angew. Chem., Int. Ed.* **2005**, *44*, 153.

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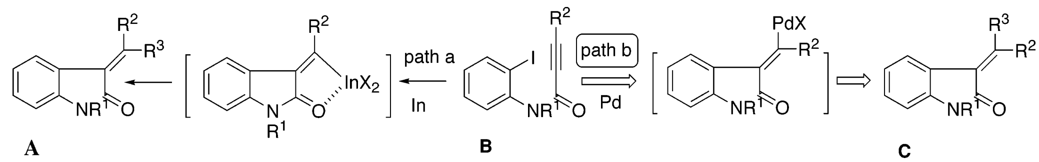
SCHEME 1



SCHEME 2

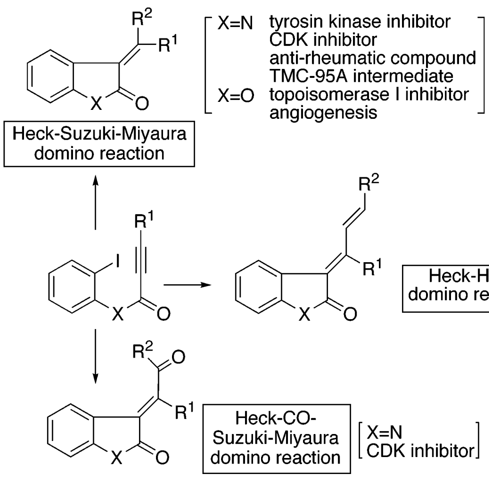
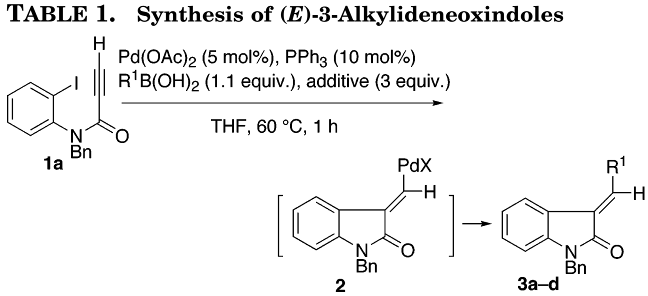


TABLE 1. Synthesis of (*E*)-3-Alkylideneoxindoles

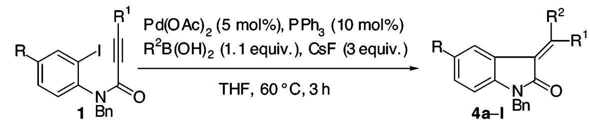


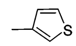
run	R^1	additive	(*E*)-**3**	yield (%)
1	Ph	NaOH (aq)	a	88:4 (*E*:*Z*)
2	Ph	CsF	a	95
3	*p*-MeO–Ph	CsF	b	77
4	*p*-CF_3–Ph	CsF	c	78
5	Bu	CsF	d	70

catalyzed Heck/Suzuki–Miyaura domino reaction was carried out with starting material **B**, the other stereoisomer **C** of **A** should be obtained stereoselectively via path b. Herein we report the palladium-catalyzed domino reaction of compound **B** to yield (*E*)-, (*Z*)-, and disubstituted-3-alkylideneoxindoles as single stereoisomers. We applied this procedure to the palladium-catalyzed Heck/Heck domino reaction and to the Heck/carbonylation/Suzuki–Miyaura domino reaction (Scheme 2).

Preparation of the starting materials **1** was easily achieved according to our recently reported method.[8] We initially examined the reaction of **1** in the presence of a catalytic amount of $Pd(OAc)_2$, PPh_3, and 1.1 equiv of aryl- and alkylboronic acids (Table 1). When sodium hydroxide was used as a base, a mixture of (*E*)- and (*Z*)-3-alkylideneoxindoles **3a** (*E*:*Z* = 22:1) was obtained (run 1). After some trials, we found that cesium fluoride was an appropriate additive as an activator for boronic acids of this Heck/Suzuki–Miyaura domino coupling reaction. Then, we examined the reaction of alkyneamide **1a** and some aryl- and alkylboronic acids in the presence of cesium fluoride. The cascade reaction proceeded to completion to produce (*E*)-alkenes **3a–d** exclusively in high yields (runs 2–5). The vinylic protons of (*E*)-isomers **3** appeared at a lower field in the ^1H NMR spectra than the corresponding signals of the (*Z*)-isomers due to the effect of the amide carbonyl oxygen. As we envisaged, the (*E*)-alkenes **3** might be produced via (*E*)-vinylpalladium intermediate **2**. This feature is in contrast to the possibility that the vinylindium intermediate might be a (*Z*)-vinylindium intermediate due to the strong coordination of the indium atom to the amide carbonyl group.[8]

TABLE 2. Synthesis of Disubstituted 3-Alkylideneoxindoles

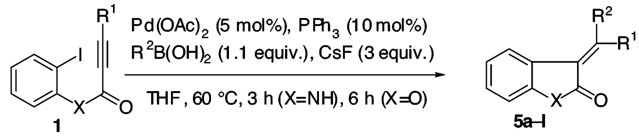


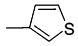
run	**1**	R	R^1	R^2	**4**	yield (%)
1	**b**	H	Ph	Ph	**a**	95
2	**c**	H	*p*-Tol	Ph	(*Z*)-**b**	96
3	**b**	H	Ph	*p*-Tol	(*E*)-**b**	93
4	**b**	H	*p*-MeO-Ph	Ph	**c**	92
5	**d**	H	*p*-CF_3-Ph	Ph	(*Z*)-**d**	95
6	**b**	H	Ph	*p*-CF_3-Ph	(*E*)-**d**	80
7	**e**	H		Ph	**e**	96
8	**f**	H	Bu	Ph	(*E*)-**f**	90
9	**g**	H	CH_2OBn	Ph	**g**	90
10	**g**	H	CH_2OBn	*p*-MeO-Ph	**h**	90
11	**b**	H	Ph	Bu	(*Z*)-**f**	45
12	**h**	Me	Bu	Ph	**i**	92
13	**i**	CN	Bu	Ph	**j**	91
14[a]	**j**	CF_3	Bu	Ph	**k**	71

[a] Reaction time was 10 h, and starting material (18%) was recovered.

Having succeeded in the synthesis of (*E*)-3-alkylideneoxindoles, we next applied this method to the stereoselective synthesis of disubstituted 3-alkylideneoxindoles **4** using aryl- and alkyl-boronic acids. While this paper was in preparation, Player et al. published a complementary stereoselective synthesis of disubstituted 3-alkylideneoxindoles with N-containing heterocycles.[13] They found that copper(I) thiophen-2-carboxylate (CuTC) was an appropriate additive for obtaining high stereoselectivity. Table 2 shows our results. In most cases, the corresponding disubstituted 3-alkylideneoxindoles **4a–h** were obtained in high yields with no contamination of other stereoisomers (runs 1–10). Only when aliphatic boronic acid was used was the product yield low (run 11), as usually seen in the Suzuki–Miyaura reaction. The

TABLE 3. Synthesis of Disubstituted 3-Alkylideneoxindoles and 3-Alkylidenebenzofuran-2-ones



run	1	X	R^1	R^2	5	yield (%)	run	1	X	R^1	R^2	5	yield (%)
1	**k**	NH	Ph	*p*-Tol	**a**	96	6	**n**	O	H	Ph	**f**	80
2	**k**	NH	Ph	*p*-MeO-Ph	**b**	92	7	**o**	O	Ph	*p*-Tol	**g**	93
3	**k**	NH	Ph	*p*-CF_3-Ph	**c**	90	8	**o**	O	Ph	*p*-MeO-Ph	**h**	90
4	**l**	NH		Ph	**d**	85	9	**o**	O	Ph	*p*-CF_3-Ph	**i**	70
5	**m**	NH	Et	Ph	**e**	88	10	**p**	O	Bu	Ph	**j**	94

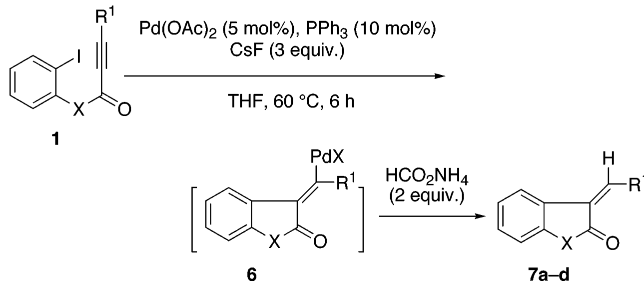
reaction of compounds **1** bearing an electron-donating or electron-withdrawing group on the aromatic ring also gave stereoselectively the desired cyclized products **4i**−**k** in good yields (runs 12−14). By our previous method,[8] it was not possible to obtain compounds (*E*)-**4f** or **4g**−**k** containing alkyl groups as R^1 substituents. The Heck/Suzuki−Miyaura domino reaction mentioned here can achieve the synthesis of these compounds exclusively. The stereoselectivity of compounds **4** was unambiguously confirmed using the authentic samples or by comparison with the tendencies of their ^{1}H NMR spectra.[8]

Encouraged by these results, we applied these optimized conditions to *N*-free alkyneamide **1** and alkynester **1**. Our radical cyclization method with indium was not a suitable method for *N*-free alkyneamides **1**, but the palladium-catalyzed cyclization reactions mentioned here fortunately proceeded smoothly and stereoselectively to yield disubstituted 3-alkylideneoxindoles **5a**−**e** (X = NH, Table 3, runs 1−5) and 3-alkylidenebenzofuran-2-ones known as topoisomerase inhibitors and angiogenesis[14] **5f**[15]−**j** (X = O, runs 6−10) in high yields.

To obtain (*Z*)-3-alkylideneoxindoles and benzofuran-2-one, compound **1** was treated with a catalytic amount of $Pd(OAc)_2$ and PPh_3 in the presence of cesium fluoride in THF. In the presence of ammonium formate, the reaction proceeded smoothly to regenerate the Pd(0) catalyst from the intermediate σ-vinylpalladium complexes **6**. Under these conditions, the desired (*Z*)-**7a**−**7c** and **7e**[15] were cleanly obtained in good yields (Table 4, runs 1−3, 5). Unfortunately, our attempted synthesis of compound **7d** bearing an aliphatic substituent was unsuccessful (R^1 = Bu, run 4).

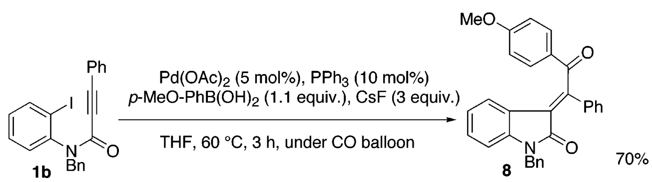
Next, we applied these methods to the synthesis of compound **8** known as a a CDK inhibitor[14] via a Heck/carbonylation/Suzuki−Miyaura domino reaction (Scheme 3). This reaction proceeded smoothly under a carbon monoxide atmosphere to produce compound **8** in 70% yield. The (*E*)-configuration of the double bond is unambiguously supported by the NOESY spectrum for the interaction between the aromatic proton of anisole and the aromatic proton in the 4-position of the indolone moiety. We also applied our method to the synthesis of compound **9**. As shown in Table 5, Heck/Heck domino reactions proceeded to give compounds **9** as a single isomer in high yields (runs 1−3). The stereostructure of the newly introduced olefins was found to be of trans geometry and confirmed by the large olefinic coupling constant of their ^{1}H NMR. Only when we used allyl acetate as an olefin did we obtain the unusual product **9d** in 80% yield (run 4). This product would be produced by intramolecular Heck cyclization, followed by intermolecular Heck reaction, and then maybe a palladium-β-alkoxy elimination. Lautens reported Pd-catalyzed intramolecular coupling reaction between aryl iodide and allyl moieties.[9] He wrote that the amine base should be the reductant of Pd(II) to Pd(0) after the catalytic cycle, and inorganic bases instead of the amine base gave very

TABLE 4. Synthesis of (*Z*)-3-Alkylideneoxindoles



run	1	X	R^1	base	(*Z*)-**7**	yield (%)
1	b	NBn	Ph	CsF	a	80
2	c	NBn	Tol	CsF	b	70
3	d	NBn	*p*-CF_3−Ph	CsF	c	70
4	f	NBn	Bu	CsF	d	0
5	o	O	Ph	CsF	e	65

SCHEME 3. Heck Carbonylation/Suzuki−Miyaura Domino Reaction

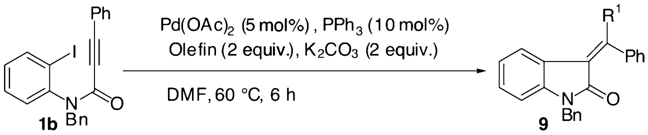


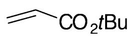
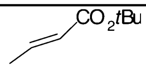
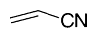
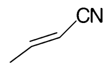
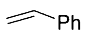
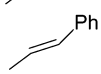
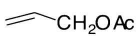
(13) Cheung, W. S.; Patch, R. J.; Player, M. R. *J. Org. Chem.* **2005**, *70*, 3741.

(14) (a) Woodard, C. L.; Li, Z.; Kathcart, A. K.; Terrell, J.; Gerena, L.; L.-Sanchez, M.; Kyle, D. E.; Bhattacharjee, A. K.; Nichols, D. A.; Ellis, W.; Prigge, S. T.; Geyer, J. A.; Waters, N. C. *J. Med. Chem.* **2003**, *46*, 3877. (b) Adams, C.; Aldous, D. J.; Amendola, S.; Bamborough, P.; Bright, C.; Crowe, S.; Eastwood, P.; Fenton, G.; Foster, M.; Harrison, T. K. P.; King, S.; Lai, J.; Lawrence, C.; Letallec, J.-P.; McCarthy, C.; Moorcroft, N.; Page, K.; Rao, S.; Redford, J.; Sadiq, S.; Smith, K.; Souness, J. E.; Thurairatnam, S.; Vine, M.; Wyman, B. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 3105.

(15) Msaddek, M.; Rammah, M.; Ciamala, K.; Vebrel, J.; Laude, B. *Synthesis* **1997**, 1495.

TABLE 5. Heck/Heck Domino Reaction



run	olefin	R[1]	9	yield (%)
1			**a**	90
2			**b**	92
3			**c**	90
4			**d**	80

low product yields. In our experiment, when we used potassium carbonate as a base, compound **9** was obtained exclusively. This is an interesting result, and we are currently investigating the same type of reaction.

Conclusion

We have developed efficient catalytic methods for the stereoselective and diversity-generating synthesis of various (*E*)-, (*Z*)-, and disubstituted 3-alkylideneoxindoles and 3-alkylidenebenzofuran-2-ones via palladium-catalyzed Heck/Suzuki−Miyaura, Heck/Heck, and Heck/carbonylation/Suzuki−Miyaura domino reactions. Our method provides a versatile tool for further expansion of the synthetic utility such as the total synthesis of natural products and random screening in the search for drug candidates.

Experimental Section

General Procedure for the Synthesis of (*E*)- and Disubstituted Compounds (3−5). To a solution of iodoalkyne **1a** (36.1 mg, 0.10 mmol) in THF were added palladium(II) acetate (1.12 mg, 5×10^{-3} mmol), triphenylphosphine (2.62 mg, 0.01 mmol), phenylboronic acid (13.3 mg, 0.11 mmol), and cesium fluoride (45.3 mg, 0.30 mmol), and the solution was stirred for 1 h at 60 °C under an argon atmosphere. After being quenched with water, the mixture was extracted with AcOEt and dried over $MgSO_4$. The residue was purified by column chromatography on silica gel (hexane/AcOEt = 5/1) to give **(*E*)-3a** (29.5 mg, 95%).

General Procedure for the Synthesis of (*Z*)-3-Alkylideneoxindoles 7. To a solution of iodoalkyne **1b** (43.7 mg, 0.10 mmol) in THF were added palladium(II) acetate (1.12 mg, 5×10^{-3} mmol), triphenylphosphine (2.62 mg, 0.01 mmol), cesium fluoride (45.3 mg, 0.30 mmol), and ammonium formate (12.6 mg, 0.20 mmol), and the solution was stirred for 6 h at 60 °C under an argon atmosphere. After being quenched with water, the mixture was extracted with AcOEt and dried over $MgSO_4$. The residue was purified by column chromatography on silica gel (hexane/AcOEt = 5/1) to give **(*Z*)-7b** (24.9 mg, 80%).

Heck/Carbonylation/Suzuki−Miyaura Domino Reaction: Synthesis of Compound 8. To a solution of iodoalkyne **1b** (36.1 mg, 0.10 mmol) in THF were added palladium(II) acetate (1.12 mg, 5×10^{-3} mmol), triphenylphosphine (2.62 mg, 0.01 mmol), 4-methoxyphenylboronic acid (16.6 mg, 0.11 mmol), and cesium fluoride (45.3 mg, 0.30 mmol), and the solution was stirred for 3 h at 60 °C under a carbon monoxide atmosphere. After being quenched with water, the mixture was extracted with AcOEt and dried over $MgSO_4$. The residue was purified by column chromatography on silica gel (hexane/AcOEt = 5/1) to give **8** (31.2 mg, 70%).

(*E*)-1-Benzyl-3-(2-(4-methoxyphenyl)-2-oxo-1-phenylethylidene)indolin-2-one (8): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, J = 7.9 Hz, 2H), 7.44−7.24 (m, 8H), 7.05 (t, J = 7.6 Hz, 1H), 6.97−6.88 (m, 4H), 6.68−6.66 (m, 3H), 4.92 (s, 2H), 3.87 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.8, 163.3, 160.8, 155.4, 140.4, 140.3, 137.5, 165.6, 133.6, 131.7, 130.7, 129.3, 128.5, 127.8, 124.5, 123.8, 123.0, 121.2, 114.2, 113.5, 109.5, 55.3; IR ($CHCl_3$) ν 2980, 1602 cm^{-1}; MS (FAB) *m/z* 446 (MH$^+$); HRMS (FAB) calcd for $C_{30}H_{24}NO_3$ (MH$^+$) 446.1756, found 446.1758.

Heck/Heck Domino Reaction: Synthesis of Compound 9. To a solution of iodoalkyne **1b** (36.1 mg, 0.10 mmol) in DMF were added palladium(II) acetate (1.12 mg, 5×10^{-3} mmol), triphenylphosphine (2.62 mg, 0.01 mmol), *tert*-butyl acrylate (25.6 mg, 0.20 mmol), and potassium carbonate (27.6 mg, 0.20 mmol), and the mixture was stirred for 6 h at 60 °C under an argon atmosphere. After being quenched with water, the mixture was extracted with AcOEt and dried over $MgSO_4$. The residue was purified by column chromatography on silica gel (hexane/AcOEt = 5/1) to give **9** (39.3 mg, 90%).

(2*E*,4*Z*)-*tert*-Butyl 4-(1-Benzyl-2-oxindolin-3-ylidene)-4-phenylbut-2-enoate (9a): ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.50 (d, J = 15.5 Hz, 1H), 7.52−7.50 (m, 4H), 7.33−7.22 (m, 6H), 7.05−7.03 (m, 1H), 6.63 (d, J = 7.9 Hz, 1H), 6.56 (m, 1H), 5.77 (d, J = 7.6 Hz, 1H), 5.67 (d, J = 15.5 Hz, 1H), 4.98 (s, 2H), 1.50 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.9, 147.8, 143.1, 140.4, 136.1, 131.4, 129.7, 129.5, 129.3, 128.8, 128.3, 127.6, 127.4, 127.0, 124.7, 122.6, 121.8, 108.7, 80.8, 43.3, 28.0; IR ($CHCl_3$) ν 2950, 1640 cm^{-1}; MS (FAB) *m/z* 438 (MH$^+$); HRMS (FAB) calcd for $C_{29}H_{28}NO_3$ (MH$^+$) 438.2069, found 438.2070.

(2*E*,4*Z*)-4-(1-Benzyl-2-oxindolin-3-ylidene)-4-phenylbut-2-enenitrile (9b): ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.48 (d, J = 16.2 Hz, 1H), 7.59−7.54 (m, 3H), 7.34−7.20 (m, 8H), 7.07 (t, J = 6.4 Hz, 1H), 6.59 (t, J = 7.7 Hz, 1H), 5.79 (d, J = 8.0 Hz, 1H), 5.21 (d, J = 16.2 Hz, 1H), 4.96 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9, 147.2, 145.4, 143.6, 135.7, 134.9, 130.6, 129.8, 129.4, 128.9, 128.4, 127.8, 127.8, 127.4, 125.2, 122.2, 122.0, 118.0, 109.0, 106.3, 43.5; IR ($CHCl_3$) ν 2960, 1605 cm^{-1}; MS (FAB) *m/z* 363 (MH$^+$); HRMS (FAB) calcd for $C_{25}H_{19}N_2O$ (MH$^+$) 363.1497, found 363.1495.

(3*Z*)-1-Benzyl-3-((*E*)-1,3-diphenylallylidene)indolin-2-one (9c): ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.42 (d, J = 12.2 Hz, 1H), 7.58−7.53 (m, 5H), 7.37−7.24 (m, 10H), 7.00 (t, J = 7.6 Hz, 1H), 6.67 (d, J = 6.3 Hz, 1H), 6.57 (t, J = 7.6 Hz, 1H), 6.50 (d, J = 12.2 Hz, 1H), 5.75−5.72 (m, 1H), 5.02 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.1, 151.6, 141.8, 137.6, 136.4, 129.3, 129.1, 128.8, 128.7, 128.6, 128.5, 128.2, 128.0, 127.7, 127.5, 127.3, 123.7, 123.4, 121.6, 108.4, 96.9, 43.3; IR ($CHCl_3$) ν 3002, 1640 cm^{-1}; MS (FAB) *m/z* 414 (MH$^+$); HRMS (FAB) calcd for $C_{30}H_{24}NO$ (MH$^+$) 414.1858, found 414.1860.

(*Z*)-1-Benzyl-3-(1-phenylbut-3-enylidene)indolin-2-one (9d). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.84 (d, J = 8.0 Hz, 1H), 9.56 (d, J = 15.8 Hz, 1H), 7.55−7.53 (m, 3H), 7.36−7.22 (m, 9H), 7.08 (t, J = 5.6 Hz, 1H), 6.68 (d, J = 7.7 Hz, 1H), 6.60 (t, J = 7.7 Hz, 1H), 5.97 (q, J = 8.0 Hz, 1H), 5.89 (d, J = 8.0 Hz, 1H), 4.98 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9, 155.1, 142.5, 141.4, 139.9, 136.4, 132.2, 132.1, 130.2, 129.4, 129.2, 129.0, 128.8, 128.7, 128.6, 128.5, 127.8, 127.5, 127.3, 127.2, 124.0, 123.4, 123.2, 121.4, 108.7, 43.4; IR ($CHCl_3$) ν 3002, 1652 cm^{-1}; MS (FAB) *m/z* 352 (MH$^+$); HRMS (FAB) calcd for $C_{25}H_{22}NO$ (MH$^+$) 352.1701, found 352.1703.

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Supporting Information Available: Characterization data and ^{1}H and ^{13}C NMR spectra of synthetic new compounds This material is available free of charge via the Internet at http://pubs.acs.org.

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