JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

Lewis Acid Catalyzed Dehydrogenative Coupling of Tertiary Propargylic Alcohols with Quinoline *N*-Oxides

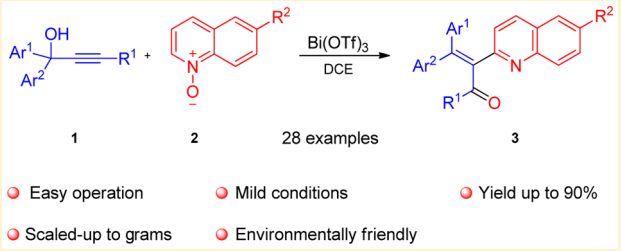
Ya-Ping Han,[†] Xue-Song Li,[†] Xin-Yu Zhu,[†] Ming Li,[†] Li Zhou,[†] Xian-Rong Song,[‡] and Yong-Min Liang*[,†]

[†]State Key Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou 730000, China

[‡]Jiangxi Key Laboratory of Organic Chemistry, Jiangxi Science Technology Normal University, Nanchang 330013, China

Supporting Information

ABSTRACT: An unprecedented Lewis acid catalyzed, high-efficiency synthesis of valuable 2-(quinolin-2-yl)prop-2-en-1-ones via dehydrogenative coupling of propargylic alkynols with quinoline *N*-oxides is described. This protocol, which tolerates a broad range of functional groups, provides a straightforward pathway to the products 2-(quinolin-2-yl)prop-2-en-1-one scaffolds in satisfactory yields. The conversion could be scaled up to gram scale efficiently, which underlines a latent application of this methodology.



INTRODUCTION

The functionalized quinoline derivatives represent an important class of heterocycles because they are the key skeletal structures in a wide array of pharmacologically and biologically relevant natural products.[1,2] It has been shown that these compounds exhibit potential biological activity, especially with antileishmanial activity,[3] biological antagonist activity,[4] and antimalarial and antimicrobial activities.[5] They play a key role in molecular recognition processes as well.[6] Previous methods to synthesize quinolines or quinolinones relied on the use of transition-metal catalysts such as Pd or Cu via a cross-coupling reaction. In 2013, the Wu group disclosed a novel employing quinoline *N*-oxides with aryl sulfonyl chlorides to construct 2-arylsulfonyl-quinolines (Scheme 1a).[7] Recently, the dehydrogenative amidation of quinoline *N*-oxides with lactams/cyclamines to generate 2-aminoquinolines was developed by Sun and co-workers in the presence of a Cu catalyst (Scheme 1b).[8] Very recently, Wu et al. accomplished a ^{t}BuOLi-promoted cross-dehydrogenative coupling (CDC) of quinoline *N*-oxides with 1,3-azoles to construct quinoline derivatives (Scheme 1c).[9] Nevertheless, the use of expensive metal reagents, extra bases, or complicated operation imposes restrictions on further application in organic synthetic chemistry. Thus, there is still a need for a versatile, practical, and environmentally benign access to 2-alkenylquinolones.

Propargylic alcohols have extensively used as synthons in organic synthesis due to their high reactivity and lower cost. The employment of propargylic alcohols as the substrates for the construction of various compounds, such as azepines,[10a] tetrazoles,[10b] furans,[10c] and thiazoles,[10d] has been widely investigated. Inspired by these intriguing studies and our advancing aspiration on the transformation of propargylic alcohols, we herein report an unprecedented Lewis acid catalyzed dehydrogenative coupling of quinoline *N*-oxides with propargylic alcohols, which enables the convergent synthesis of 2-(quinolin-2-yl)prop-2-en-1-ones under neutral conditions.

RESULTS AND DISCUSSION

The initial investigation began by employing the alkynol **1a** (0.1 mmol) with quinoline *N*-oxide **2a** (2.0 equiv) as the model substrates to optimize the reaction conditions. To our delight, the expected product **3a** was isolated in 60% yield in the presence of $Hf(OTf)_3$ (20 mol %) in DCE at 80 °C for 2 h (Table 1, entry 1). The molecular structure of **3a** was further elucidated by NMR spectra and X-ray crystal structure analysis (see the Supporting Information).[11] Notably, different Lewis acids were tested in this reaction system, and it was found that $Bi(OTf)_3$ was effective in providing the desired product in 71% yield (entries 2−8). Subsequently, investigation of the temperature revealed that 100 °C was the most suitable for this transformation (entries 9−11). A yield of 81% was obtained by prolonging the reaction time to 4 h (entries 12 and 13). The yield was slightly reduced to 80% by decreasing the catalyst loading to 15 mol % (entries 14 and 15). Reactions in other solvents such as CH_3NO_2, CH_3CN, $PhCH_3$, 1,4-dioxane, and THF did not result in any improvement in the yield (entries 16−20). Ultimately, the optimal conditions for the generation of **3a** were eventually finalized with the use of **1a** (0.1 mmol) and quinoline *N*-oxide **2a** (2.0 equiv) in the presence of $Bi(OTf)_3$ (15 mol %) in DCE (2.0 mL) at 100 °C for 4 h.

With the optimized reaction conditions in hand, the scope of the dehydrogenative coupling reactions was explored by employing various propargylic alcohols with quinoline *N*-oxides.

Received: December 6, 2016
Published: January 6, 2017

DOI: 10.1021/acs.joc.6b02882
J. Org. Chem. 2017, 82, 1697−1704

Scheme 1. Summary of Previous Studies and Our New Anticipation toward Quinoline Derivatives

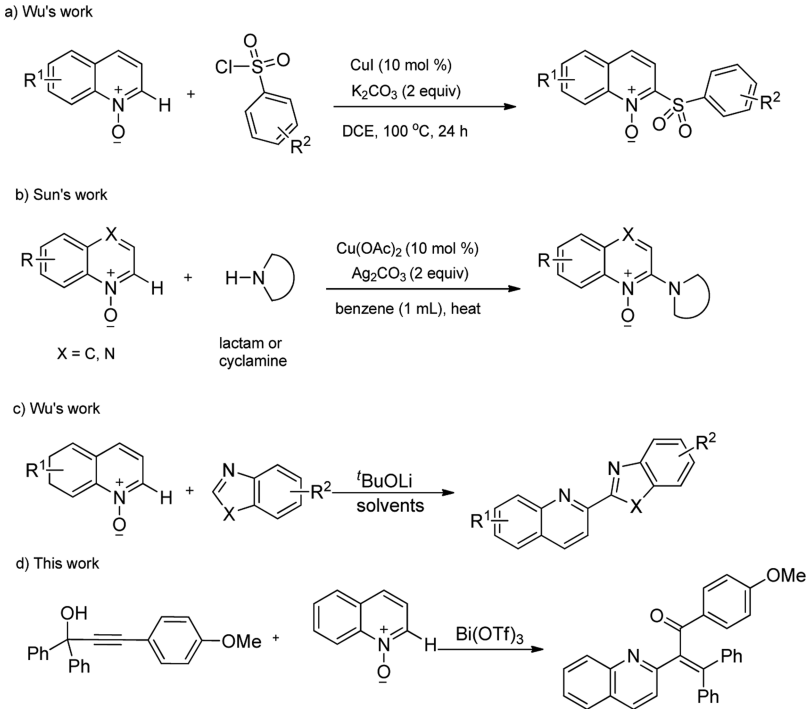
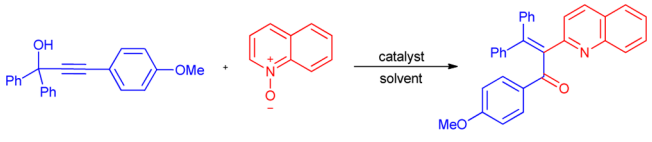


Table 1. Optimization of the Reaction Conditions of 1a with Quinoline *N*-Oxide[a,b]



1a 2a 3a

entry	catalyst (mol %)	solvent	temp (°C)	time (h)	yield[b] (%)
1	$Hf(OTf)_3$ (20)	DCE	80	2	60
2	$Yb(OTf)_3$ (20)	DCE	80	2	66
3	$Y(OTf)_3$ (20)	DCE	80	2	62
4	$Al(OTf)_3$ (20)	DCE	80	2	59
5	$Zn(OTf)_2$ (20)	DCE	80	2	54
6	$Bi(OTf)_3$ (20)	DCE	80	2	71
7	$BiCl_3$ (20)	DCE	80	2	45
8	BiI_3 (20)	DCE	80	2	27
9	$Bi(OTf)_3$ (20)	DCE	60	2	52
10	$Bi(OTf)_3$ (20)	DCE	100	2	76
11	$Bi(OTf)_3$ (20)	DCE	120	2	69
12	$Bi(OTf)_3$ (20)	DCE	100	4	81
13	$Bi(OTf)_3$ (20)	DCE	100	6	72
14	**$Bi(OTf)_3$ (15)**	**DCE**	**100**	**4**	**80**
15	$Bi(OTf)_3$ (10)	DCE	100	4	70
16	$Bi(OTf)_3$ (15)	CH_3NO_2	100	4	71
17	$Bi(OTf)_3$ (15)	CH_3CN	100	4	67
18	$Bi(OTf)_3$ (15)	$PhCH_3$	100	4	63
19	$Bi(OTf)_3$ (15)	1,4-dioxane	100	4	59
20	$Bi(OTf)_3$ (15)	THF	100	4	72

[a]Unless otherwise noted, all reactions were performed with **1a** (0.1 mmol) and quinoline *N*-oxide **2a** (2.0 equiv) in solvent (2.0 mL). [b]Yields are given for isolated products.

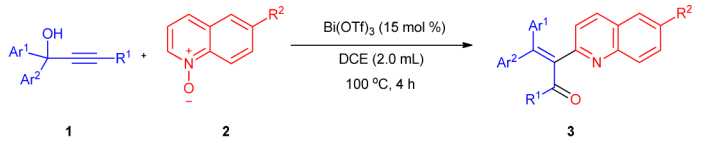
Substrates containing electron-donating groups on the *para*- or *meta*-positions to the benzene ring, such as OMe, Et, Me, and 3,5-DiMe, were efficiently coupled with quinoline *N*-oxide, furnishing the corresponding products **3a–f** in moderate to good yields (71–80%, Table 2). Notably, the alkynols bearing electron-withdrawing groups such as Ph, F, Cl, Br, NO_2, and $COOCH_3$ also performed well and were easily converted to the corresponding dehydrogenative coupling products **3g–l** with yields ranging from 51% to 90%. It is noteworthy that halo-substituted quinoline *N*-oxide derivatives are readily applied in further cross-coupling reactions (**3h–j**).

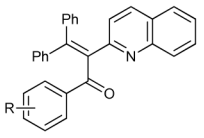
For substrates bearing either electron-rich (Me, OMe) or electron-deficient substituents (F, Cl) on the benzene rings of symmetrical propargylic alcohols (Ar^1, Ar^2), the dehydrogenative coupling reactions worked well to give the desired products with yields ranging from 68% to 81% (**3m–p**). Unsymmetrical propargylic alcohols with different electronic natures (Me, OMe, F, Cl) on the aromatic ring of Ar^1 also proceeded smoothly in the reaction, leading to the efficient generation of the corresponding products **3q–t** in 71–85% yields. Moreover, various heteroaryl-substituted (R^1, Ar^2) propargylic alcohols (**1u,v**) were suitable substrates for this protocol and generated anticipated products in moderate yields. The reactions of alkyl-substituted (R^1) propargylic alcohols **1w** and **1x** with quinoline *N*-oxide **2a** were well implemented to give the corresponding products **3w** and **3x** in 84% and 65% yields. Substituents with different electronic nature (Me, OMe, Cl, Br) on the aromatic ring of **2** also reacted smoothly in the reaction, allowing the facile formation of 1-(4-methoxyphenyl)-3,3-diphenylprop-2-(6-quinolin-2-yl)-2-en-1-ones with yields ranging from 52% to 85% (**3y–ab**). Regrettably, secondary propargylic alcohol 3-(4-methoxyphenyl)-1-phenylprop-2-yn-1-ol (**1ac**) could not progress well under the optimal conditions. This might be attributed to the fact that one aryl group hard to stabilize the allenyl cation intermediate **B** generated by propargylic alcohol (see Scheme 4).

It is interesting to note that our developed reaction system could be scaled up to grams efficiently under the standard conditions. The corresponding product **3a** was isolated in a

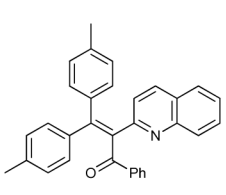
DOI: 10.1021/acs.joc.6b02882
J. Org. Chem. 2017, 82, 1697–1704

Table 2. Condensation of Various Propargylic Alcohols with Various Quinoline *N*-Oxide Derivatives[a−c]

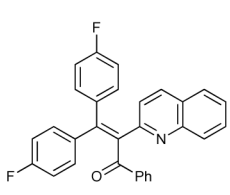




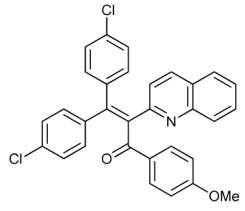
3a: 80% (R = *p*-OMe)
3b: 72% (R = *m*-OMe)
3c: 71% (R = *p*-Et)
3d: 74% (R = H)
3e: 78% (R = *p*-Me)
3f: 80% (R = 3,5-DiMe)
3g: 51% (R = *p*-Ph)
3h: 78% (R = *p*-F)
3i: 86% (R = *p*-Cl)
3j: 87% (R = *p*-Br)
3k: 82% (R = *p*-NO_2)
3l: 90% (*p*-$COOCH_3$)



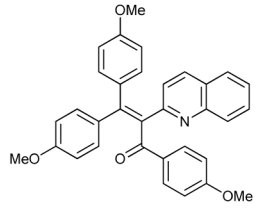
3m: 81%



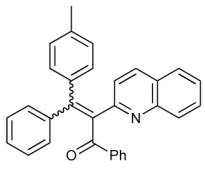
3n: 80%



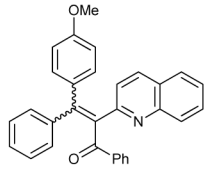
3o: 81%



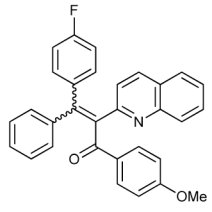
3p: 68%



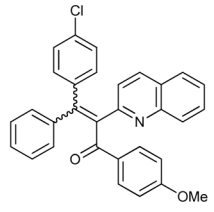
3q: 79%[c]



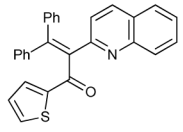
3r: 85%[c]



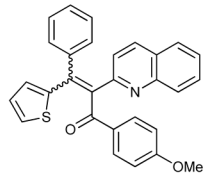
3s: 71%[c]



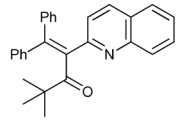
3t: 81%[c]



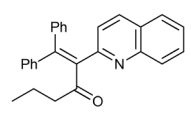
3u: 76%



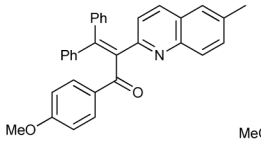
3v: 65%[c]



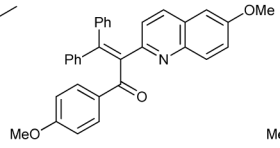
3w: 84%



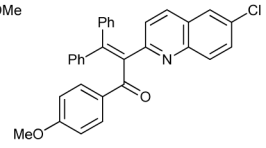
3x: 65%



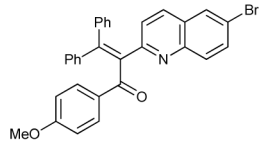
3y: 85%



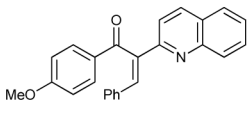
3z: 60%



3aa: 57%



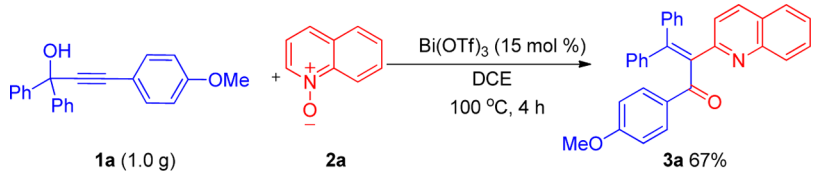
3ab: 52%



3ac: trace

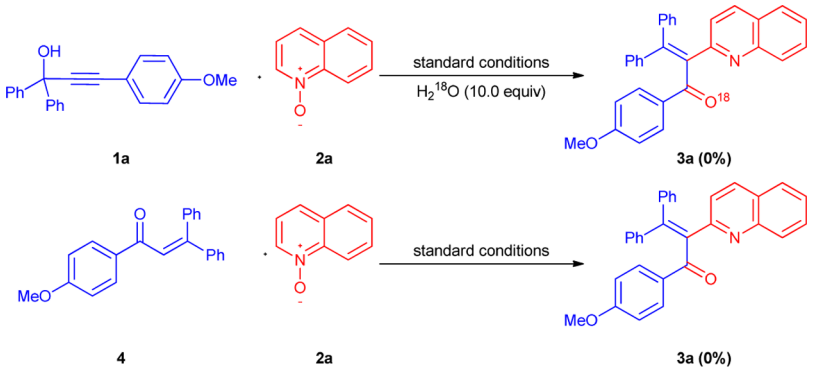
[a]Unless otherwise noted, all reactions were performed with **1** (0.1 mmol) and **2** (2.0 equiv) in the presence of $Bi(OTf)_3$ (15 mol %) in DCE (2.0 mL) at 100 °C for 4 h. [b]Yields are given for isolated products. [c]The olefin isomer *E*/*Z* ratios of **3q−t,v** are 1:1, 1:1, 1.12:1, 1.19:1, and 1.10:1, which are assigned by the integral area of ^{1}H NMR spectra.

Scheme 2. Scale-up Experiment

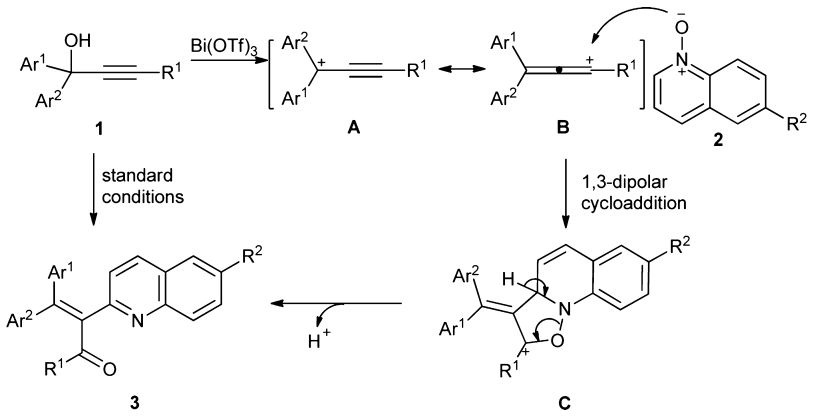


DOI: 10.1021/acs.joc.6b02882
J. Org. Chem. 2017, 82, 1697−1704

Scheme 3. Investigation of the Possible Key Intermediate



Scheme 4. Proposed Mechanism for the Formation of Quinoline Derivatives



moderate yield of 67%, which might offer a potential application in synthetic industry (Scheme 2).

To gain insight into the novel transformation, additional mechanistic studies have been conducted (Scheme 3). According to the previous literature,[1a,12,13] the cross-coupling might be achieved via 1,3-dipolar cycloaddition of carbocation intermediate **B** (see Scheme 4) with quinoline *N*-oxide **2a**, which formed the five-membered intermediate **C**. When the reaction of propargylic alcohol **1a** with **2a** was carried out in the presence of $H_2{}^{18}O$ (10.0 equiv), the desired product **3a** with ^{18}O was not detected, indicating that the oxygen of the product **3a** is from the quinoline *N*-oxide **2a**. Furthermore, isomerization of propargylic alcohols bearing an internal alkyne moiety into the corresponding α,β-unsaturated ketones is well-known as the Meyer−Schuster rearrangement. Thus, the reaction of 1-(4-methoxyphenyl)-3,3-diphenylprop-2-en-1-one (**4**) with quinolone *N*-oxide was carried out under the standard conditions, but the desired product **3a** was not obtained, which indicated that the α,β-unsaturated ketone **4** was excluded as the intermediate in the transformation.

A plausible mechanism is proposed on the basis of the literature[14,15] as shown in Scheme 4. Initially, the dehydration of propargylic alcohol **1** generates propargyl cation **A** in the presence of $Bi(OTf)_3$, which could resonate with resonance-stabilized **B**. Then, it might proceed 1,3-dipolar cycloaddition of intermediate **B** with quinoline *N*-oxide derivative **2** to generate the five-membered intermediate **C**. Finally, the desired product **3** was afforded by the release of a proton.

CONCLUSIONS

In summary, the challenging generation of functionalized 2-alkenylquinolines via Lewis acid catalyzed cross-coupling of propargylic alcohols with quinoline *N*-oxides has been achieved, leading to the high-efficiency synthesis of versatile quinoline derivatives in generally moderate to excellent yields. This protocol provides a straightforward and atom-economical route for the construction of the quinoline derivative scaffold, which acts as an important structural motif in a wide variety of pharmaceuticals and bioactive molecules.

EXPERIMENTAL SECTION

General Procedure for the Synthesis of 3a. The reaction of propargylic acohol **1a** (31.4 mg, 0.1 mmol), quinoline *N*-oxide **2a** (2.0 equiv), and $Bi(OTf)_3$ (15 mol %) in DCE (2.0 mL) was conducted at 100 °C under an air atmosphere. The reaction was completed within 4.0 h by TLC monitoring. The resulting mixture was cooled to room temperature. The solvent was evaporated under reduced pressure. The residue was further purified by chromatography on silica gel (petroleum ether/ethyl acetate, 10:1) to afford 35.3 mg of **3a**.

Compounds **1a**−**w**[2a] are known compounds. Compounds **2** are known compounds synthesized on the basis of literature reports.[1a]

General Remarks. Column chromatography was carried out on silica gel. ^1H NMR spectra were recorded on 400 MHz in $CDCl_3$. ^{13}C NMR spectra were recorded on 100 MHz in $CDCl_3$. Chemical shifts (ppm) were recorded with tetramethylsilane (TMS) as the internal reference standard. Multiplicities are given as s (singlet), d (doublet), t (triplet), dd (doublet of doublets), q (quartet), or m (multiplet). Their ^1H NMR and ^{13}C NMR spectra are provided in the Supporting Information. Solvents were dried using standard methods. Commercially available reagents were used with further purification. THF was distilled immediately before use from Na/benzophenone. The HRMS was obtained using a Q-TOF instrument equipped with ESI source.

DOI: 10.1021/acs.joc.6b02882
J. Org. Chem. 2017, 82, 1697−1704

Data collections for crystal structure were performed at room temperature (293 K) using Mo Kα radiation on a Bruker APEXII diffractometer;

Characterization Data of 3a−aa. *1-(4-Methoxyphenyl)-3,3-diphenyl-2-(quinolin-2-yl)prop-2-en-1-one (**3a**).* The resultant residue was purified by flash silica gel column chromatography to afford **3a** as a colorless solid (35.3 mg, 80%). R_f = 0.31 Mp: 220−222 °C. ^{1}H NMR (400 MHz, $CDCl_3$): 7.97−7.95 (m, 2H), 7.86 (d, J = 8.4 Hz, 1H), 7.79 (d, J = 8.8 Hz, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.58−7.54 (m, 1H), 7.44−7.40 (m, 1H), 7.25−7.19 (m, 3H), 7.17−7.16 (m, 4H), 7.14−7.12 (m, 3H), 7.06 (d, J = 8.4 Hz, 1H), 6.77−6.75 (m, 2H), 3.76 (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 197.1, 162.9, 158.9, 148.0, 146.8, 141.2, 140.8, 140.2, 135.2. 132.1, 131.2, 131.0, 130.0, 129.7, 129.0, 128.3, 128.1, 128.0, 127.2, 126.4, 126.4, 123.6, 113.4, 55.3. IR (KBr): 3368, 2923, 2854, 2373, 1655, 1597, 1422, 1254, 1163, 1072, 1029, 843, 766, 700, 598 cm^{-1}. HRMS (ESI): calcd for $C_{31}H_{23}NO_2$ ([M + H]$^+$) = 442.1802, found 442.1801 (0.2 ppm).

*1-(3-Methoxyphenyl)-3,3-diphenyl-2-(quinolin-2-yl)prop-2-en-1-one (**3b**).* The resultant residue was purified by flash silica gel column chromatography to afford **3b** as a colorless liquid (31.8 mg, 72%). R_f = 0.35. ^{1}H NMR (400 MHz, $CDCl_3$): 7.87 (d, J = 8.4 Hz, 1H), 7.79 (d, J = 8.4 Hz, 1H), 7.64 (d, J = 8.4 Hz, 1H), 7.59−7.54 (m, 2H), 7.49−7.48 (m, 1H), 7.45−7.41 (m, 1H), 7.25−7.22 (m, 1H), 7.20−7.17 (m, 7H), 7.15−7.13 (m, 3H), 7.05 (d, J = 8.4 Hz, 1H), 6.92−6.90 (m, 1H), 3.75 (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 198.2, 159.3, 158.7, 148.0, 147.6, 141.1, 140.6, 140.2, 139.6, 135.2, 131.1, 130.1, 129.7, 129.1, 129.0, 128.4, 128.3, 128.2, 128.0, 127.3, 126.5, 126.4, 123.5, 122.8, 119.1, 113.4, 55.3. IR (KBr): 3057, 2933, 2836, 1665, 1595, 1486, 1426, 1333, 1265, 1211, 1157, 1033, 764, 735, 702, 638, 597, 540 cm^{-1}. HRMS (ESI): calcd for $C_{31}H_{23}NO_2$ ([M + H]$^+$) = 442.1802, found 442.1801 (0.2 ppm).

*1-(4-Ethylphenyl)-3,3-diphenyl-2-(quinolin-2-yl)prop-2-en-1-one (**3c**).* The resultant residue was purified by flash silica gel column chromatography to afford **3c** as a colorless liquid (31.2 mg, 71%). R_f = 0.32. ^{1}H NMR (400 MHz, $CDCl_3$): 7.90−7.86 (m, 3H), 7.80 (d, J = 8.8 Hz, 1H), 7.65 (d, J = 8.0 Hz, 1H), 7.59−7.54 (m, 1H), 7.45−7.41 (m, 1H), 7.25−7.16 (m, 7H), 7.14−7.12 (m, 3H), 7.11−7.09 (m, 2H), 7.08−7.06 (m, 1H), 2.59 (q, J = 7.6 Hz, 2H), 1.17 (t, J = 7.6 Hz, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 198.0, 158.8, 149.1, 148.0, 147.2, 141.2, 140.8, 140.3, 135.9, 135.2, 131.1, 130.1, 129.9, 129.8, 129.0, 128.3, 128.2, 128.1, 128.0, 127.6, 127.2, 126.5, 126.4, 123.5, 28.8, 14.9. IR (KBr): 3281, 2925, 2860, 2366, 1649, 1597, 1444, 1265, 1167, 1118, 939, 764, 699, 599, 575 cm^{-1}. HRMS (ESI): calcd for $C_{32}H_{25}NO$ ([M + H]$^+$) = 440.2009, found 440.2011 (0.5 ppm).

*1,3,3-Triphenyl-2-(quinolin-2-yl)prop-2-en-1-one (**3d**).* The resultant residue was purified by flash silica gel column chromatography to afford **3d** as a colorless liquid (30.4 mg, 74%). R_f = 0.30. ^{1}H NMR (400 MHz, $CDCl_3$): 7.97−7.95 (m, 2H), 7.86 (d, J = 8.4 Hz, 1H), 7.79 (d, J = 8.8 Hz, 1H), 7.65 (d, J = 7.6 Hz, 1H), 7.58−7.54 (m, 1H), 7.45−7.41 (m, 1H), 7.37−7.33 (m, 1H), 7.28−7.23 (m, 3H), 7.19−7.17 (m, 6H), 7.12−7.11 (m, 3H), 7.06 (d, J = 8.8 Hz, 1H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 198.7, 158.9, 148.0, 147.5, 141.1, 140.6, 140.1, 138.3, 135.2, 132.2, 131.1, 130.2, 129.7, 129.7, 129.1, 128.4, 128.3, 128.2, 128.0, 128.0, 127.3, 126.5, 126.4, 123.6. IR (KBr): 3056, 2927, 1958, 1660, 1600, 1501, 1446, 1424, 1266, 1228, 1098, 1026, 957, 737, 699, 636, 574 cm^{-1}. HRMS (ESI): calcd for $C_{30}H_{21}NO$ ([M + H]$^+$) = 412.1696, found 412.1695 (0.2 ppm).

*3,3-Diphenyl-2-(quinolin-2-yl)-1-(p-tolyl)prop-2-en-1-one (**3e**).* The resultant residue was purified by flash silica gel column chromatography to afford **3e** as a colorless liquid (33.2 mg, 78%). R_f = 0.38. ^{1}H NMR (400 MHz, $CDCl_3$): 7.88−7.84 (m, 3H), 7.78 (d, J = 8.4 Hz, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.58−7.53 (m, 1H), 7.44−7.40 (m, 1H), 7.25−7.22 (m, 1H), 7.20−7.18 (m, 2H), 7.17−7.16 (m, 4H), 7.14−7.12 (m, 3H), 7.08−7.05 (m, 3H), 2.29 (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 198.0, 158.8, 148.0, 147.1, 143.0, 141.2, 140.7, 140.3, 135.7, 135.2, 131.1, 130.1, 129.9, 129.7, 129.0, 128.8, 128.3, 128.2, 128.2, 128.0, 127.2, 126.5, 126.4, 123.5, 21.6. IR (KBr): 3364, 2923, 2372, 1665, 1596, 1444, 1262, 1167, 1088, 1032, 832, 763, 699, 644, 587 cm^{-1}. HRMS (ESI): calcd for $C_{31}H_{23}NO$ ([M + H]$^+$) = 426.1852, found 426.1851 (0.2 ppm).

*1-(3,5-Dimethylphenyl)-3,3-diphenyl-2-(quinolin-2-yl)prop-2-en-1-one (**3f**).* The resultant residue was purified by flash silica gel column chromatography to afford **3f** as a colorless liquid (35.1 mg, 80%). R_f = 0.35. ^{1}H NMR (400 MHz, $CDCl_3$): 7.88 (d, J = 8.4 Hz, 1H), 7.79 (d, J = 8.8 Hz, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.58−7.54 (m, 3H), 7.44−7.41 (m, 1H), 7.24−7.22 (m, 1H), 7.21−7.19 (m, 1H), 7.17−7.16 (m, 5H), 7.14−7.12 (m, 3H), 7.06 (d, J = 8.4 Hz, 1H), 6.98 (s, 1H), 2.23 (s, 6H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 198.5, 158.9, 148.0, 147.4, 141.3, 140.8, 140.4, 138.0, 137.5, 135.1, 134.1, 131.1, 130.1, 129.8, 129.0, 128.3, 128.2, 128.1, 127.9, 127.6, 127.2, 126.4, 126.4, 123.6, 21.1. IR (KBr): 3316, 3056, 2922, 2305, 1663, 1595, 1501, 1444, 1301, 1265, 1197, 1156, 738, 701, 681, 640 cm^{-1}. HRMS (ESI): calcd for $C_{32}H_{25}NO$ ([M + H]$^+$) = 440.2009, found 440.2007 (0.5 ppm).

*1-([1,1′-Biphenyl]-4-yl)-3,3-diphenyl-2-(quinolin-2-yl)prop-2-en-1-one (**3g**).* The resultant residue was purified by flash silica gel column chromatography to afford **3g** as a colorless liquid (24.9 mg, 51%). R_f = 0.32. ^{1}H NMR (400 MHz, $CDCl_3$): 8.04−8.02 (m, 2H), 7.88 (d, J = 8.4 Hz, 1H), 7.81 (d, J = 8.4 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.57−7.54 (m, 3H), 7.52−7.50 (m, 2H), 7.45−7.39 (m, 4H), 7.36−7.34 (m, 1H), 7.23−7.18 (m, 6H), 7.14−7.12 (m, 3H), 7.08 (d, J = 8.4 Hz, 1H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 198.1, 158.8, 148.0, 147.5, 144.7, 141.1, 140.7, 140.1, 140.1, 137.0, 135.2, 131.1, 130.3, 130.2, 129.8, 129.1, 128.8, 128.4, 128.3, 128.2, 128.0, 128.0, 127.3, 127.2, 126.8, 126.5, 126.5, 123.6. IR (KBr): 3316, 2923, 2854, 2370, 1661, 1596, 1444, 1252, 1030, 831, 767, 696, 591 cm^{-1}. HRMS (ESI): calcd for $C_{36}H_{25}NO$ ([M + H]$^+$) = 488.2009, found 488.2007 (0.4 ppm).

*1-(4-Fluorophenyl)-3,3-diphenyl-2-(quinolin-2-yl)prop-2-en-1-one (**3h**).* The resultant residue was purified by flash silica gel column chromatography to afford **3h** as a colorless liquid (33.5 mg, 78%). R_f = 0.43. ^{1}H NMR (400 MHz, $CDCl_3$): 7.90−7.86 (m, 2H), 7.76 (d, J = 8.8 Hz, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.59−7.55 (m, 1H), 7.45−7.41 (m, 1H), 7.27−7.23 (m, 2H), 7.21−7.19 (m, 2H), 7.17−7.14 (m, 7H), 7.05−7.01 (m, 2H), 6.85−6.80 (m, 1H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 195.2, 162.0, 159.5, 158.5, 147.9 (d, J = 16.0 Hz), 141.6, 141.2, 140.7, 134.8, 133.6 (d, J = 9.0 Hz), 131.5, 131.0, 130.2, 129.7, 129.0, 128.4 (d, J = 8.0 Hz), 128.2, 128.0, 127.3, 126.5, 124.0, 123.7 (d, J = 3.0 Hz), 116.1, 115.9. IR (KBr): 3300, 2925, 2853, 2371, 1659, 1595, 1452, 1264, 1224, 1116, 1078, 1029, 765, 742, 700, 634 cm^{-1}. HRMS (ESI): calcd for $C_{30}H_{20}FNO$ ([M + H]$^+$) = 430.1602, found 430.1601 (0.2 ppm).

*1-(4-Chlorophenyl)-3,3-diphenyl-2-(quinolin-2-yl)prop-2-en-1-one (**3i**).* The resultant residue was purified by flash silica gel column chromatography to afford **3i** as a colorless liquid (38.3 mg, 86%). R_f = 0.49. ^{1}H NMR (400 MHz, $CDCl_3$): 7.90−7.88 (m, 2H), 7.85 (d, J = 8.4 Hz, 1H), 7.79 (d, J = 8.8 Hz, 1H), 7.65 (d, J = 8.0 Hz, 1H), 7.59−7.55 (m, 1H), 7.46−7.42 (m, 1H), 7.25−7.23 (m, 3H), 7.18−7.14 (m, 9H), 7.03 (d, J = 8.4 Hz, 1H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 197.6, 158.7, 148.0, 147.6, 140.9, 140.4, 139.5, 138.5, 136.7, 135.3, 131.0, 131.0, 130.1, 129.6, 129.2, 128.6, 128.5, 128.4, 128.3, 128.1, 127.3, 126.6, 126.5, 123.5. IR (KBr): 3331, 3056, 2924, 2305, 1672, 1590, 1443, 1264, 1166, 1091, 1012, 741, 700, 639 cm^{-1}. HRMS (ESI): calcd for $C_{30}H_{20}ClNO$ ([M + H]$^+$) = 446.1306, found 446.1305 (0.2 ppm).

*1-(4-Bromophenyl)-3,3-diphenyl-2-(quinolin-2-yl)prop-2-en-1-one (**3j**).* The resultant residue was purified by flash silica gel column chromatography to afford **3j** as a colorless liquid (42.5 mg, 87%). R_f = 0.51. ^{1}H NMR (400 MHz, $CDCl_3$): 7.86−7.78 (m, 4H), 7.65 (d, J = 8.0 Hz, 1H), 7.59−7.55 (m, 1H), 7.46−7.39 (m, 3H), 7.25−7.23 (m, 1H), 7.18−7.13 (m, 9H), 7.03 (d, J = 8.8 Hz, 1H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 197.8, 158.7, 148.0, 147.7, 140.9, 140.3, 139.5, 137.1, 135.3, 131.4, 131.1, 131.0, 130.1, 129.6, 129.2, 128.6, 128.5, 128.3, 128.1, 127.3, 126.6, 126.4, 123.5. IR (KBr): 3321, 2925, 2305, 1657, 1595, 1264, 1167, 1071, 1009, 743, 637, 658, 542 cm^{-1}. HRMS (ESI): calcd for $C_{30}H_{20}BrNO$ ([M + H]$^+$) = 490.0801, found 490.082 (0.2 ppm).

*1-(4-Nitrophenyl)-3,3-diphenyl-2-(quinolin-2-yl)prop-2-en-1-one (**3k**).* The resultant residue was purified by flash silica gel column chromatography to afford **3k** as a colorless liquid (37.4 mg, 82%). R_f =

DOI: 10.1021/acs.joc.6b02882
J. Org. Chem. 2017, 82, 1697−1704

0.36. ^{1}H NMR (400 MHz, $CDCl_3$): 8.11−8.04 (m, 4H), 7.85−7.81 (m, 2H), 7.69−7.57 (m, 3H), 7.48−7.44 (m, 1H), 7.38−7.34 (m, 1H), 7.29−7.25 (m, 1H), 7.23−7.21 (m, 1H), 7.19−7.18 (m, 2H), 7.14−7.13 (m, 4H), 7.04 (d, J = 8.8 Hz, 1H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 197.6, 158.7, 149.4, 148.7, 148.0, 144.3, 143.4, 140.6, 139.9, 139.1, 135.4, 132.5, 131.0, 130.3, 130.2, 129.5, 129.3, 129.0, 128.8, 128.4, 128.4, 128.3, 128.0, 127.4, 126.8, 126.5, 126.0, 123.5, 123.4, 123.2. IR (KBr): 3403, 3058, 2926, 1955, 1670, 1597, 1526, 1445, 1425, 1266, 1224, 1107, 1031, 846, 733, 701, 639 cm^{-1}. HRMS (ESI): calcd for $C_{30}H_{20}N_2O_3$ ([M + H]$^+$) = 457.1547, found 457.1549 (0.4 ppm).

*Methyl 4-(3,3-Diphenyl-2-(quinolin-2-yl)acryloyl)benzoate (**3l**).* The resultant residue was purified by flash silica gel column chromatography to afford **3l** as a colorless liquid (42.2 mg, 90%). R_f = 0.45. ^{1}H NMR (400 MHz, $CDCl_3$): 8.00−7.91 (m, 4H), 7.85−7.79 (m, 2H), 7.66 (d, J = 7.6 Hz, 1H), 7.59−7.55 (m, 1H), 7.46−7.42 (m, 1H), 7.28−7.24 (m, 2H), 7.19−7.18 (m, 4H), 7.15−7.10 (m, 4H), 7.04 (d, J = 8.4 Hz, 1H), 3.87 (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 198.4, 166.4, 158.8, 148.1, 148.0, 141.9, 140.8, 140.3, 139.6, 135.3, 132.8, 131.0, 130.2, 129.6, 129.3, 129.3, 129.2, 128.7, 128.5, 128.3, 128.3, 128.1, 127.3, 126.6, 126.4, 126.0, 123.5, 52.2. IR (KBr): 3335, 3056, 2954, 2305, 1718, 1675, 1594, 1502, 1438, 1278, 1106, 910, 871, 735, 700, 639, 590 cm^{-1}. HRMS (ESI): calcd for $C_{32}H_{23}NO_3$ ([M + H]$^+$) = 470.1751, found 470.1750 (0.2 ppm).

*1-Phenyl-2-(quinolin-2-yl)-3,3-di(p-tolyl)prop-2-en-1-one (**3m**).* The resultant residue was purified by flash silica gel column chromatography to afford **3m** as a colorless liquid (35.6 mg, 81%). R_f = 0.37. ^{1}H NMR (400 MHz, $CDCl_3$): 7.96−7.93 (m, 2H), 7.85 (d, J = 8.8 Hz, 1H), 7.78 (d, J = 8.4 Hz, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.57−7.53 (m, 1H), 7.43−7.39 (m, 1H), 7.36−7.32 (m, 1H), 7.28−7.24 (m, 2H), 7.08−7.04 (m, 5H), 6.97 (d, J = 8.0 Hz, 2H), 6.91 (d, J = 8.0 Hz, 2H), 2.29 (s, 3H), 2.21 (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 198.8, 159.2, 148.0, 147.8, 139.2, 138.5, 138.4, 138.3, 137.9, 135.1, 132.1, 131.1, 130.1, 129.7, 129.7, 129.0, 128.9, 128.7, 128.0, 127.2, 126.4, 123.7, 21.3, 21.2. IR (KBr): 3374, 2924, 2374, 1656, 1595, 1423, 1265, 1159, 1115, 1064, 745, 699, 659 cm^{-1}. HRMS (ESI): calcd for $C_{32}H_{25}NO$ ([M + H]$^+$) = 440.2009, found 440.2010 (0.2 ppm).

*3,3-Bis(4-fluorophenyl)-1-phenyl-2-(quinolin-2-yl)prop-2-en-1-one (**3n**).* The resultant residue was purified by flash silica gel column chromatography to afford **3n** as a colorless liquid (35.8 mg, 80%). R_f = 0.34. ^{1}H NMR (400 MHz, $CDCl_3$): 7.95−7.93 (m, 2H), 7.87−7.84 (m, 2H), 7.67 (d, J = 8.4 Hz, 1H), 7.60−7.56 (m, 1H), 7.47−7.43 (m, 1H), 7.40−7.36 (m, 1H), 7.31−7.27 (m, 2H), 7.16−7.11 (m, 4H), 7.06 (d, J = 8.8 Hz, 1H), 6.90−6.80 (m, 4H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 198.3, 163.9 (d, J = 3.0 Hz), 161.5 (d, J = 3.0 Hz), 158.4, 148.0, 145.2, 140.5, 138.0, 136.9 (d, J = 3.0 Hz), 136.4 (d, J = 4.0 Hz), 135.6, 132.9, 132.8, 132.5, 132.0, 131.9, 129.7, 129.6, 129.3, 128.2, 127.3, 126.7, 126.5, 123.3, 115.5, 115.3 (d, J = 3.0 Hz), 115.1. IR (KBr): 3397, 2924, 2365, 1666, 1595, 1449, 1412, 1228, 1155, 1096, 743, 660, 555 cm^{-1}. HRMS (ESI): calcd for $C_{30}H_{19}F_2NO$ ([M + H]$^+$) = 448.1507, found 448.1508 (0.2 ppm).

*3,3-Bis(4-chlorophenyl)-1-(4-methoxyphenyl)-2-(quinolin-2-yl)-prop-2-en-1-one (**3o**).* The resultant residue was purified by flash silica gel column chromatography to afford **3o** as a colorless liquid (41.3 mg, 81%). R_f = 0.54. ^{1}H NMR (400 MHz, $CDCl_3$): 7.95−7.93 (m, 2H), 7.88−7.84 (m, 2H), 7.68 (d, J = 8.0 Hz, 1H), 7.61−7.57 (m, 1H), 7.48−7.44 (m, 1H), 7.16−7.12 (m, 6H), 7.09−7.05 (m, 3H), 6.81−6.79 (m, 2H), 3.80 (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 196.3, 163.3, 157.9, 148.0, 144.0, 141.3, 139.3, 138.8, 135.7, 134.5, 134.4, 132.3, 132.1, 131.2, 130.8, 129.7, 129.3, 129.0, 128.6, 128.4, 127.3, 126.8, 126.5, 123.1, 113.6, 55.4. IR (KBr): 3395, 3057, 2927, 2374, 1663, 1596, 1260, 1163, 1091, 1026, 837, 738, 607 cm^{-1}. HRMS (ESI): calcd for $C_{31}H_{21}Cl_2NO_2$ ([M + H]$^+$) = 510.1022, found 510.1021 (0.2 ppm).

*1,3,3-Tris(4-methoxyphenyl)-2-(quinolin-2-yl)prop-2-en-1-one (**3p**).* The resultant residue was purified by flash silica gel column chromatography to afford **3p** as a colorless liquid (34.1 mg, 68%). R_f = 0.41. ^{1}H NMR (400 MHz, $CDCl_3$): 7.99−7.96 (m, 2H), 7.90 (d, J = 8.4 Hz, 1H), 7.83 (d, J = 8.4 Hz, 1H), 7.68 (d, J = 7.2 Hz, 1H), 7.61−7.56 (m, 1H), 7.47−7.43 (m, 1H), 7.17−7.15 (m, 2H), 7.12−7.09 (m, 3H), 6.80−6.77 (m, 2H), 6.73−6.68 (m, 4H), 3.80 (s, 3H), 3.78 (s, 3H), 3.74 (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 197.6, 162.8, 159.7, 159.7, 148.0, 146.8, 138.3, 135.2, 134.0, 133.3, 132.7, 132.2, 132.0, 131.7, 131.4, 129.6, 129.0, 127.2, 126.3, 126.3, 123.9, 113.5, 113.4, 113.4, 55.3, 55.2, 55.1. IR (KBr): 3284, 2924, 2371, 1736, 1597, 1262, 1157, 1115, 1067, 1030, 746, 612, 562 cm^{-1}. HRMS (ESI): calcd for $C_{33}H_{27}NO_4$ ([M + H]$^+$) = 502.2013, found 502.2011 (0.4 ppm).

*1,3-Diphenyl-2-(quinolin-2-yl)-3-(p-tolyl)prop-2-en-1-one (**3q**).* The resultant residue was purified by flash silica gel column chromatography to afford **3q** as a colorless liquid (33.6 mg, 79%). R_f = 0.35. ^{1}H NMR (400 MHz, $CDCl_3$): 7.97−7.93 (m, 4H), 7.88−7.84 (m, 2H), 7.81−7.76 (m, 2H), 7.66−7.62 (m, 2H), 7.58−7.53 (m, 2H), 7.45−7.40 (m, 2H), 7.35−7.32 (m, 2H), 7.29−7.23 (m, 6H), 7.17−7.16 (m, 6H), 7.11−7.07 (m, 4H), 7.06−7.03 (m, 4H), 6.98 (d, J = 8.0 Hz, 2H), 6.92 (d, J = 8.0 Hz, 2H), 2.29 (s, 3H), 2.21 (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 198.8, 198.7, 159.2, 158.9, 148.0, 148.0, 147.7, 147.6, 141.3, 140.8, 139.6, 138.4, 138.3, 138.3, 137.6, 135.2, 135.1, 132.2, 132.1, 131.1, 131.0, 130.2, 130.1, 129.7, 129.6, 129.0, 129.0, 128.9, 128.8, 128.3, 128.2, 128.2, 128.0, 128.0, 127.9, 127.3, 126.4, 126.4, 123.7, 123.6, 21.3, 21.2. IR (KBr): 3404, 3056, 2924, 2304, 1959, 1663, 1595, 1557, 1501, 1447, 1424, 1333, 1265, 1228, 1168, 1023, 739, 701, 613, 566 cm^{-1}. HRMS (ESI): calcd for $C_{31}H_{23}NO$ ([M + H]$^+$) = 426.1852, found 426.1849 (0.7 ppm).

*3-(4-Methoxyphenyl)-1,3-diphenyl-2-(quinolin-2-yl)prop-2-en-1-one (**3r**).* The resultant residue was purified by flash silica gel column chromatography to afford **3r** as a colorless liquid (37.5 mg, 85%). R_f = 0.42. ^{1}H NMR (400 MHz, $CDCl_3$): 7.98−7.92 (m, 4H), 7.89−7.76 (m, 4H), 7.67−7.63 (m, 2H), 7.59−7.54 (m, 2H), 7.45−7.40 (m, 2H), 7.36−7.31 (m, 2H), 7.29−7.23 (m, 6H), 7.18−7.17 (m, 6H), 7.12−7.09 (m, 6H), 7.07−7.02 (m, 2H), 6.71−6.63 (m, 4H), 3.75 (s, 3H), 3.70 (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 199.0, 198.8, 159.8, 159.8, 158.4, 159.2, 148.0, 148.0, 147.6, 141.4, 140.9, 139.2, 139.1, 138.4, 138.4, 135.3, 135.1, 133.6, 132.9, 132.6, 132.2, 132.1, 131.7, 131.2, 130.3, 129.7, 129.0, 128.4, 128.3, 128.2, 128.1, 128.0, 128.0, 127.3, 127.2, 126.4, 126.4, 123.8, 123.7, 113.6, 113.5, 55.2, 55.1. IR (KBr): 3312, 3055, 2984, 2305, 1661, 1604, 1509, 1447, 1265, 1168, 1032, 738, 702, 567 cm^{-1}. HRMS (ESI): calcd for $C_{31}H_{23}NO_2$ ([M + H]$^+$) = 442.1802, found 442.1801 (0.2 ppm).

*3-(4-Fluorophenyl)-1-(4-methoxyphenyl)-3-phenyl-2-(quinolin-2-yl)prop-2-en-1-one (**3s**).* The resultant residue was purified by flash silica gel column chromatography to afford **3s** as a colorless liquid (30.5 mg, 71%). R_f = 0.47. ^{1}H NMR (400 MHz, $CDCl_3$): 7.97−7.93 (m, 4H), 7.88−7.79 (m, 4H), 7.68−7.64 (m, 2H), 7.60−7.55 (m, 2H), 7.46−7.43 (m, 2H), 7.20−7.18 (m, 4H), 7.16−7.12 (m, 8H), 7.11−7.09 (m, 2H), 7.07−7.04 (m, 2H), 6.87−6.83 (m, 4H), 6.79−6.75 (m, 4H), 3.78 (s, 3H), 3.77 (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 196.9 (d, J = 29.0 Hz), 163.0 (d, J = 8.0 Hz), 158.6 (d, J = 8.0 Hz), 148.0 (d, J = 4.0 Hz), 145.7 (d, J = 14.0 Hz), 141.0, 140.6, 140.4, 137.3, 136.8 (d, J = 3.0 Hz), 135.5, 135.3, 132.9, 132.8, 132.1, 131.9, 131.8, 131.0 (d, J = 4.0 Hz), 130.0, 129.7 (d, J = 3.0 Hz), 129.2, 129.1, 128.5, 128.3, 128.2, 128.1, 127.3 (d, J = 3.0 Hz), 126.6, 126.5 (d, J = 7.0 Hz), 123.4 (d, J = 7.0 Hz), 115.3, 115.2, 115.1, 115.0, 113.5, 113.4, 55.3, 55.3. IR (KBr): 3277, 3055, 2932, 2841, 1903, 1713, 1653, 1598, 1507, 1423, 1263, 1162, 1030, 860, 736, 701, 603 cm^{-1}. HRMS (ESI): calcd for $C_{31}H_{22}FNO_2$ ([M + H]$^+$) = 460.1707, found 460.1708 (0.2 ppm).

*3-(4-Chlorophenyl)-1-(4-methoxyphenyl)-3-phenyl-2-(quinolin-2-yl)prop-2-en-1-one (**3t**).* The resultant residue was purified by flash silica gel column chromatography to afford **3t** as a colorless liquid (38.5 mg, 81%). R_f = 0.31. ^{1}H NMR (400 MHz, $CDCl_3$): 7.97−7.93 (m, 4H), 7.87−7.79 (m, 4H), 7.69−7.64 (m, 2H), 7.61−7.55 (m, 2H), 7.47−7.42 (m, 2H), 7.34−7.29 (m, 2H), 7.19−7.17 (m, 4H), 7.15−7.12 (m, 10H), 7.10−7.08 (m, 2H), 7.08−7.04 (m, 2H), 6.80−6.75 (m, 4H), 3.79 (s, 3H), 3.77 (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 196.7, 196.6, 163.1, 163.0, 158.4, 158.4, 148.0, 147.9, 145.5, 145.4, 140.8, 140.7, 140.4, 139.7, 139.2, 135.7, 135.3, 134.3, 134.2, 132.4, 132.1, 131.3, 131.0, 130.9, 130.0, 129.7, 129.7, 129.3, 129.2, 128.5, 128.4, 128.4, 128.3, 128.3, 128.1, 127.3, 127.3, 126.7, 126.6, 126.5, 123.3, 113.6, 113.5, 55.3, 55.3. IR (KBr): 3408, 2926, 2849,

DOI: 10.1021/acs.joc.6b02882
J. Org. Chem. 2017, 82, 1697−1704

2252, 1712, 1656, 1597, 1422, 1363, 1258, 1222, 1163, 1091, 1029, 912, 838, 737, 638, 603 cm^{-1}. HRMS (ESI): calcd for $C_{31}H_{22}ClNO_2$ ($[M + H]^+$) = 476.1412, found 476.1413 (0.2 ppm).

*3,3-Diphenyl-2-(quinolin-2-yl)-1-(thiophene-2-yl)prop-2-en-1-one (**3u**).* The resultant residue was purified by flash silica gel column chromatography to afford **3u** as a colorless liquid (31.7 mg, 76%). R_f = 0.41. ^1H NMR (400 MHz, $CDCl_3$): 7.89 (d, J = 8.4 Hz, 1H), 7.80 (d, J = 8.8 Hz, 1H), 7.67−7.62 (m, 2H), 7.60−7.56 (m, 1H), 7.47−7.42 (m, 2H), 7.28−7.23 (m, 3H), 7.19−7.16 (m, 7H), 7.05 (d, J = 8.4 Hz, 1H), 6.92−6.90 (m, 1H). $^{13}C\{H\}$ NMR (100 MHz, $CDCl_3$): δ 190.6, 158.5, 148.0, 147.6, 145.5, 141.2, 140.6, 140.0, 135.2, 134.1, 133.6, 131.1, 130.2, 129.8, 129.1, 128.5, 128.3, 128.2, 128.1, 127.7, 127.3, 126.6, 126.5, 123.6. IR (KBr): 3274, 3057, 2926, 1956, 1639, 1595, 1500, 1413, 1264, 1080, 1060, 1035, 739, 658 cm^{-1}. HRMS (ESI): calcd for $C_{28}H_{19}NOS$ ($[M + H]^+$) = 418.1260, found 418.1259 (0.2 ppm).

*1-(4-Methoxyphenyl)-3-phenyl-2-(quinolin-2-yl)-3-(thiophene-2-yl)prop-2-en-1-one (**3v**).* The resultant residue was purified by flash silica gel column chromatography to afford **3v** as a colorless liquid (29.1 mg, 65%). R_f = 0.41. ^1H NMR (400 MHz, $CDCl_3$): 8.07 (d, J = 8.8 Hz, 2H), 8.00−7.82 (m, 4H), 7.76−7.72 (m, 2H), 7.63−7.61 (m, 2H), 7.57−7.47 (m, 2H), 7.43−7.39 (m, 2H), 7.32−7.30 (m, 4H), 7.28−7.25 (m, 2H), 7.23−7.15 (m, 8H), 7.07−6.98 (m, 2H), 6.85−6.81 (m, 4H), 6.77−6.74 (m, 2H), 3.80 (s, 3H), 3.77 (s, 3H). $^{13}C\{H\}$ NMR (100 MHz, $CDCl_3$): δ 197.2, 196.1, 163.2, 163.0, 158.3, 158.2, 148.2, 147.9, 143.6, 142.9, 140.6, 140.4, 139.9, 139.4, 139.1, 138.8, 135.9, 135.1, 132.2, 132.1, 131.0, 130.9, 130.5, 130.1, 129.8, 129.7, 129.2, 129.0, 128.6, 128.6, 128.4, 128.2, 128.2, 127.9, 127.4, 127.2, 127.0, 126.7, 126.7, 126.5, 126.3, 123.4, 123.2, 113.6, 113.4, 55.3, 55.3. IR (KBr): 3296, 3056, 2929, 2840, 1957, 1654, 1596, 1501, 1423, 1312, 1252, 1167, 1028, 834, 738, 702, 582 cm^{-1}. HRMS (ESI): calcd for $C_{29}H_{21}NO_2S$ ($[M + H]^+$) = 448.1366, found 448.1369 (0.7 ppm).

*4,4-Dimethyl-1,1-diphenyl-2-(quinolin-2-yl)pent-1-en-3-one (**3w**).* The resultant residue was purified by flash silica gel column chromatography to afford **3w** as a colorless liquid (32.8 mg, 84%). R_f = 0.37. ^1H NMR (400 MHz, $CDCl_3$): 7.99−7.97 (m, 1H), 7.70−7.61 (m, 3H), 7.47−7.43 (m, 1H), 7.31 (s, 5H), 7.24−7.20 (m, 1H), 7.18−7.14 (m, 2H), 7.12−7.10 (m, 2H), 6.86 (d, J = 8.4 Hz, 1H), 1.13 (s, 9H). $^{13}C\{H\}$ NMR (100 MHz, $CDCl_3$): δ 217.3. 158.8, 147.7, 142.4, 142.2, 141.6, 141.0, 134.6, 131.0, 130.9, 129.3, 129.1, 128.5, 128.3, 128.2, 128.1, 127.4, 126.5, 123.7, 45.0, 28.1. IR (KBr): 3345, 2924, 2860, 2374, 1595, 1264, 1093, 1074, 1028, 765, 745, 703, 642, 581 cm^{-1}. HRMS (ESI): calcd for $C_{28}H_{25}NO$ ($[M + H]^+$) = 392.2009, found 392.2008 (0.3 ppm).

*1,1-Diphenyl-2-(quinolin-2-yl)hex-1-en-3-one (**3x**).* The resultant residue was purified by flash silica gel column chromatography to afford **3w** as a colorless liquid (24.6 mg, 65%). R_f = 0.34. ^1H NMR (400 MHz, $CDCl_3$): 7.99 (d, J = 8.0 Hz, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.67−7.63 (m, 2H), 7.48−7.45 (m, 1H), 7.35−7.34 (m, 3H), 7.28−7.27 (m, 2H), 7.22−7.18 (m, 1H), 7.14−7.11 (m, 2H), 7.07−7.05 (m, 2H), 6.90 (d, J = 8.4 Hz, 1H), 2.49 (t, J = 7.2 Hz, 2H), 1.59 (q, J = 7.2 Hz, 2H), 0.77 (t, J = 7.2 Hz, 3H). $^{13}C\{H\}$ NMR (100 MHz, $CDCl_3$): δ 208.8, 158.9, 147.8, 145.1, 142.5, 141.1, 140.4, 135.1, 130.9, 130.0, 129.5, 129.2, 128.7, 128.4, 128.2, 128.1, 127.4, 126.5, 123.7, 46.4, 17.3, 13.6. IR (KBr): 3459, 3025, 2920, 2854, 1665, 1589, 1154, 1021, 1009, 795, 775, 748, 703, 642, 581, 572, cm^{-1}. HRMS (ESI): calcd for $C_{27}H_{23}NO$ ($[M + H]^+$) = 378.1852, found 378.1858 (0.2 ppm).

*1-(4-Methoxyphenyl)-2-(6-methylquinolin-2-yl)-3,3-diphenylprop-2-en-1-one (**3y**).* The resultant residue was purified by flash silica gel column chromatography to afford **3y** as a colorless liquid (38.5 mg, 85%). R_f = 0.43. ^1H NMR (400 MHz, $CDCl_3$): 7.96−7.94 (m, 2H), 7.77−7.70 (m, 2H), 7.41−7.38 (m, 2H), 7.21−7.19 (m, 3H), 7.16−7.12 (m, 7H), 7.03 (d, J = 8.4 Hz, 1H), 6.77−6.75 (m, 2H), 3.77 (s, 3H), 2.46 (s, 3H). $^{13}C\{H\}$ NMR (100 MHz, $CDCl_3$): δ 197.1, 162.9, 157.9, 146.6, 146.6, 141.3, 140.9, 140.3, 136.4, 134.6, 132.1, 131.3, 131.2, 131.1, 130.1, 129.4, 128.2, 128.1, 128.0, 128.0, 126.5, 126.2, 123.6, 113.4, 55.3, 21.5. IR (KBr): 3344, 2924, 2372, 1596, 1460, 1382, 1257, 1162, 1113, 1028, 834, 739, 700, 589 cm^{-1}. HRMS (ESI): calcd for $C_{32}H_{25}NO_2$ ($[M + H]^+$) = 456.1958, found 456.1959 (0.2 ppm).

*1-(4-Methoxyphenyl)-2-(6-methoxyquinolin-2-yl)-3,3-diphenylprop-2-en-1-one (**3z**).* The resultant residue was purified by flash silica gel column chromatography to afford **3z** as a colorless liquid (28.3 mg, 60%). R_f = 0.42. ^1H NMR (400 MHz, $CDCl_3$): 7.95−7.92 (m, 2H), 7.53 (d, J = 8.4 Hz, 1H), 7.51−7.47 (m, 4H), 7.43−7.40 (m, 2H), 7.33−7.31 (m, 2H), 7.30−7.27 (m, 2H), 7.18−7.17 (m, 1H), 7.17−7.14 (m, 2H), 6.98−6.97 (m, 1H), 6.82−6.79 (m, 2H), 3.88 (s, 3H), 3.73 (s, 3H). $^{13}C\{H\}$ NMR (100 MHz, $CDCl_3$): δ 198.5, 159.5, 158.0, 155.6, 143.5, 139.4, 139.1, 135.5, 133.9, 131.4, 130.0, 129.1, 128.7, 128.4, 128.3, 128.2, 128.1, 127.9, 127.2, 125.9, 125.8, 122.3, 118.7, 113.8, 108.1, 107.7, 104.9, 55.5, 55.2. IR (KBr): 3060, 2934, 2838, 2051, 1819, 1713, 1597, 1509, 1449, 1381, 1261, 1162, 1030, 946, 907, 835, 738, 701, 530 cm^{-1}. HRMS (ESI): calcd for $C_{32}H_{25}NO_3$ ($[M + H]^+$) = 472.1907, found 472.1905 (0.2 ppm).

*2-(6-Chloroquinolin-2-yl)-1-(4-methoxyphenyl)-3,3-diphenylprop-2-en-1-one (**3aa**).* The resultant residue was purified by flash silica gel column chromatography to afford **3aa** as a colorless liquid (27.1 mg, 57%). R_f = 0.35. ^1H NMR (400 MHz, $CDCl_3$): 7.94 (d, J = 8.4 Hz, 2H), 7.78 (d, J = 9.2 Hz, 1H), 7.68 (d, J = 8.4 Hz, 1H), 7.61−7.60 (m, 1H), 7.50−7.47 (m, 1H), 7.25 (s, 1H), 7.21−7.19 (m, 3H), 7.17−7.15 (m, 3H), 7.13−7.12 (m, 3H), 7.06 (d, J = 8.4 Hz, 1H), 6.76 (d, J = 8.8 Hz, 2H), 3.75 (s, 3H). $^{13}C\{H\}$ NMR (100 MHz, $CDCl_3$): δ 197.0, 163.0, 159.3, 147.2, 146.3, 141.0, 140.6, 139.7, 134.2, 132.1, 132.0, 131.2, 131.1, 131.0, 130.0, 129.9, 128.4, 128.3, 128.2, 128.0, 127.0, 125.9, 124.4, 113.4, 55.3. IR (KBr): 3298, 2924, 2853, 2364, 1714, 1596, 1258, 1158, 1123, 831, 700, 677, 576 cm^{-1}. HRMS (ESI): calcd for $C_{31}H_{22}ClNO_2$ ($[M + H]^+$) = 476.1412, found 476.1414 (0.4 ppm).

*2-(6-Bromoquinolin-2-yl)-1-(4-methoxyphenyl)-3,3-diphenylprop-2-en-1-one (**3ab**).* The resultant residue was purified by flash silica gel column chromatography to afford **3ab** as a colorless liquid (27.0 mg, 52%). R_f = 0.38. ^1H NMR (400 MHz, $CDCl_3$): 7.94 (d, J = 8.8 Hz, 2H), 7.79−7.78 (m, 1H), 7.72−7.67 (m, 2H), 7.62−7.59 (m, 1H), 7.25−7.24 (m, 1H), 7.22−7.17 (m, 4H), 7.15−7.12 (m, 5H), 7.06 (d, J = 8.8 Hz, 1H), 6.76 (d, J = 8.8 Hz, 2H), 3.76 (s, 3H). $^{13}C\{H\}$ NMR (100 MHz, $CDCl_3$): δ 196.9, 163.0, 159.4, 147.2, 146.5, 141.0, 140.6, 139.7, 134.1, 132.5, 132.0, 131.3, 131.0, 131.0, 130.0, 129.3, 128.4, 128.3, 128.2, 128.0, 127.5, 124.4, 120.3, 113.4, 55.3. IR (KBr): 3300, 2926, 2851, 2362, 1596, 1443, 1261, 1159, 1115, 1028, 764, 745, 700, 664, 588 cm^{-1}. HRMS (ESI): calcd for $C_{31}H_{22}BrNO_2$ ($[M + H]^+$) = 520.0907, found 520.0904 (0.4 ppm).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02882.

^1H and ^{13}C NMR spectra for all products (PDF)

X-ray crystallographic data for product **3a** (CIF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: liangym@lzu.edu.cn.

ORCID

Yong-Min Liang: 0000-0001-8280-8211

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the National Science Foundation (NSF 21272101, 21472073, and 21532001), the Program for Changjiang Scholars and Innovative Research Team in University (IRT15R28), and The "111" Project, J1103307.

■ REFERENCES

(1) (a) Xia, H.; Liu, Y.; Zhao, P.; Gou, S.; Wang, J. *Org. Lett.* **2016**, *18*, 1796. (b) Gong, X.; Song, G.; Zhang, H.; Li, X. *Org. Lett.* **2011**, *13*,

1766. (c) Bharate, J. B.; Vishwakarma, R. A.; Bharate, S. B. *RSC Adv.* **2015**, *5*, 42020. (d) Prajapati, S. M.; Patel, K. D.; Vekariya, R. H.; Panchal, S. N.; Patel, H. D. *RSC Adv.* **2014**, *4*, 24463. (e) Khusnutdinov, R. I.; Bayguzina, A. R.; Dzhemilev, U. M. *J. Organomet. Chem.* **2014**, *768*, 75. (f) Xiao, B.; Liu, Z.-J.; Liu, L.; Fu, Y. *J. Am. Chem. Soc.* **2013**, *135*, 616. (g) Chen, X.; Zhu, C.; Cui, X.; Wu, Y. *Chem. Commun.* **2013**, *49*, 6900. (h) Hughes, R. A.; Moody, C. J. *Angew. Chem., Int. Ed.* **2007**, *46*, 7930. (i) Couturier, M.; Caron, L.; Tumidajski, S.; Jones, K.; White, T. D. *Org. Lett.* **2006**, *8*, 1929.

(2) (a) Zhu, C.; Yi, M.; Wei, D.; Chen, X.; Wu, Y.; Cui, X. *Org. Lett.* **2014**, *16*, 1840. (b) Jeong, J.; Patel, P.; Hwang, H.; Chang, S. *Org. Lett.* **2014**, *16*, 4598. (c) Wu, Z.; Pi, C.; Cui, X.; Bai, J.; Wu, Y. *Adv. Synth. Catal.* **2013**, *355*, 1971. (d) Wen, P.; Li, Y.; Zhou, K.; Ma, C.; Lan, X.; Ma, C.; Huang, G. *Adv. Synth. Catal.* **2012**, *354*, 2135. (e) Zhao, D.; Wang, W.; Yang, F.; Lan, J.; Yang, L.; Gao, G.; You, J. *Angew. Chem., Int. Ed.* **2009**, *48*, 3296. (f) Campeau, L.-C.; Stuart, D. R.; Leclerc, J.-P.; Bertrand-Laperle, M.; Villemure, E.; Sun, H.-Y.; Lasserre, S.; Guimond, N.; Lecavallier, M.; Fagnou, K. *J. Am. Chem. Soc.* **2009**, *131*, 3291. (g) Michael, J. P. *Nat. Prod. Rep.* **2008**, *25*, 166. (h) Cho, S. H.; Hwang, S. J.; Chang, S. *J. Am. Chem. Soc.* **2008**, *130*, 9254.

(3) Michael, J. P. *Nat. Prod. Rep.* **2005**, *22*, 627.

(4) (a) Ivachtchenko, A. V.; Golovina, E. S.; Kadieva, M. G.; Kysil, V. M.; Mitkin, O. D.; Tkachenko, S. E.; Okun, I. M. *J. Med. Chem.* **2011**, *54*, 8161. (b) Liu, K. G.; Robichaud, A. J.; Bernotas, R. C.; Yan, Y.; Lo, J. R.; Zhang, M.-Y.; Hughes, Z. A.; Huselton, C.; Zhang, G. M.; Zhang, J. Y.; Kowal, D. M.; Smith, D. L.; Schechter, L. E.; Comery, T. A. *J. Med. Chem.* **2010**, *53*, 7639. (c) Clark, D. E.; Higgs, C.; Wren, S. P.; Dyke, H. J.; Wong, M.; Norman, D.; Lockey, P. M.; Roach, A. G. *J. Med. Chem.* **2004**, *47*, 3962. (d) Zwaagstra, M. E.; Schoenmakers, S. H. H. F.; Nederkoorn, P. H. J.; Gelens, E.; Timmerman, H.; Zhang, M.-Q. *J. Med. Chem.* **1998**, *41*, 1439.

(5) Ridley, R. G. *Nature* **2002**, *415*, 686.

(6) (a) Li, J.-S.; Gold, B. *J. Org. Chem.* **2005**, *70*, 8764. (b) Li, J.-S.; Chen, F.-X.; Shikiya, R.; Marky, L. A.; Gold, B. *J. Am. Chem. Soc.* **2005**, *127*, 12657. (c) Nakatani, K.; Sando, S.; Kumasawa, H.; Kikuchi, J.; Saito, I. *J. Am. Chem. Soc.* **2001**, *123*, 12650. (d) Nakatani, K.; Sando, S.; Saito, I. *J. Am. Chem. Soc.* **2000**, *122*, 2172.

(7) Wu, Z.; Song, H.; Cui, X.; Pi, C.; Du, W.; Wu, Y. *Org. Lett.* **2013**, *15*, 1270.

(8) Li, G.; Jia, C.; Sun, K. *Org. Lett.* **2013**, *15*, 5198.

(9) Chen, X.; Cui, X.; Yang, F.; Wu, Y. *Org. Lett.* **2015**, *17*, 1445.

(10) (a) Han, Y.-P.; Song, X.-R.; Qiu, Y.-F.; Zhang, H.-R.; Li, L.-H.; Jin, D.-P.; Sun, X.-Q.; Liu, X.-Y.; Liang, Y.-M. *Org. Lett.* **2016**, *18*, 940. (b) Song, X.-R.; Han, Y.-P.; Qiu, Y.-F.; Qiu, Z.-H.; Liu, X.-Y.; Xu, P.-F.; Liang, Y.-M. *Chem. - Eur. J.* **2014**, *20*, 12046. (c) Hosseyni, S.; Su, Y.; Shi, X. *Org. Lett.* **2015**, *17*, 6010. (d) Zhang, X.; Teo, W. T.; Sally; Chan, P. W. H. *J. Org. Chem.* **2010**, *75*, 6290.

(11) CCDC 1502039.

(12) (a) Kumar, R.; Kumar, I.; Sharma, R.; Sharma, U. *Org. Biomol. Chem.* **2016**, *14*, 2613. (b) Jin, J.-J.; Niu, H.-Y.; Qu, G.-R.; Guo, H.-M.; Fossey, J. S. *RSC Adv.* **2012**, *2*, 5968. (c) Loska, R.; Mąkosza, M. *Chem. - Eur. J.* **2008**, *14*, 2577. (d) Lewis, J. C.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2007**, *129*, 5332. (e) Heaney, F.; Lawless, E.; Mahon, M.; McArdle, P.; Cunningham, D. *Org. Biomol. Chem.* **2006**, *4*, 2408. (f) Abramovitch, R. A.; Grins, G.; Rogers, R. B.; Shinkai, I. *J. Am. Chem. Soc.* **1976**, *98*, 5671. (g) Abramovitch, R. A.; Rogers, R. B.; Singer, G. M. *J. Org. Chem.* **1975**, *40*, 41.

(13) (a) Shibata, T.; Takano, H. *Org. Chem. Front.* **2015**, *2*, 383. (b) Loska, R.; Szachowicz, K.; Szydlik, D. *Org. Lett.* **2013**, *15*, 5706. (c) Ryu, J.; Cho, S. H.; Chang, S. *Angew. Chem., Int. Ed.* **2012**, *51*, 3677. (d) Zhao, J.; Wu, C.; Li, P.; Ai, W.; Chen, H.; Wang, C.; Larock, R. C.; Shi, F. *J. Org. Chem.* **2011**, *76*, 6837. (e) Guan, B.-T.; Hou, Z. *J. Am. Chem. Soc.* **2011**, *133*, 18086. (f) Raminelli, C.; Liu, Z.; Larock, R. C. *J. Org. Chem.* **2006**, *71*, 4689. (g) Valenciano, J.; Sánchez-Pavón, E.; Cuadro, A. M.; Vaquero, J. J.; Alvarez-Builla, J. *J. Org. Chem.* **2001**, *66*, 8528.

(14) (a) Han, Y.-P.; Song, X.-R.; Qiu, Y.-F.; Li, X.-S.; Zhang, H.-R.; Zhu, X.-Y.; Liu, X.-Y.; Liang, Y.-M. *Org. Lett.* **2016**, *18*, 3866. (b) Zhao, T. S. N.; Yang, Y.; Lessing, T.; Szabó, K. J. *J. Am. Chem. Soc.* **2014**, *136*, 7563. (c) Hao, L.; Wu, F.; Ding, Z.-C.; Xu, S.-X.; Ma, Y.-L.; Chen, L.; Zhan, Z.-P. *Chem. - Eur. J.* **2012**, *18*, 6453. (d) Zhu, H.-T.; Ji, K.-G.; Yang, F.; Wang, L.-J.; Zhao, S.-C.; Ali, S.; Liu, X.-Y.; Liang, Y.-M. *Org. Lett.* **2011**, *13*, 684. (e) Wang, T.; Chen, X.-l.; Chen, L.; Zhan, Z.-p. *Org. Lett.* **2011**, *13*, 3324. (f) Wang, D.; Zhang, Y.; Harris, A.; Gautam, L. N. S.; Chen, Y.; Shi, X. *Adv. Synth. Catal.* **2011**, *353*, 2584. (g) Engel, D. A.; Dudley, G. B. *Org. Lett.* **2006**, *8*, 4027.

(15) (a) Zhang, H.; Tanimoto, H.; Morimoto, T.; Nishiyama, Y.; Kakiuchi, K. *Org. Lett.* **2013**, *15*, 5222. (b) Wang, L.; Xie, X.; Liu, Y. *Angew. Chem., Int. Ed.* **2013**, *52*, 13302. (c) Zhang, L.; Zhu, Y.; Yin, G.; Lu, P.; Wang, Y. *J. Org. Chem.* **2012**, *77*, 9510. (d) Trost, B. M.; Luan, X.; Miller, Y. *J. Am. Chem. Soc.* **2011**, *133*, 12824. (e) Pennell, M. N.; Unthank, M. G.; Turner, P.; Sheppard, T. D. *J. Org. Chem.* **2011**, *76*, 1479. (f) He, W.; Li, C.; Zhang, L. *J. Am. Chem. Soc.* **2011**, *133*, 8482.

DOI: 10.1021/acs.joc.6b02882
J. Org. Chem. 2017, 82, 1697−1704