Note

Stereoselective Synthesis of 3-(1,3-Diarylallylidene)oxindoles via a Palladium-Catalyzed Tandem Reaction

Yoseb Yu, Kye Jung Shin, and Jae Hong Seo

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.6b02909 • Publication Date (Web): 06 Jan 2017

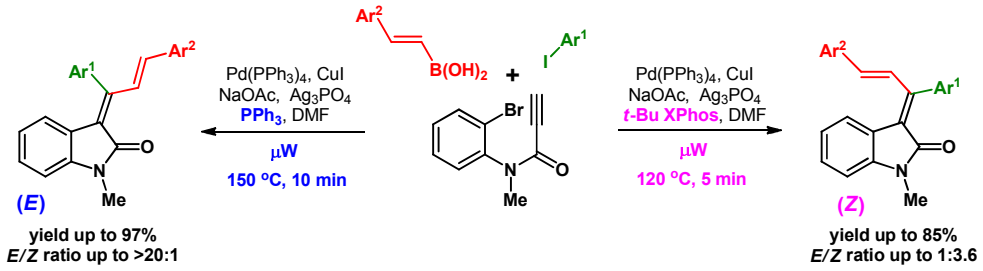
Stereoselective Synthesis of 3-(1,3-Diarylallylidene)oxindoles via a Palladium-Catalyzed Tandem Reaction

Yoseb Yu, Kye Jung Shin, and Jae Hong Seo*

Integrated Research Institute of Pharmaceutical Sciences, College of Pharmacy, The Catholic University of Korea, Bucheon-si, Gyeonggi-do 14662, Korea

jaehongseo@catholic.ac.kr

■ Table of Contents



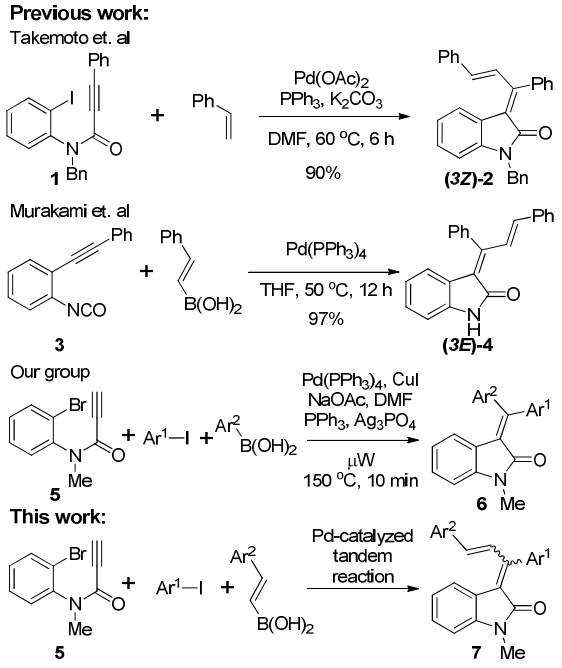
■ Abstract

We have developed an efficient three-component tandem reaction for the synthesis of 3-(1,3-diarylallylidene)oxindoles combining three palladium-catalyzed reactions: the Sonogashira, Heck, and Suzuki-Miyaura reactions. This method allows a stereoselective approach to each (*E*)- and (*Z*)-isomer by ligand change and controlling the reaction temperature.

3-Methylene oxindole is a prevalent skeleton in various biologically active compounds[1] and synthetic intermediates.[2] 3-(Diarylmethylene)oxindole derivatives[3] are gaining attention recently because of novel activities, such as AMPK activation[3b] and estrogen receptor-related anti-breast-cancer activity.[3c] To increase the value of 3-(diarylmethylene)oxindoles as a chemical entity for future drug discovery and development, modifications or expansion of the core structure has been requested by the medicinal chemistry sector. 3-(1,3-Diarylallylidene)oxindoles bearing a vinyl linker between one of the aryl substituents and the methylene group of the oxindoles could be an ideal candidate for this purpose. Although numerous methods for the synthesis of 3-(diarylmethylene)oxindoles have been reported,[4]

synthetic studies on 3-(1,3-diarylallylidene)oxindoles are relatively rare. and the substrate scopes of the methods are either not well studied or limited in number.[5,6] In 2005, Takemoto and coworkers reported that a (*3Z*)-3-(1,3-diphenylallylidene)oxindole (*3Z*)-**2** could be prepared via an intra- and intermolecular double Heck reaction of 3-phenylpropiolamide **1** and styrene with a 90% yield.[4c] In 2008, the Murakami group disclosed an elegant palladium-catalyzed oxidative cyclization/transmetallation of 2-(alkynyl)phenyl isocyanate **3** with styrylboronic acid to afford a counter stereoisomer, (*3E*)-3-(1,3-diphenyallylidene)oxindole (*3E*) **4**, in a 97% yield.[4g] As described above, stereoselective synthesis of (*3E*)- and (*3Z*)-3-(1,3-diarylallylidene)oxindoles has been achieved, but there is still a need to develop a more efficient and stereoselective method for the synthesis of this key intermediate. Recently, our group reported a microwave-assisted three-component tandem reaction of propiolamide **5**, aryliodide, and arylboronic acid to yield 3-(diarylmethylene)oxindoles **6** with a short reaction time (10 min) and a high stereoselectivity via three palladium-catalyzed reactions: the Sonogashira, Heck, and Suzuki-Miyaura reactions.[7] We then applied our palldium-catalyzed tandem reaction conditions to the synthesis of (1,3-diarylallylidene)oxindoles **7** by displacing arylboronic acid with 2-arylvinylboronic acid. (Scheme 1)

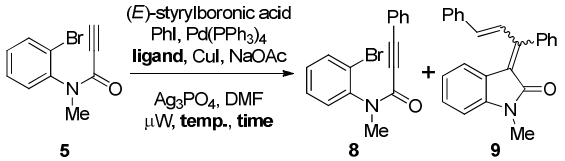
Scheme 1. Synthetic Approaches for 3-(1,3-Diarylallylidene)oxindoles



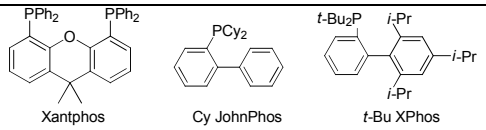
First, a mixture of propiolamide **5**, phenyl iodide, and styrylboronic acid was exposed to the previously optimized reaction conditions (150 °C, 10 min), which afforded 3-(allylidene)oxindole **9** as a single isolable product at a 97% yield (Table 1, entry 1). To our surprise, an extensive NMR study, including a ROESY experiment, unambiguously elucidated the stereochemistry of the newly formed olefin of **9** as the

(*E*)- rather than the (*Z*)-configuration, which was expected from the *syn* addition mechanism during the migratory insertion of a triple bond to the arylpallaium species. In our previous work on the synthesis of 3-(diarylmethylene)oxindole,[7,8] the formation of the unexpected stereoisomer was explained by the isomerization of the vinylpalladium intermediate via a zwitterionic palladium carbenoid species.[9] This isomerization was successfully surpassed by the addition of a silver salt, such as silver phosphate (Ag_3PO_4), which is known to change the catalytic pathway of a palladium-catalyzed reaction from neutral to cationic.[10] In the cationic pathway, positively charged palladium of a vinylpalladium intermediate is presumably less likely to form zwitterionic palladium carbenoid.[11] Since Ag_3PO_4 was already used in the reaction, we speculated that (*3Z*)-**9** was mainly formed at first and then isomerized to (*3E*)-**9** under the reaction conditions. To verify this, the reaction was run at a lower temperature (130 °C), and the formation of the (*Z*)-isomer was observed as a minor product (*E*/*Z* ratio = 1.4:1, entry 2) whilst a longer reaction time (20 min) at the same temperature (130 °C) increased the ratio of the (*E*)-isomer (*E*/*Z* ratio = 2.9:1, entry 3). When the reaction was run at a 120 °C for 10 min, the (*Z*)-isomer was obtained as a major product with a moderate yield (67% yield, *E*/*Z* ratio = 1:2.5) but a small amount of the Sonogashira adduct **8** remained (17% yield; entry 4). An additional 10 min of reaction time increased the yield to 78% but the *E*/*Z* ratio was lower, at 1:1.4 (entry 5). Lowering the reaction temperature to 110 °C made the reaction rate very slow, giving yields of **9** of 44% (10 min) and 58% yield (20 min) as well as substantial amounts of intermediate **8**, but the *E*/*Z* ratio of the products obtained was within an acceptable range (entries 6 and 7). All of the above results imply that the (*Z*)-isomer is generated as the major isomer at first in the reaction but that isomerization to the (*E*)-isomer is easily facilitated by the reaction conditions, especially high temperature and long reaction time. Extensive efforts to find the optimal conditions for a high yield and (Z)-stereoselectivity were exerted by screening various catalysts, ligands, bases, solvents, and silver additives. However, all trials were fruitless except for the ligand change. A reaction with P(*o*-tol)$_3$ resulted in moderate selectivity (*E*/*Z* ratio = 1:2.7) but with a low yield of 30% (entry 8). Xantphos, a bidentate phosphine ligand, increased the yield to 57% but had a very low *E*/*Z* stereoselectivity (*E*/*Z* ratio = 1:1.3; entry 9). Cy Johnphos gave similar results to P(*o*-tol)$_3$ (entry 10). The best result from a ligand change was from *t*-Bu XPhos, which gave a high yield with moderate stereoselectivity (75% yield, *E*/*Z* ratio = 1:2.0; entry 11). After conducting several experiments varying the reaction time and temperature with *t*-Bu XPhos, a reaction temperature of 120 °C for 5 min with *t*-Bu XPhos was found to result in a yield of 85% with a 1:2.5 *E*/*Z* ratio (entry 12). When the amount of *t*-Bu XPhos was increased to 40 mol%, a better *E*/*Z* stereoselectivity (*E*/*Z* ratio = 1:2.9) was obtained but the yield dropped slightly to 73% (entry 13). The addition of water (40 mol%)[12] gave mediocre results in both yield and stereoselectivity (81% yield, *E*/*Z* ratio = 1:2.6; entry 14).

Table 1. Optimization of Reaction Conditions[a]



Entry	Ligand	Temp. (°C)	Time (h)	Yield (%)[b] 8	Yield (%)[b] 9	*E*:*Z* Ratio[c] of **9**
1	PPh_3	150	10	-	97	>20:1
2	PPh_3	130	10	-	85	1.4:1
3	PPh_3	130	20	-	95	2.9:1
4	PPh_3	120	10	17	67	1:2.5
5	PPh_3	120	20	9	78	1:1.4
6	PPh_3	110	10	46	44	1.2.7
7	PPh_3	110	20	29	58	1:3.2
8	P(*o*-tol)$_3$	110	20	43	30	1:2.7
9	Xantphos	110	20	38	57	1:1.3
10	Cy JohnPhos	110	20	68	30	1:2.0
11	*t*-Bu XPhos	110	20	15	75	1:2.0
12	*t*-Bu XPhos	120	5	8	85	1:2.5
13[d]	*t*-Bu XPhos	120	5	8	73	1:2.9
14[e]	*t*-Bu XPhos	120	5	11	81	1:2.8

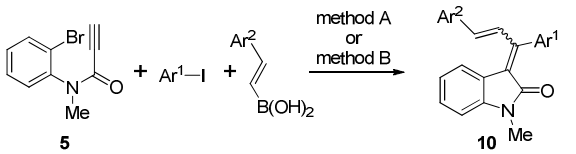


[a]Reaction conditions: **5** (0.2 mmol), PhI (1.1 eq), (*E*)-styrylboronic acid (1.2 eq), $Pd(PPh_3)_4$ (10 mol%), ligand (30 mol%), CuI (5 mol%), NaOAc (3.0 eq), Ag_3PO_4 (1.1 eq), DMF (5.0 mL). [b]Isolated yield. [c]Ratio was determined by ^{1}H NMR of crude product; each stereoisomer could be separated. [d]40 mol% of *t*-Bu XPhos was used. [e]40 mol% of H_2O was added.

Based on the results of Table 1, we chose two reaction conditions for the synthesis of each (*3E*)- and (*3Z*)-3-(diarylallylidene)oxindole (method A for the (*3E*)-isomer, Table 1, entry 1; method B for the (*3Z*)-isomer, Table 1, entry 13). The substrate scopes of those two methods were investigated with various aryl iodides and 2-arylvinylboronic acids (Table 2). First, the efficiencies of our reaction conditions for the synthesis of (*3E*)-3-(diarylallylidene)oxindoles (method A) were tested. The reaction with a combination of phenyl iodide and 4-chlorostyrylboronic acid under method A conditions afforded the oxindole **10a** with a 92% yield and a high stereoselectivity (*E*/*Z* ratio = >20:1; entry 1). Styrylboronic acid with a 4-MeO substituent was a less suitable reagent for this type of tandem reaction, which needed an increase in the amount of boronic acid (1.5 eq) used to provide **8b** in a moderate yield and stereoselectivity (66% yield, *E*/*Z* ratio = 9:1; entry 2). Under method A conditions, 4-chlorophenyl iodide gave a moderate yield (67–72%) and *E*/*Z* ratio (10–15:1) regardless of the 2-arylvinylboronic acid used (entries 4–6). Both 4-nitrophenyl iodide and 4-methoxyphenyl iodide gave excellent stereoselectivity (*E*/*Z* ratio = >20:1) in reactions with all three 2-arylvinylboronic acids (entries 7–11). However, generally, reactions of 4-nitrophenyl iodide gave slightly better yield than those of 4-methoxyphenyl iodide. Next, we screened the substrate scope of method B, which was devised for a more challenging target, (*3Z*)-3-(diarylallylidene)oxindoles. Under standard conditions of method B, (4-chlorostyryl)boronic acid produced an oxindole **10a** with an 80% yield and a moderate *E*/*Z* ratio (1:2.2; entry 12). (4-

Methoxystyryl)boronic acid needed further modifications, including an increased amount of boronic acids (1.5 eq), the addition of water (40 mol%), and a longer reaction time (10 min) to produce **10b** in a 59% yield with a 1:2.5 *E*/*Z* ratio (entry 13). The reaction of 4-chlorophenyl iodide and styrylboronic acid (1.5 eq) gave a good yield (82%) and *E*/*Z* ratio (1:3.6; entry 14). (4-Chlorostyryl)boronic acid gave 82% yield and a 1:2 *E*/*Z* ratio in the reaction with 4-chlorophenyl iodide (entry 15). The less-reactive (4-methoxystyryl)boronic acid required an increase in the amount used (1.5 eq) and the aid of water to obtain a moderate yield (57%) with 1:3.6 *E*/*Z* ratio (entry 16). Reactions of 4-nitrophenyl iodide with three 2-arylvinylboronic acids provided moderate *E*/*Z* ratios (1:1.9–3.3) in moderate to good yields (51–91%; entries 17–19). Despite extensive efforts to find the right conditions for high stereoselectivity, the reactions of 4-methoxyphenyl iodide with all three 2-arylvinylboronic acids gave slightly lower stereoselectivity (*E*/*Z* ratio = 1:1.2–1.6) in moderate yields (51–91%; entries 20–22). Similar low stereoselectivity from 4-methoxyphenyl iodide was observed in our previous work on the synthesis of 3-(diarylmethylene)oxindoles, which was presumably due to the rapid isomerization of the vinylpalladium intermediate bearing the 4-methoxy substituent.[8]

Table 2. Substrate Scope of the Reaction[a]

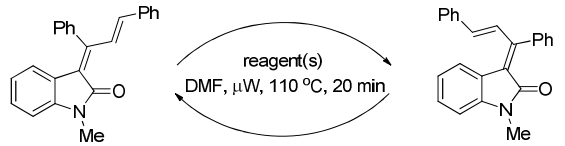


Entry	Ar^1	Ar^2	10	Method	Yield[b] (%)	*E*:*Z* Ratio[c]
1	Ph	4-Cl-C_6H_4	**10a**	A	92	>20:1
2	Ph	4-MeO-C_6H_4	**10b**	A[d]	66	9:1
3	4-Cl-C_6H_4	Ph	**10c**	A	72	10:1
4	4-Cl-C_6H_4	4-Cl-C_6H_4	**10d**	A	69	15:1
5	4-Cl-C_6H_4	4-MeO-C_6H_4	**10e**	A	67	10:1
6	4-NO_2-C_6H_4	Ph	**10f**	A	85	>20:1
7	4-NO_2-C_6H_4	4-Cl-C_6H_4	**10g**	A	83	>20:1
8	4-NO_2-C_6H_4	4-MeO-C_6H_4	**10h**	A	63	>20:1
9	4-MeO-C_6H_4	Ph	**10i**	A	79	>20:1
10	4-MeO-C_6H_4	4-Cl-C_6H_4	**10j**	A	61	>20:1
11	4-MeO-C_6H_4	4-MeO-C_6H_4	**10k**	A	54	>20:1
12	Ph	4-Cl-C_6H_4	**10a**	B	80	1:2.5
13	Ph	4-MeO-C_6H_4	**10b**	B[d,e,f]	59	1:2.5
14	4-Cl-C_6H_4	Ph	**10c**	B[d]	82	1:3.6
15	4-Cl-C_6H_4	4-Cl-C_6H_4	**10d**	B	82	1:2
16	4-Cl-C_6H_4	4-MeO-C_6H_4	**10e**	B[d,e]	57	1:3.6
17	4-NO_2-C_6H_4	Ph	**10f**	B	64	1:3.6
18	4-NO_2-C_6H_4	4-Cl-C_6H_4	**10g**	B[f]	91	1:2
19	4-NO_2-C_6H_4	4-MeO-C_6H_4	**10h**	B[f]	51	1:1.9
20	4-MeO-C_6H_4	Ph	**10i**	B	63	1:1.2
21	4-MeO-C_6H_4	4-Cl-C_6H_4	**10j**	B[g]	80	1:1.6
22	4-MeO-C_6H_4	4-MeO-C_6H_4	**10k**	B[d]	69	1:1.3

[a]Reagents and conditions for method A: **5** (0.2 mmol), Ar^1I (1.1 eq), (*E*)-2-Ar^2-vinylboronic acid (1.2 eq), $Pd(PPh_3)_4$ (10 mol%), PPh_3 (30 mol%), CuI (5 mol%), NaOAc (3.0 eq), Ag_3PO_4 (1.1 eq), DMF, microwave irradiation, 150 °C, 10 min. Method B: **5** (0.2 mmol), Ar^1I (1.1 eq), (*E*)-2-Ar^2-vinylboronic acid (1.2 eq), $Pd(PPh_3)_4$ (10 mol%), *t*-Bu XPhos (40 mol%), CuI (5 mol%), NaOAc (3.0 eq), Ag_3PO_4 (1.1 eq), DMF, microwave irradiation, 120 °C, 5 min. [b]Isolated yield. [c]Ratio was determined by ^1H NMR of the crude product; each regioisomer could be separated. [d]1.5 equiv of (*E*)-2-Ar^2-vinylboronic acid was used. [e]40 mol% of H_2O was added. [f]Reaction was run for 10 min. [g]Reaction was run at 100 °C for 10 min.

In order to better understand the isomerization mechanism, we examined the isomerization rate of pure (*3E*)- and (*3Z*)-**9** under several reaction conditions (Table 3). First, the reactions of each (*3E*)- and (*3Z*)-**9** were run with all reagents of method B at 100 °C for 20 min. Very small amounts (2%) of (*3E*)-**9** were transformed into (*3Z*)-**9** under these conditions (entry 1), and (*3Z*)-**9** showed a relatively high conversion rate (66%) (entry 2). These results are consistent with the fact that the (*E*)-isomer's ratio was increased with longer reaction times and higher temperatures. Even without any reagent, the conversion from the (*Z*)- to (*E*)-isomer occurred at a 14% rate (entry 3). Yamamoto and coworkers reported that the *E*/*Z* isomerization of 3-(propynylidene)oxindole using a palladium-catalyzed reaction was mainly facilitated by a phosphine ligand.[13] However, there was no additional enhancement of the isomerization by PPh_3 and *t*-Bu XPhos in our reaction (entries 4 and 5). Both silver additive (Ag_3PO_4) and base (NaOAc) showed negligible effect on isomerization (entries 6 and 7). CuI gave a relatively high rate of conversion (58%) considering the small amount (5 mol%) of addition (entry 8). Under the reaction with palladium catalyst ($Pd(PPh_3)_4$), (*3Z*)-**9** was almost completely transformed into (*3E*)-**9** (entry 9). All of the above results imply that the major contributors to isomerization in the reaction are $Pd(PPh_3)_4$ and CuI. Since both Pd and Cu are able to coordinate to multiple π-systems, isomerization might proceed via metal chelation to a dienone system of 3-allylideneoxindoles.[14,15]

Table 3. *E*/*Z* Isomerization Study



(*3E*)-**9** (*3Z*)-**9**

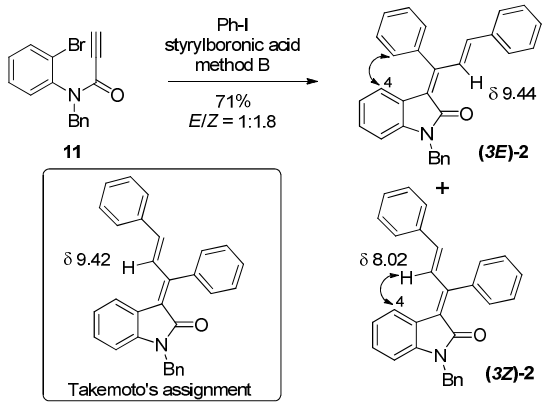
Entry	Starting material	Reagent(s)	Conversion Rate (%)[a]
1	(3*E*)-**9**	reagents for method B[b]	2
2	(3*Z*)-**9**	reagents for method B[b]	66
3	(3*Z*)-**9**	none	14
4	(3*Z*)-**9**	PPh_3 (40 mol%)	14
5	(3*Z*)-**9**	*t*-Bu XPhos (40 mol%)	14
6	(3*Z*)-**9**	Ag_3PO_4 (1.2 eq)	16
7	(3*Z*)-**9**	NaOAc (3.0 eq)	31
8	(3*Z*)-**9**	CuI (5 mol%)	58
9	(3*Z*)-**9**	$Pd(PPh_3)_4$ (10 mol%)	98

[a]Rate was determined by ^{1}H NMR of the crude mixture. [b]$Pd(PPh_3)_4$ (10 mol%), $Pd(PPh_3)_4$ (10 mol%), *t*-Bu XPhos (40 mol%), CuI (5 mol%), NaOAc (3.0 eq), Ag_3PO_4 (1.2 eq).

NMR analysis performed for structural elucidation of all the products revealed that the vinyl protons near the oxindole ring have a certain range of chemical shifts in ^{1}H NMR spectroscopy for each (*3E*)- and (*3Z*)-isomer. The vinyl protons of the (*3E*)-isomers are found in the range of 9.23–9.39 ppm, whereas those of the (*3E*)-isomers are in the range of 7.82–8.02 ppm. Although the chemical shift (9.32 ppm) for

the vinyl proton of (*3E*)-**4** in Murakami's spectral data is very similar to our own observations, Takemoto's data (9.42 ppm) for (*3Z*)-**2** is out of range and seems likely to be that of the (*3E*)-isomer. To resolve the structural ambiguity of **2**, we decided to prepare two stereoisomers of **2** using our tandem reaction (Scheme 2). The reaction of *N*-Bn propiolamide **11** with phenyl iodide and styrylboronic acid under method B conditions provided 3-(1,3-diphenylallylidene)oxindole **2** in a 71% yield with a 1:1.8 *E*/*Z* ratio. The structure of each isomer was elucidated by a detailed 2D NMR study including HSQC, HMBC, COSY, and ROESY experiments. The *E*/*Z* stereochemistry of **2** was found by looking for a correlation between the proton at the 4-position and one of protons around each side in the ROESY data, which is depicted in Scheme 2. Comparing the entirety of the spectral data led us to conclude that the compound, which was originally assigned by Takemoto as (*3Z*)-**2**, is actually (*3E*)-**2**. Thus, our tandem reaction is the first general method to make (*3Z*)-(diarylallylidene)oxindoles.

Scheme 2. Synthesis and NMR Analysis of 2[a]



[a]Reagents and conditions: Method B: **11** (0.2 mmol), PhI (1.1 eq), (*E*)-styrylboronic acid (1.2 eq), $Pd(PPh_3)_4$ (10 mol%), *t*-Bu XPhos (40 mol%), CuI (5 mol%), NaOAc (3.0 eq), Ag_3PO_4 (1.2 eq), DMF, microwave irradiation, 120 °C, 5 min.

In conclusion, various 3-(1,3-diarylallylidne)oxindoles could be synthesized by a palladium-catalyzed three-component tandem reaction from simple propiolamide, aryl iodide, and 2-arylvinylboronic acid with a short reaction time (up to 10 min) by the assistance of microwave irradiation. A stereoselective approach for each (3*E*)- or (3*Z*)-isomer is even possible by simple changes of the phosphine ligand, reaction time, and reaction temperature. (*3E*)-Isomers could be obtained in excellent stereoselectivity with PPh_3 at high temperatures. Reaction with *t*-Bu XPhos at lower temperatures gave (*3Z*)-isomers with moderate stereoselectivity.

■ Experimental Section

1. General information

Microwave reactions were conducted in a microwave reactor (Biotage Initiator^{+}). All reactions were performed under an argon atmosphere with dry solvents unless otherwise stated. Dry tetrahydrofuran (THF) was obtained using a solvent purification system. Other dry solvents were purchased as anhydrous grade. All commercially available reagents were purchased and used without further purification. Reactions were monitored by thin-layer chromatography (TLC) on silica gel plates using UV light, PMA (an ethanolic solution of phosphomolybdic acid), or ANIS (an ethanolic solution of *para*-anisaldehyde) as a visualizing agent. Purification of products was conducted by column chromatography through silica gel. NMR spectra were obtained at 500 MHz using residual undeuterated solvent or TMS (tetramethylsilane) as an internal reference. High-resolution mass spectra (HR-MS) were recorded with EI (electron impact) method on a quadrupole mass spectrometer.

2. Experimental procedures and spectroscopic data analysis

General procedure for preparation of *N*-alkylpropiolamides

To a stirred suspension of NaH (44 mg, 60% in mineral oil, 1.1 mmol, 1.1 equiv) in THF (5.0 mL) was added a solution of *N*-(2-bromophenyl)propiolamide[7] (224 mg, 1.0 mmol) in THF (5 mL) at 0 °C. After 30 min stirring, MeI (0.08 mL, 1.3 mmol, 1.3 equiv) or BnBr (0.14 mL, 1.2 mmol, 1.2 equiv) was added dropwise at the same temperature. Then, the temperature was gradually raised to 25 °C. The mixture was stirred for 6 h at 25 °C and diluted with sat. aq. NH_4Cl (50 mL). The mixture was extracted with EtOAc (50 mL x 2). The combined organic layer was dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography (silica gel, hexanes:EtOAc 5:1) to yield *N*-alkylpropiolamides **5** or **11**.

***N*-(2-bromophenyl)-*N*-methylpropiolamide (5)**:[4a] 89% Yield; off white solid; mp = 72.8 °C (lit.[4a] 88-89 °C); R_f = 0.32 (silica gel, hexanes:EtOAc 4:1); IR (film) 3221, 2107, 1646, 1372, 763 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, 7:1 atropisomeric mixture, major peaks): δ 7.68 (dd, J = 8.0, 1.0 Hz, 1H), 7.41–7.21 (m, 3H), 3.25 (s, 3H), 2.73 (s, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 153.3, 141.7, 133.9, 133.8, 130.5, 130.4, 129.9, 129.3, 128.9, 128.8, 123.8, 80.0, 78.9, 76.1, 39.0, 35.4 ppm; HRMS (ESI-TOF): calcd for $C_{10}H_8{}^{79}BrNO$ [M + H$^+$]: 237.9868, found 237.9872.

***N*-benzyl-*N*-(2-bromophenyl)propiolamide (11)**: White solid; mp = 52.5 °C; R_f = 0.3 (silica gel, hexanes:EtOAc 5:1); IR (film) 3214, 3064, 2106, 1640, 722, 697, 697 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500MHz) δ

7.67 (dd, J =7.8, 1.8 Hz, 1H), 7.28–7.26 (m, 3H), 7.24–7.19 (m, 4H), 6.84 (dd, J = 12.9, 6.9 Hz, 1H), 5.58 (d, J = 14.3 Hz, 1H), 4.16 (d, J =14.1 Hz, 1H), 2.73 (s, 1H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 153.3, 139.7, 136.0, 133.7, 132.1, 130.4, 129.6, 128.9, 128.8, 128.7, 128.1, 128.0, 124.2, 79.2, 76.2, 51.2; HRMS (EI): calcd for $C_{16}H_{12}BrNO$ [M^+]: 313.0102, found 313.0099.

General procedures for palladium-catalyzed tandem reaction

A microwave reaction vial was charged with *N*-methylpropiolamide **5** (47.6 mg, 0.20 mmol, 1.0 equiv), aryliodide (0.22 mmol, 1.1 equiv), 2-arylvinylboronic acid (0.24 mmol, 1.2 equiv), CuI (1.9 mg, 0.01 mmol, 5 mol%), NaOAc (49 mg, 0.6 mmol, 3.0 equiv), $Pd(PPh_3)_4$ (23.3 mg, 0.02 mmol, 10 mol%), phosphine ligand (method A: PPh_3 (15.7 mg, 0.06 mmol, 30 mol%), method B: *t*-Bu XPhos (33.9 mg, 0.08 mmol, 40 mol%), Ag_3PO_4 (92.1 mg, 0.22 mmol, 1.1 equiv) and DMF (2 mL). The reaction vial was sealed and then exposed to microwave irradiation under conditions with a set time and temperature. The mixture was cooled to 25 °C and diluted with EtOAc (50 mL). The organic layer was washed with H_2O (30 mL x 3) and brine (30 mL), and then dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography (silica gel, hexane:EtOAc) to yield Sonogashira adduct **8** and 3-(1,3-diarylallylidene)oxindoles **9** or **10**.

***N*-(2-bromophenyl)-*N*-methyl-3-phenylpropiolamide (8)**:[16] white solid; mp = 93.9 °C; R_f = 0.24 (silica gel, hexanes:EtOAc 4:1); IR (film) 2217, 1644, 1583, 1477, 1442, 1361, 1312, 1131, 1027, 933, 759 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, 10:1 atropisomeric mixture, major peaks): δ 7.72 (dd, J = 8.0, 1.5 Hz, 1H), 7.43–7.41 (m, 2H), 7.33–7.29 (m, 2H), 7.22 (t, J = 7.5 Hz, 2H), 7.08 (dd, J = 8.3, 1.3 Hz, 1H), 3.32 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 154.6, 142.3, 133.9, 133.7, 132.7, 132.6, 130.8, 130.2, 130.1, 128.9, 128.7, 128.4, 124.1, 120.4, 90.6, 82.3, 39.8, 35.3 ppm; HRMS (ESI-TOF): calcd for $C_{16}H_{12}{}^{79}BrNO$ [M + H^+]: 314.0181, found 314.0186.

(*E*)-3-((*E*)-1,3-diphenylallylidene)-1-methylindolin-2-one ((*3E*)-9): Yellow solid; mp = 125.7 °C; R_f = 0.4 (silica gel, hexanes:EtOAc 4:1); IR (film) 3055, 2957, 1678, 1089, 786, 692, 544 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.38 (d, J = 16.0 Hz, 1H), 7.55–7.51 (m, 5H), 7.33–7.25 (m, 5H), 7.08 (td, J = 8.2, 7.6 Hz, 1H), 6.74 (d, J = 7.8 Hz, 1H), 6.60 (t, J = 7.7 Hz, 1H), 6.47 (d, J = 16.0 Hz, 1H), 5.72 (d, J = 7.8 Hz, 1H), 3.3 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.1, 151.2, 142.9, 141.6, 137.8, 136.9, 129.3, 129.2, 128.8, 128.7, 128.6, 128.3, 128.0, 127.7, 123.7, 123.4, 122.6, 121.6, 107.6, 25.9 ppm; HRMS (EI): calcd for $C_{24}H_{19}NO$ [M^+]: 337.1467, found 337.1466.

(*Z*)-3-((*E*)-1,3-diphenylallylidene)-1-methylindolin-2-one ((*3Z*)-9): Yellow solid; mp = 153.5 °C; R_f = 0.3 (silica gel, hexanes:EtOAc 4:1); IR (film) 3368, 3052, 2928, 1691, 1096, 689, 540 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.01 (d, J = 15.8 Hz, 1H), 7.75 (d, J = 7.6 Hz, 1H), 7.5–7.47 (m, 5H), 7.39 (t, J =

7.3 Hz, 2H), 7.35–7.30 (m, 4H), 7.11 (td, *J* = 7.7, 1.0 Hz, 1H), 6.85 (d, *J* = 7.7 Hz, 1H), 6.62 (d, *J* = 15.7 Hz, 1H), 3.16 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.1, 150.6, 143.7, 142.9, 138.0, 136.5, 129.7, 129.5, 129.1, 128.8, 128.7, 128.5, 128.3, 127.7, 124.6, 123.6, 123.5, 121.9, 108.1, 25.9 ppm; HRMS (EI): calcd for $C_{24}H_{19}NO$ [M^+]: 337.1467, found 337.1466.

(*E*)-3-((*E*)-3-(4-chlorophenyl)-1-phenylallylidene)-1-methylindolin-2-one ((*3E*)-10a): Yellow solid; mp = 123.2 °C; R_f = 0.32 (silica gel, hexanes:EtOAc 8:1); IR (film) 3044, 2930, 1681, 1484, 1086, 811, 746, 720, 544 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.36 (d, *J* = 16 Hz, 1H), 7.57–7.53 (m, 3H), 7.44 (dt, *J* = 13.3, 2.3 Hz, 2H), 7.29–7.26 (m, 4H), 7.10 (td, *J* = 7.7, 1.1 Hz, 1H), 6.75 (d, *J* = 7.7 Hz, 1H), 6.59 (td, *J* = 7.7, 1.0 Hz, 1H), 6.40 (d, *J* = 16.0 Hz, 1H), 5.72 (d, *J* = 7.8 Hz, 1H), 3.30 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.1, 150.8, 143.0, 139.9, 137.5, 135.5, 134.8, 129.4, 129.1, 129.0, 128.7, 128.6, 128.5, 128.2, 123.8, 123.3, 123.0, 121.7, 170.7, 25.9 ppm; HRMS (EI): calcd for $C_{24}H_{18}ClNO$ [M^+]: 371.1077, found 371.1077.

(*Z*)-3-((*E*)-3-(4-chlorophenyl)-1-phenylallylidene)-1-methylindolin-2-one ((*3Z*)-10a): Yellow solid; mp = 162.0 °C; R_f = 0.2 (silica gel, hexanes:EtOAc 4:1); IR (film) 3376, 3053, 2946, 1696, 1093, 816, 770, 741, 544cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.96 (d, *J* = 15.8 Hz, 1H), 7.72 (d, *J* = 7.6 Hz, 1H), 7.49–7.47 (m, 3H), 7.41 (d, *J* = 8.5, 2H), 7.36–7.28 (m, 5H), 7.11 (td, 7.6, 1.0 Hz, 1H), 6.8 (d, *J* = 7.7 Hz, 1H), 6.55 (d, *J* = 15.8 Hz, 1H), 3.15 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.1, 150.1, 143.8, 141.3, 137.9, 135.3, 135.1, 129.7, 129.3, 129.2, 129.0, 128.8, 128.6, 128.3, 124.6, 124.0, 123.2, 122.0, 108.2, 25.9 ppm; HRMS (EI): calcd for $C_{24}H_{18}ClNO$ [M^+]: 371.1077, found 371.1081.

(*E*)-3-((*E*)-3-(4-methoxyphenyl)-1-phenylallylidene)-1-methylindolin-2-one ((*3E*)-10b): Yellow solid; mp = 135.5 °C; R_f = 0.2 (silica gel, hexanes:EtOAc 5:1); IR (film) 3053, 2838, 1249, 1023, 747, 694 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.27 (d, *J* = 16.0 Hz, 1H), 7.55–7.52 (m, 3H), 7.48 (d, *J* = 8.7 Hz, 2H), 7.28–7.27 (m, 2H), 7.08 (td, *J* = 7.7, 1.1 Hz, 1H), 6.84 (dt, *J* = 14.3, 2.9 Hz, 2H), 6.75 (d, *J* = 7.7 Hz, 1H), 6.59 (td, *J* = 7.7, 1.0 Hz, 1H), 6.44 (d, *J* = 16 Hz, 1H), 5.70 (d, *J* = 7.7 Hz, 1H), 3.82 (s, 3H), 3.30(s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.2, 160.7, 151.9, 142.7, 141.5, 137.9, 129.9, 129.6, 129.3, 128.7, 128.5, 128.0, 125.7, 123.6, 123.5, 121.5, 114.3, 107.5, 55.5, 29.8, 25.9 ppm; HRMS (EI): calcd for $C_{25}H_{21}NO_2$ [M^+]: 367.1572, found 367.1572.

(*Z*)-3-((*E*)-3-(4-methoxyphenyl)-1-phenylallylidene)-1-methylindolin-2-one ((*3Z*)-10b): Yellow solid; mp = 167.7 °C; R_f = 0.2 (silica gel, hexanes:EtOAc 4:1); IR (film) 3055, 2989, 2840, 1683, 1557, 1252, 827, 744 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.89 (d, *J* = 15.7 Hz, 1H), 7.76 (d, *J* = 7.6 Hz, 1H), 7.50–7.44 (m, 5H), 7.31–7.29 (m, 3H), 7.10 (td, *J* = 7.7, 0.6 Hz, 1H), 6.92 (d, *J* = 8.7 Hz, 2H), 6.84 (d, *J* = 7.7 Hz, 1H), 6.58 (d, *J* = 15.7 Hz, 1H), 3.85 (s, 3H), 3.16 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.2, 160.9, 151.2, 143.5, 142.7, 138.2, 129.7, 129.6, 129.3, 128.4, 128.3, 128.2, 126.5, 124.3, 123.5, 122.5, 121.8, 114.5, 108.0, 55.5, 25.9 ppm; HRMS (EI): calcd for $C_{25}H_{21}NO_2$ [M^+]: 367.1572, found 367.1571.

(*E*)-3-((*E*)-1-(4-chlorophenyl)-3-phenylallylidene)-1-methylindolin-2-one ((*3E*)-10c): Yellow solid; mp = 178.2 °C; R_f = 0.3 (silica gel, hexanes:EtOAc 6:1); IR (film) 3058, 2930, 1680, 1469, 1085, 745, 544 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 9.37 (d, *J* = 16.1 Hz, 1H), 7.56–7.53 (m, 4H), 7.33 (t, *J* = 7.3 Hz, 2H), 7.29 (d, *J* = 7.1 Hz, 1H), 7.24 (dt, *J* = 12.8, 2.2 Hz, 2H), 7.13 (td, *J* = 7.7, 1.0 Hz, 1H), 6.76 (d, *J* = 7.7 Hz, 1H), 6.66 (td, *J* = 7.7, 0.9 Hz, 1H), 6.43 (d, *J* = 16.1 Hz, 1H), 5.86 (d, *J* = 7.7 Hz, 1H), 3.29 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.9, 149.6, 143.0, 141.4, 136.8, 136.1, 134.6, 130.3, 129.7, 129.3, 128.9, 128.6, 128.0, 127.5, 123.5, 123.1, 122.8, 121.7, 107.8, 25.9 ppm; HRMS (EI): calcd for $C_{24}H_{18}ClNO$ [M^+]: 371.1077, found 371.1078.

(*Z*)-3-((*E*)-1-(4-chlorophenyl)-3-phenylallylidene)-1-methylindolin-2-one ((*3Z*)-10c): Yellow solid; mp = 152.6 °C; R_f = 0.2 (silica gel, hexanes:EtOAc 6:1); IR (film) 3391, 3051, 2929, 1701, 1082, 747, 695, 542 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.97 (d, *J* = 15.8 Hz, 1H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.50 (d, *J* = 7.2 Hz, 2H), 7.45 (dt, *J* = 13.1, 2.2 Hz, 2H), 7.41–7.35 (m, 3H), 7.31 (td, *J* = 15.4, 0.9 Hz, 1H), 7.24 (t, *J* = 13.3, 2.3 Hz, 2H), 7.11 (td, *J* = 7.7, 0.9 Hz, 1H), 6.85 (d, *J* = 7.7 Hz, 1H), 6.59 (d, *J* = 15.8 Hz, 1H), 3.16 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.1, 149.1, 143.7, 142.9, 136.4, 136.3, 134.5, 131.2, 129.7, 129.1, 129.0, 128.6, 128.4, 127.8, 124.6, 123.8, 123.1, 122.1, 108.2, 25.9 ppm; HRMS (EI): calcd for $C_{24}H_{18}ClNO$ [M^+]: 371.1077, found 371.1077.

(*E*)-3-((*E*)-1,3-bis(4-chlorophenyl)allylidene)-1-methylindolin-2-one ((*3E*)-10d): Yellow solid; mp = 193.0 °C; R_f = 0.27 (silica gel, hexanes:EtOAc 8:1); IR (film) 3063, 2925, 1683, 1485, 1085, 738, 545 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 9.33 (d, *J* = 16.1 Hz, 1H), 7.55 (d, *J* = 8.3 Hz, 2H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 8.3 Hz, 2H), 7.15 (t, *J* = 7.7 Hz, 1H), 6.76 (d, *J* = 7.8 Hz, 1H), 6.67 (t, *J* = 7.7 Hz, 1H), 6.35 (d, *J* = 16.1 Hz, 1H), 5.86 (d, *J* = 7.7 Hz, 1H), 3.28 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.9, 167.2, 163.1, 139.7, 135.9, 135.3, 135.0, 134.8, 130.3, 129.8, 129.1, 128.8, 128.0, 123.7, 123.2, 123.0, 121.8, 107.8, 25.9 ppm; HRMS (EI): calcd for $C_{24}H_{17}Cl_2NO$ [M^+]: 405.0687, found 405.0689.

(*Z*)-3-((*E*)-1,3-bis(4-chlorophenyl)allylidene)-1-methylindolin-2-one ((*3Z*)-10d): Yellow solid; mp = 171.8 °C; R_f = 0.28 (silica gel, hexanes:EtOAc 5:1); IR (film) 3377, 3063, 1695, 1083, 812, 739, 544 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.93 (d, *J* = 15.8 Hz, 1H), 7.70 (d, *J* = 7.7 Hz, 1H), 7.44 (dt, *J* = 13.2, 2.2 Hz, 2H), 7.42 (d, *J* = 8.5 Hz, 2H), 7.36 (d, *J* = 8.6 Hz, 2H), 7.31 (td, *J* = 7.8, 1.0 Hz, 1H), 7.22 (dt, *J* = 13.2, 2.2 Hz, 2H), 7.11 (td, *J* = 7.7, 1.0 Hz, 1H), 6.85 (d, *J* = 7.7 Hz, 1H), 6.53 (d, *J* = 15.8 Hz, 1H), 3.16 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.0, 148.6, 143.8, 141.3, 136.3, 135.5, 134.8, 134.6, 131.2, 129.4, 129.2, 128.9, 128.8, 128.7, 124.6, 124.2, 123.0, 122.1, 108.3, 25.9 ppm; HRMS (EI): calcd for $C_{24}H_{17}Cl_2NO$ [M^+]: 405.0687, found 405.0687.

(*E*)-3-((*E*)-1-(4-chlorophenyl)-3-(4-methoxyphenyl)allylidene)-1-methylindolin-2-one ((*3E*)-10e): Yellow solid; mp = 129.0 °C; R_f = 0.38 (silica gel, CH_2Cl_2:hexane 5:1); IR (film) 3056, 2929, 1681, 1252,

1171, 1085, 826, 744, 544 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 9.24 (d, *J* = 16 Hz, 1H), 7.53 (dt, *J* = 13.1, 2.2 Hz, 2H), 7.48 (d, *J* = 8.7 Hz, 2H), 7.22 (dt, *J* = 12.6, 2.1 Hz, 2H), 7.11 (td, *J* = 7.4, 1.1 Hz, 1H), 6.85 (dt, *J* = 14.4, 2.4 Hz, 2H), 6.76 (d, *J* = 7.7 Hz, 1H), 6.64 (td, *J* = 7.7, 1.0, 1H), 6.38 (d, *J* = 16 Hz, 1H), 5.83 (d, *J* = 7.5 Hz, 1H), 3.82 (s, 3H), 3.30 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.0, 160.8, 150.2, 142.8, 141.4, 136.4, 134.5, 130.3, 129.73, 129.65, 129.6, 128.3, 125.5, 123.3, 121.6, 114.4, 107.7, 55.5, 25.9. ppm; HRMS (EI): calcd for $C_{25}H_{20}ClNO_2$ [M^+]: 401.1183, found 401.1185.

(*Z*)-3-((*E*)-1-(4-chlorophenyl)-3-(4-methoxyphenyl)allylidene)-1-methylindolin-2-one ((*3Z*)-10e): Yellow solid; mp = 168.2 °C; R_f = 0.35 (silica gel, CH_2Cl_2:hexane 5:1); IR (film) 3351, 3060, 2927, 2775, 1682, 1258, 1172, 826, 744, 538 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.88 (d, *J* = 15.7Hz, 1H), 7.77 (d, *J* = 7.7 Hz, 1H), 7.48 (d, *J* = 8.4 Hz, 4H), 7.34 (t, *J* = 7.7 Hz, 1H), 7.28 (dd, *J* = 6.9, 0.9 Hz, 2H), 7.15 (t, *J* = 7.7 Hz, 1H), 6.95 (d, *J* = 8.2 Hz, 2H), 6.87 (d, *J* = 7.8 Hz, 1H), 6.57 (d, *J* = 15.7 Hz, 1H), 3.88 (s, 3H), 3.19 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.2, 161.1, 149.7, 143.6, 142.7, 136.6, 134.4, 131.2, 129.4, 129.2, 128.7, 128.6, 126.2, 124.4, 123.3, 122.7, 122.0, 114.6, 108.1, 55.6, 25.9 ppm; HRMS (EI): calcd for $C_{25}H_{20}ClNO_2$ [M^+]: 401.1183, found 401.1183.

(*E*)-1-methyl-3-((*E*)-1-(4-nitrophenyl)-3-phenylallylidene)indolin-2-one ((*3E*)-10f): Yellow solid; mp = 228.2 °C; R_f = 0.3 (silica gel, hexanes:EtOAc 3:1); IR (film) 3100, 2925, 1678, 1512, 1343, 1089, 747, 688, 544 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 9.39 (d, *J* = 16.2 Hz, 1H), 8.45 (d, *J* = 8.8 Hz, 2H), 7.53–7.50 (m, 4H), 7.35–7.30 (m, 3H), 7.15 (td, *J* = 7.7, 1.1 Hz, 1H), 6.78 (d, *J* = 7.7 Hz, 1H), 6.62 (td, *J* = 7.7, 1.0 Hz, 1H), 6.30 (d, *J* = 16.2 Hz, 1H), 5.70 (d, *J* = 7.5 Hz, 1H), 3.31 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.7, 148.1, 148.0, 144.7, 143.2, 141.5, 136.5, 130.2, 129.6, 129.2, 123.0, 128.0, 126.8, 124.8, 123.3, 122.9, 122.6, 121.9, 108.1, 26.0 ppm; HRMS (EI): calcd for $C_{24}H_{18}N_2O_3$ [M^+]: 382.1317, found 382.1318.

(*Z*)-1-methyl-3-((*E*)-1-(4-nitrophenyl)-3-phenylallylidene)indolin-2-one ((*3Z*)-10f): Yellow solid; mp = 233.0 °C; R_f = 0.2 (silica gel, hexanes:EtOAc 5:1); IR (film) 3367, 3048, 2884, 1689, 1342, 1098, 747, 688, 541 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 8.35 (d, *J* = 8.7, 2H), 8.00 (d, *J* = 15.9 Hz, 1H), 7.79 (d, *J* = 7.6 Hz, 1H), 7.49–7.46 (m, 4H), 7.42–7.34 (m, 4H), 7.14 (td, *J* = 7.7, 0.7 Hz, 1H), 6.87 (d, *J* = 7.8 Hz, 1H), 6.47 (d, *J* = 15.9 Hz, 1H), 3.15 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.0, 147.8, 147.2, 145.5, 144.1, 143.0, 136.0, 130.6, 130.0, 129.6, 129.2, 127.8, 127.3, 124.8, 124.3, 123.7, 122.5, 122.4, 108.5, 25.9 ppm; HRMS (EI): calcd for $C_{24}H_{18}N_2O_3$ [M^+]: 382.1317, found 382.1319.

(*E*)-3-((*E*)-3-(4-chlorophenyl)-1-(4-nitrophenyl)allylidene)-1-methylindolin-2-one ((*3E*)-10g): Yellow solid; mp = 249.5 °C; R_f = 0.34 (silica gel, hexanes:EtOAc 5:1); IR (film) 3100, 2923, 2852, 1678, 1342, 1085, 816, 742, 543 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 9.37 (d, *J* = 16.2 Hz, 1H), 8.44 (dt, *J* = 12.9, 2.3 Hz, 2H), 7.50 (dt, *J* = 13.0, 2.3 Hz, 2H), 7.43 (d, *J* = 8.5 Hz, 2H), 7.30 (d, *J* = 8.6 Hz, 2H), 7.15 (td, *J* = 7.7, 0.9 Hz, 1H), 6.78 (d, *J* = 7.8 Hz, 1H), 6.62 (td, *J* = 7.7, 0.8 Hz, 1H), 6.23 (d, *J* = 16.2 Hz, 1H), 5.71

(d, J = 7.7 Hz, 1H), 3.30 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.6, 148.2, 147.5, 144.4, 143.3, 139.8, 135.4, 135.0, 130.2, 129.4, 129.3, 129.2, 129.1, 128.3, 127.3, 127.1, 124.8, 124.3, 123.4, 123.3, 122.5, 122.0, 108.2, 26.0 ppm; HRMS (EI): calcd for $C_{24}H_{17}ClN_2O_3$ [M^+]: 416.0928, found 416.0928.

(*Z*)-3-((*E*)-3-(4-chlorophenyl)-1-(4-nitrophenyl)allylidene)-1-methylindolin-2-one ((*3Z*)-10g): Yellow solid; mp = 273.3 °C; R_f = 0.2 (silica gel, hexanes:EtOAc 5:1); IR (film) 3103, 2930, 1694, 1505, 1345, 1099, 817, 747, 543 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.34 (dt, J = 13.3, 2.2 Hz, 2H), 7.97 (d, J = 15.9 Hz, 1H), 7.75 (d, J = 7.6 Hz, 1H), 7.44 (dt, J = 13.3, 2.3 Hz, 2H), 7.42–7.34 (m, 5H), 7.14 (td, J = 7.7, 0.9 Hz, 1H), 6.87 (d, J = 7.8 Hz, 1H), 6.41 (d, J = 15.9 Hz, 1H), 3.15 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.9, 147.8, 146.7, 145.3, 144.2, 141.4, 135.8, 134.5, 130.5, 129.8, 129.5, 128.9, 127.8, 124.8, 124.6, 123.8, 122.4, 108.5, 26.0 ppm; HRMS (EI): calcd for $C_{24}H_{17}ClN_2O_3$ [M^+]: 416.0928, found 416.0928.

(*E*)-3-((*E*)-3-(4-methoxyphenyl)-1-(4-nitrophenyl)allylidene)-1-methylindolin-2-one ((*3E*)-10h): Yellow solid; mp = 197.0 °C; R_f = 0.23 (silica gel, hexanes:EtOAc 4:1); IR (film) 3100, 2928, 1675, 1509, 1343, 1253, 1088, 744, 542 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.27 (d, J = 16.2 Hz, 1H), 8.43 (dt, J = 13.0, 2.3 Hz, 2H), 7.50 (dt, J = 13, 2.3 Hz, 2H), 7.46 (d, J = 8.8 Hz, 2H), 7.13 (td, J = 7.7, 0.9 Hz, 1H), 6.9 (d, J = 8.8 Hz, 2H), 6.78 (d, J = 7.8 Hz, 1H), 6.60 (td, J = 7.7, 0.8 Hz, 1H), 6.26 (d, J = 16.2 Hz, 1H), 5.68 (,d J = 7.7 Hz, 1H), 3.82 (s, 3H), 3.30 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.8, 161.1, 148.6, 148.1, 144.9, 143.0, 141.4, 130.2, 129.7, 129.4, 128.8, 124.8, 124.7, 123.1, 122.8, 121.8, 121.7, 114.5, 108.0, 55.5, 25.9 ppm; HRMS (EI): calcd for $C_{25}H_{20}N_2O_4$ [M^+]: 412.1423, found 412.1422.

(*Z*)-3-((*E*)-3-(4-methoxyphenyl)-1-(4-nitrophenyl)allylidene)-1-methylindolin-2-one ((*3Z*)-10h): Yellow solid; mp = 191.4 °C; R_f = 0.2 (silica gel, hexanes:EtOAc 4:1); IR (film) 3367, 3072, 2838, 1687, 1507, 1345, 1253, 1173, 1098, 745, 542 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.34 (d, J = 8.7 Hz, 2H), 7.89 (d, J = 15.8 Hz, 1H), 7.79 (d, J = 7.6 Hz, 1H), 7.46–7.42 (m, 4H), 7.34 (t, J = 7.7 Hz, 1H), 7.15 (t, J = 7.6 Hz, 1H), 6.92 (d, J = 8.8 Hz, 2H), 6.86 (d, J = 7.8 Hz, 1H), 6.41 (d, J = 15.8 Hz, 1H), 3.85 (s, 3H), 3.14 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.1, 161.3, 147.8, 147.7, 145.7, 143.9, 142.9, 130.5, 129.5, 129.3, 128.8, 125.2, 124.6, 123.7, 123.1, 122.7, 122.3, 114.7, 108.4, 55.6, 25.9 ppm; HRMS (EI): calcd for $C_{25}H_{20}N_2O_4$ [M^+]: 412.1423, found 412.1423.

(*E*)-3-((*E*)-1-(4-methoxyphenyl)-3-phenylallylidene)-1-methylindolin-2-one ((*3E*)-10i): Yellow solid; mp = 153.6 °C; R_f = 0.3 (silica gel, hexanes:EtOAc 4:1); IR (film) 3069, 2929, 2834, 1685, 1242, 1088, 1028, 689, 545 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.36 (d, J = 16 Hz, 1H), 7.55 (d, J = 7.4 Hz, 2H), 7.32 (t, J = 7.4 Hz, 2H), 7.27 (d, J = 5.8 Hz, 1H), 7.21 (d, J = 8.5 Hz, 2H), 7.12 (t, J = 7.6 Hz, 1H), 7.08 (d, J = 8.5 Hz, 2H), 6.75 (d, J = 7.7 Hz, 1H), 6.65 (t, J = 7.6 Hz, 1H), 6.53 (d, J = 16 Hz, 1H), 5.92 (d, J = 7.7 Hz, 1H), 3.94 (s, 3H), 3.30 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.1, 159.8, 151.2, 142.8,

141.4, 137.0, 130.1, 129.9, 129.1, 128.8, 128.21, 128.19, 128.0, 123.64, 123.58, 122.8, 121.6, 114.7, 107.6, 55.5, 25.8 ppm; HRMS (EI): calcd for $C_{25}H_{21}NO_2$ [M^+]: 367.1572, found 367.1571.

(*Z*)-3-((*E*)-1-(4-methoxyphenyl)-3-phenylallylidene)-1-methylindolin-2-one ((*3Z*)-10i): Yellow solid; mp = 185.8 °C; R_f = 0.23 (silica gel, hexanes:EtOAc 3:1); IR (film) 3116, 2956, 1698, 1251, 1098, 747, 544 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.94 (d, *J* = 15.8 Hz, 1H), 7.68 (d, *J* = 7.6 Hz, 1H), 7.51 (d, *J* = 7.2 Hz, 2H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.36–7.32 (m, 1H), 7.30–7.28 (m, 3H), 7.09 (td, *J* = 7.6, 0.9 Hz, 1H), 7.00 (dt, *J* = 14.3, 2.9 Hz, 2H), 6.84 (d, *J* = 7.7 Hz, 1H), 6.70 (d, *J* = 15.7 Hz, 1H), 3.89 (s, 3H), 3.18 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.2, 160.2, 150.8, 143.4, 142.8, 136.6, 131.8, 129.9, 129.4, 129.3, 129.1, 128.5, 127.7, 124.5, 123.7, 123.2, 121.9, 113.6, 108.0, 55.4, 25.9 ppm; HRMS (EI): calcd for $C_{25}H_{21}NO_2$ [M^+]: 367.1572, found 367.1570.

(*E*)-3-((*E*)-3-(4-chlorophenyl)-1-(4-methoxyphenyl)allylidene)-1-methylindolin-2-one ((*3E*)-10j): Yellow solid; mp = 143.1 °C; R_f = 0.36 (silica gel, hexanes:EtOAc 5:1); IR (film) 3064, 2948, 1678, 1247, 1087, 751, 544 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 9.31 (d, *J* = 16.0 Hz, 1H), 7.45 (d, *J* = 8.5 Hz, 2H), 7.27 (d, *J* = 8.6 Hz, 2H), 7.19 (d, *J* = 8.6 Hz, 2H), 7.12 (t, *J* = 7.7 Hz, 1H), 7.07 (d, *J* = 8.6 Hz, 2H), 6.74 (d, *J* = 7.8 Hz, 1H), 6.65 (t, *J* = 7.8 Hz, 1H), 6.45 (d, *J* = 16.0 Hz, 1H), 5.92 (d, *J* = 7.7 Hz, 1H), 3.93 (s, 3H), 3.28 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.1, 159.9, 150.7, 142.9, 139.7, 135.6, 134.7, 130.1, 129.6, 129.04, 128.97, 128.7, 128.4, 123.7, 123.5, 123.2, 121.6, 114.7, 107.6, 55.5, 25.8 ppm; HRMS (EI): calcd for $C_{25}H_{20}ClNO_2$ [M^+]: 401.1185, found 401.1185.

(*Z*)-3-((*E*)-3-(4-chlorophenyl)-1-(4-methoxyphenyl)allylidene)-1-methylindolin-2-one ((*3Z*)-10j): Yellow solid; mp = 156.1 °C; R_f = 0.35 (silica gel, hexanes:EtOAc 5:1); IR (film) 3375, 3049, 2840, 1696, 1243, 1087, 830, 744, 547 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.90 (d, *J* = 15.8 Hz, 1H), 7.64 (d, *J* = 7.6 Hz, 1H), 7.43 (d, *J* = 8.6 Hz, 2H), 7.35 (dt, *J* = 13.1, 2.9 Hz, 2H), 7.29 (td, *J* = 7.7, 1.0 Hz, 1H), 7.26 (dt, *J* = 14.3, 2.3 Hz, 2H), 7.09 (td, *J* = 7.7, 1.0 Hz, 1H), 7.00 (dt, *J* = 14.3, 2.4 Hz, 2H), 6.84 (d, *J* = 7.7 Hz, 1H), 6.63 (d, *J* = 15.8 Hz, 1H), 3.89 (s, 3H), 3.17 (s, 3H)ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.2, 160.3, 150.3, 143.5, 141.2, 135.2, 135.1, 131.7, 129.79, 129.76, 129.3, 128.8, 128.7, 124.5, 123.6, 123.5, 121.9, 113.7, 108.1, 55.4, 25.9 ppm; HRMS (EI): calcd for $C_{25}H_{20}ClNO_2$ [M^+]: 401.1183, found 401.1183.

(*E*)-3-((*E*)-1,3-bis(4-methoxyphenyl)allylidene)-1-methylindolin-2-one ((*3E*)-10k): Yellow solid; mp = 131.7 °C; R_f = 0.21 (silica gel, hexanes:EtOAc 5:1); IR (film) 3066, 3051, 2835, 1686, 1241, 1087, 816, 745, 538 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 9.23 (d, *J* = 15.9 Hz, 1H), 7.49 (d, *J* = 8.8 Hz, 2H), 7.19 (dt, *J* = 13.9, 2.3 Hz, 2H), 7.09 (td, *J* = 7.7, 0.8 Hz, 1H), 7.06 (dt, *J* = 14.0, 2.4 Hz, 2H), 6.85 (d, *J* = 8.8 Hz, 2H), 6.74 (d, *J* = 7.7 Hz, 1H), 6.63 (td, *J* = 7.7, 0.8 Hz, 1H), 6.48 (d, *J* = 15.9 Hz, 1H), 5.89 (d, *J* = 7.7 Hz, 1H), 3.9 (s, 3H), 3.82 (s, 3H), 3.30 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.2, 160.6, 159.8,

151.8, 142.6, 141.3, 130.1, 130.0, 129.6, 127.9, 126.2, 123.8, 123.4, 121.8, 121.5, 114.6, 114.3, 107.5, 55.49, 55.46, 25.8 ppm; HRMS (EI): calcd for $C_{26}H_{23}NO_3$ [M^+]: 397.1678, found 397.1677.

(*Z*)-3-((*E*)-1,3-bis(4-methoxyphenyl)allylidene)-1-methylindolin-2-one ((*3Z*)-10k): Yellow solid; mp = 160.2 °C; R_f = 0.2 (silica gel, hexanes:EtOAc 3:1); IR (film) 3054, 2839, 1684, 1248, 1171, 830, 747, 546 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.82 (d, *J* = 15.7 Hz, 1H), 7.69 (d, *J* = 7.7 Hz, 1H), 7.46 (d, *J* = 8.5 Hz, 2H), 7.30–7.25 (m, 3H), 7.09 (t, *J* = 7.6 Hz, 1H), 7.00 (d, *J* = 7.4 Hz, 2H), 6.92 (d, *J* = 8.5 Hz, 2H), 6.83 (d, *J* = 7.8 Hz, 1H), 6.65 (d, *J* = 15.7 Hz, 1H), 3.89 (s, 3H), 3.85 (s, 3H), 3.17 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.3, 160.9, 160.1, 151.4, 143.2, 142.6, 131.7, 130.1, 129.4, 129.3, 128.2, 127.1, 124.3, 123.8, 122.2, 121.8, 114.6, 113.6, 107.9, 55.6, 55.4, 25.9 ppm; HRMS (EI): calcd for $C_{26}H_{23}NO_3$ [M^+]: 397.1678, found 397.1677.

(E)-1-benzyl-3-((E)-1,3-diphenylallylidene)indolin-2-one ((*3E*)-2): Yellow solid; mp = 174.2 °C; R_f = 0.35 (silica gel, hexanes:EtOAc 8:1); IR (film) 3728, 3064, 2917, 1675, 1174, 746, 684, 553 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 9.44 (d, *J* = 16.1 Hz, 1H), 7.58–7.52 (m, 5H), 7.38–7.27 (m, 10H), 6.99 (td, *J* = 7.7, 0.8 Hz, 1H), 6.48 (d, *J* = 7.8 Hz, 1H), 6.59 (t, *J* = 7.7 Hz, 1H), 6.52 (d, *J* = 16 Hz, 1H), 5.75 (d, *J* = 7.8 Hz, 1H), 5.04 (s, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.1, 151.7, 142.1, 141.9, 137.7, 136.9, 136.5, 129.4, 129.2, 128.9, 128.8, 128.7, 128.3, 128.1, 127.8, 127.6, 127.4, 126.6, 123.8, 123.5, 122.4, 121.7, 108.6, 43.5 ppm; HRMS (EI): calcd for $C_{30}H_{23}NO$ [M^+]: 413.1780, found 413.1780.

(*Z*)-1-benzyl-3-((*E*)-1,3-diphenylallylidene)indolin-2-one ((*3Z*)-2): Yellow solid; mp = 155.9 °C; R_f = 0.18 (silica gel, hexanes:EtOAc 8:1); IR (film) 3720, 3023, 2915, 1691, 1364, 1175, 746, 694, 556 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 8.02 (d, *J* = 15.8 Hz, 1H), 7.76 (d, *J* = 7.6 Hz., 1H), 7.51–7.49 (m, 5H), 7.41–7.35 (m, 5H), 7.29–7.26 (m, 4H), 7.24–7.21 (m, 1H), 7.17 (td, *J* = 7.7, 1 Hz, 1H), 7.06 (td, *J* = 7.6, 1 Hz, 1H), 6.72 (d, *J* = 7.7 Hz, 1H), 6.64 (d, *J* = 15.8 Hz, 1H), 4.88 (s, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.1, 151.0, 143.0, 142.8, 138.0, 136.5, 136.5, 129.9, 129.5, 129.1, 128.8, 128.7, 128.7, 128.6, 128.3, 127.8, 127.5, 127.4, 127.6, 123.5, 123.3, 122.0, 109.1, 43.5 ppm; HRMS (EI): calcd for $C_{30}H_{23}NO$ [M^+]: 413.1780, found 413.1780.

■ Associated content

Supporting information

The supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.#######

^1H, ^{13}C and 2D NMR spectra for new compounds (PDF)

■ Author information

Corresponding Author

E-mail: jaehongseo@catholic.ac.kr

Notes

The authors declare no competing financial interest

■ Acknowledgment.

This work was supported by supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT & Future Planning (NRF-2014R1A1A1038332), and Research Fund 2013 of The Catholic University of Korea

■ References

(1) (a) 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.; Shewchuk, L.; Veal, J. M.; Walker, D. H.; Kuyper, L. F. *J. Med. Chem.* **2001**, *44*, 4339. (b) Lai, J. Y. Q.; Cox, P. J.; Patel, R.; Sadiq, S.; Alous, D. J.; Thurairatnam, S.; Smith, K.; Wheeler, D.; Jagpal, S.; Praveen, S.; Fenton, G.; Harrison, T. K. P.; McCarthy, C.; Bamborough, P. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 3111. (c) Zhang, W.; Go, M.-L. *Bioorg. Med. Chem.* **2009**, *17*, 2077. (d) Huber, K.; Schemies, J.; Uciechowska, U.; Wagner, J. M.; Rumpf, T.; Lewrick, F.; Süss, R.; Sippl, W.; Jung, M.; Bracher, F. *J. Med. Chem.* **2010**, *53*, 1383. (e) Henise, J. C.; Taunton, J. *J. Med. Chem.* **2011**, *54*, 4133. (f) Eissenstat, M.; Guerassina, T.; Gulnik, S.; Afonina, E.; Silva, A. M.; Ludtke, D.; Yokoe, H.; Yu, B.; Erickson, J. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 5078. (g) Lv, K.; Wang, L.-L.; Zhou, X.-B.; Liu, M.-L.; Liu, H.-Y.; Zheng, Z.-B.; Li, S. *Med. Chem. Res.* **2013**, *22*, 1723. (h) Roth, G. J.; Binder, R.; Colbatzky, F.; Dallinger, C.; Schlenker-Herceg, R.; Hilberg, F.; Wollin, S.-L.; Kaiser, R. *J. Med. Chem.* **2015**, *58*, 1053.

(2) (a) Lin, S.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 1967. (b) Trost, B. M.; Cramer, N.; Bernsmann, H.; *J. Am. Chem. Soc.* **2007**, *129*, 3086. (c) Antonchick, A. P.; Gerding-Reimers, C.; Catarinella, M.; Schürmann, M.; Rreut, H.; Ziegler, S.; Rauh, D.; Waldmann, H. *Nat. Chem.* **2010**, *2*, 735. (d) Singh, A.; Roth, G. P. *Org. Lett.* **2011**, *13*, 2118.

(3) (a) Sasaki, E.; Miyoshi, K.; Nozawa, Y.; Kanda, A.; Nakano, K.; Yamasaki, Y.; Miyake, H.; Matsuura, N. *Pharmacology* **2001**, *63*, 17. (b) Yu, L.-F.; Li, Y.-Y.; Su, M.-B.; Zhang, M.; Zhang, W.; Zhang, L.-N.; Pang, T.; Zhang, R.-T.; Liu, B.; Li, J.-Y.; Li, J.; Nan, F.-J. *ACS Med. Chem. Lett.* **2013**, *4*, 475. (c) Pal, A.; Ganguly, a.; Ghosh, A.; Yousuf, M.; Rathore, B.; Banerjee, R.; Adhikari, S. *ChemMedChem* **2014**, *9*, 727.

(4) (a) Brunton, S. A.; Jones, K. *J. Chem. Soc*., *Perkin Trans. 1*, **2000**, 763. (b) Yanada, R.; Obika, S.; Oyama, M.; Takemoto, Y. *Org. Lett.* **2004**, *6*, 2825. (c) Yanada, R.; Obika, S.; Inokuma, T.; Yanada, K.; Yamashita, M.; Ohta, S.; Takemoto, Y. *J. Org. Chem.* **2005**, *70*, 6972. (d) Cheung, W. S.; Patch, R. J.; Player, M. R. *J. Org. Chem.* **2005**, *70*, 3741. (e) Miura, T.; Takahashi, Y.; Murakami, M. *Org. Lett.* **2007**, *9*, 5075. (f) Pinto, A.; Neuville, L.; Zhu, J. *Angew. Chem., Int. Ed.* **2007**, *46*, 3291. (g) Miura, T.; Toyoshima, T.; Takahashi, Y.; Murakami, M. *Org. Lett.* **2008**, *10*, 4887. (h) Yang, X.-H.; Li, K.; Song, R.-J.; Li, J.-H. *Eur. J. Org. Chem.* **2014**, 616.

(5) All precedent works for the synthesis of 2-(1,3-diarylallylidne)oxindoles were shown in a limited range as an application of synthetic methods for 3-(diarylmethylene)oxindoles.

(6) For synthesis of (non-diaryl)-substituted 3-(allylidene)oxindoles, see: (a) Arthuis, M.; Pontikis, R.; Florent, J.-C. *Tetrahedron Lett.* **2007**, *48*, 6397. (b) Muthusamy, S.; Azhagan, D. *Tetrahedron Lett.* **2011**, *52*, 6732. (c) Zhao, Y.-L.; Cao, Z.-Y.; Zeng, X.-P.; Shi, J.-M.; Yu, Y.-H.; Zhou, J. *Chem. Commun.* **2016**, *52*, 3943.

(7) Park, S.; Shin, K. J.; Seo, J. H. *Synlett* **2015**, *26*, 2296.

(8) Dong, G. R.; Park, S.; Lee, D.; Shin K. J.; Seo, J. H. *Synlett* **2013**, *24*, 1993.

(9) (a) Zargarian, D.; Alper, H. *Organometallics* **1993**, *12*, 712. (b) Cacchi, S.; Fabrizi, G,; Marinelli, F.; Moro, L.; Pace, P. *Tetrahedron Lett.* **1996**, *52*, 10225. (c) Amatore, C.; Bensalem, S.; Ghalem, S.; Jutand, A. *J. Organomet. Chem.* **2004**, *689*, 4642. (d) Krasovskyiy, A.; Lipshutz, B. H. *Org. Lett.* **2011**, *13*, 3818. (e) Le, C. M.; Hou, L. X.; Sperger, T.; Schoenebeck, F.; Lautens, M. *Angew. Chem., Int. Ed.* **2015**, *54*, 15897.

(10) (a) Karabelas, K.; Westerlund, C.; Hallberg, A. *J. Org. Chem.* **1985**, *50*, 3896. (b) Cabri, W.; Candiani, I.; Bedeschi, A.; Penco, S. *J. Org. Chem.* **1992**, *57*, 1481.

(11) For more detailed discussion about the proposed mechanism for the isomerization of vinylpalladium intermediate, see ref (8).

(12) For the enhancing effect of water additive on the Suzuki-Miyaura reaction, see: (a) Kostas, I. D.; Andreadaki, F. J.; Kovala-Demertzi, D.; Prentjas, C.; Demertzis, M. A. *Tetrahedron Lett.* **2005**, *46*, 1967. (b) Dolliver, D. D.; Bhattarai, B. T.; Pandey, A.; Lanier, M. L.; Bordelon, A. S.; Adhikari, S.; Dinser, J. A.; Flowers, P. F.; Wills, V. S.; Schneider, C. L. *J. Org. Chem.* **2013**, *78*, 3676.

(13) Kamijo, S.; Sasaki, Y.; Kanazawa, C.; Schüβler, T.; Yamamoto, Y. *Agenw. Chem., Int. Ed.* **2005**, *44*, 7718.

(14) For s mechanism study on Pd(0)-catalyzed *E*/*Z*-isomerization of α,β-unsaturated ester, see Canovese, L.; Santo, C.; Visentin, F. *Organometallics* **2008**, *27*, 3577.

(15) Molecular mechanics calculations (MM2) by Chem3D indicate that (*3E*)-**9** is approximately 0.4 kcal/mol lower in energy than (*3Z*)-**9**.

(16) Tang, B.-X.; Zhang, Y.-H.; Song, R.-J.; Tang, D.-J.; Deng, G.-B.; Wang, Z.-Q.; Xie, Y.-X.; Xia, Y.-Z.; Li, J.-H. *J. Org. Chem.* **2012**, *77*, 2837.