JOC The Journal of Organic Chemistry

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One-Pot Phosphine-Catalyzed Syntheses of Quinolines

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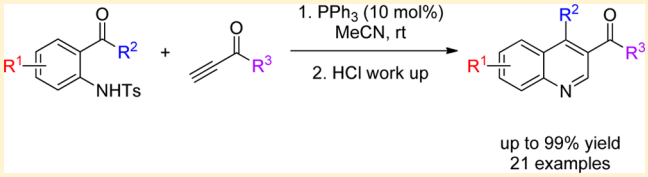
Supporting Information

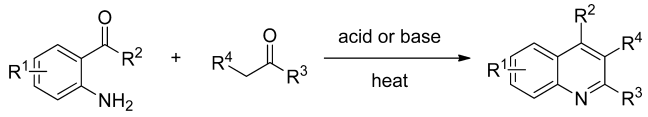
ABSTRACT: In this study we developed an efficient one-pot procedure for the preparation of 3-substituted and 3,4-disubstituted quinolines from stable starting materials (activated acetylenes reacting with *o*-tosylamidobenzaldehydes and *o*-tosylamidophenones, respectively) under mild conditions. The reaction appears to operate under a general base catalysis mechanism, instigated by the *β*-phosphonium enoate *α*-vinyl anion generated in situ through nucleophilic addition of PPh_3 to the activated alkyne. Michael addition of the deprotonated tosylamides to the activated alkynes and subsequent rapid aldol cyclization led to the formation of labile *N*-tosyldihydroquinoline intermediates. Driven by aromatization, detosylation of the dihydroquinoline intermediates occurred readily in the presence of dilute aqueous HCl to give the final quinoline products.



INTRODUCTION

The quinoline unit is found in a wide variety of pharmacologically and biologically active compounds.[1] Not surprisingly, quinoline derivatives continue to attract the attention of medicinal chemists, and strategies for accessing new scaffolds of quinoline derivatives are of great interest to synthetic chemists. In recent years, many transition metal-catalyzed processes have been developed for mild and efficient syntheses of quinolines.[2] Notably, the number of conventional metal-free paths for quinoline syntheses have also been growing.[3] Several classical methods for targeting the quinoline core, including the Skraup, Doebner–von Miller, Friedländer, Pfitzinger, Conrad–Limpach, and Combes syntheses,[4a,b] remain relevant today for the preparation of quinoline-containing materials, ligands, and pharmaceutical agents.[4a] Nevertheless, such reactions are often performed under unfavorably harsh conditions, typically with either a strong acid or base and thermal assistance.[4a,b] For example, the Friedländer quinoline synthesis, a particularly powerful tool for generating quinoline core systems, is performed at high temperature in the presence of either a strong acid or base.[4] In addition to unattractive reaction conditions, the instability of the coupling partners in the Friedländer quinoline synthesis further limits its synthetic potential.[4,5] In particular, when the synthesis of 3-substituted quinolines is attempted using Friedländer methodology (R^2 = R^3 = H), self-condensation of both aldehyde coupling partners can lower the reaction efficiency and complicate the product's purification (Scheme 1).[6] To prevent self-condensation of aminobenzaldehydes in Friedländer methodology, several classical approaches, namely the Borsche, Pfitzinger, and Niemantowski quinoline syntheses, have been developed employing alternative starting materials.[4] In a recent report, for example, aminobenzaldehydes were generated in situ from corresponding nitrobenzaldehydes and subsequently used in the Friedländer synthesis.[5]

Scheme 1. Friedländer Quinoline Synthesis



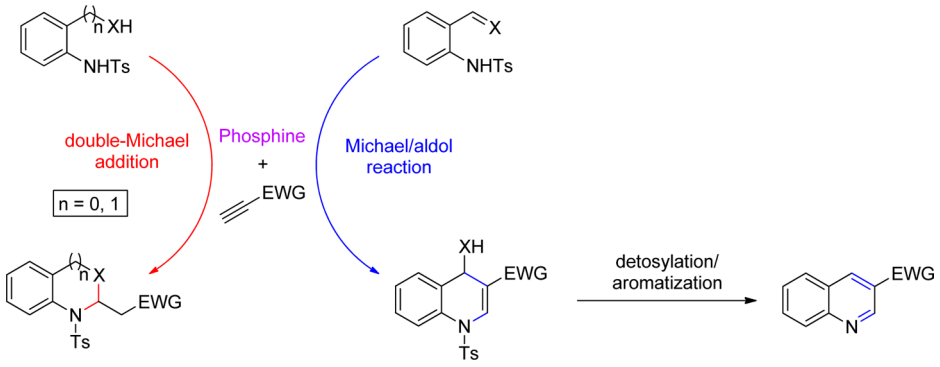
For the synthesis of 3-substituted quinolines in particular, in 2009 Verpoort reported a one-pot methodology to avoid self-condensation of the aminobenzaldehyde by employing an aminobenzyl alcohol as a precursor; they also prevented self-condensation of the other coupling partner through late introduction of the strong base.[6] This approach, however, requires an elevated temperature and a stoichiometric amount of the strong base. More recently, Li reported an alternative approach to 3-substituted quinolines by coupling alkynones with aminobenzaldehyde in the presence of a catalytic amount of Lewis acid as the activator.[7] Despite the use of a mild Lewis acid, this approach requires thermal assistance, long reaction times, and the use of unstable aminobenzaldehydes. The synthesis of 3-substituted quinolines is also generally difficult when using other methods.[4a,8] Herein, we report a simple and efficient one-pot phosphine-catalyzed procedure for the synthesis of 3-substituted quinolines under mild conditions from stable starting materials.

We developed the title quinoline synthesis during an expansion of our original double-Michael reaction.[9,10] We attempted to develop alternative modes of this tandem reaction to generate a variety of heterocyclic scaffolds (Scheme 2). The double-Michael reaction requires two pronucleophilic groups in one of the starting materials to undergo the two successive Michael additions. Replacing one pronucleophilic group with

Received: July 31, 2012
Published: August 28, 2012

dx.doi.org/10.1021/jo3015825 | J. Org. Chem. 2012, 77, 8257–8267

Scheme 2. 3-Substituted Quinoline Synthesis Versus Double-Michael Reaction

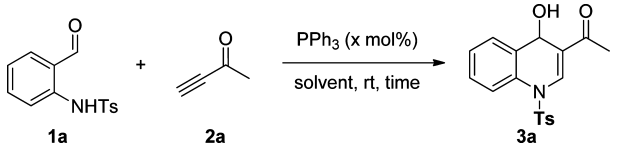


an electrophilic group would alter the nature of the reaction to a cascade of nucleophilic additions (Michael addition followed by an aldol reaction, or vice versa). The presence of an *N*-tosyl group in the substrates not only activated the pronucleophile but also completely inhibited the self-condensation normally observed for Friedländer substrates. In fact, *N*-tosylated *o*-aminobenzaldehydes are bench-stable at room temperature for months of storage without any deterioration. The activated acetylenes are likewise very stable under storage and during the reaction.

RESULTS AND DISCUSSION

In a preliminary study of the reaction, we reacted 0.1 M of *N*-tosyl-2-aminobenzaldehyde (**1a**) with 2.0 equiv of 3-butyn-2-one (**2a**) in THF in the presence of 20 mol % PPh_3 as the catalyst. We stopped the reaction prior to completion, after 17 h, for a quick evaluation of its feasibility, identifying the dihydroquinoline **3a** as the product in 28% yield (Table 1, entry 1). We suspected that the long reaction time might have caused **2a** to oligomerize in the presence of the nucleophilic catalyst PPh_3, thereby explaining the poor reaction yield. Therefore, we tested the slow addition (syringe pump, 2 h) of **2a** to the reaction mixture, but the yield was unchanged (entry 2). We observed (^{1}H NMR spectra) almost no oligomerization in a mixture of **2a** and 20 mol % PPh_3 after several days. Increasing the reaction time from 17 to 24 h barely increased the reaction yield (entry 3), implying that a significantly longer time might be required for the reaction to reach completion. Surprisingly, the addition of a stoichiometric amount of PPh_3 did not accelerate the reaction; indeed, it completely shut down the reaction and yielded no product (entry 4). ^{1}H NMR spectra revealed the complete destruction of **2a** within 5 min in the presence of a stoichiometric amount of PPh_3. When the concentration of **1a** was increased to 0.2 M or greater, the reaction yield improved significantly (entries 1 and 5–7). Among the solvents tested for the reaction, MeCN provided the highest yield (entry 8); reactions performed in DMSO and DCM (data not shown) provided product yields lower than those obtained in THF and MeCN. The reactions of **1a** in THF at concentrations of 0.4 and 0.2 M resulted in the same yields (entries 6 and 7). Because **1a** is not soluble in MeCN at a concentration of 0.4 M, we considered the optimal concentration of **1a** in MeCN to be 0.2 M. Decreasing the loading of the catalyst PPh_3 to 10 mol % improved the reaction yield by 4% (entry 10). The reaction yield decreased, however, after decreasing the catalyst loading of 5 mol % (entry 11). Increasing the number of equivalents of the activated acetylene **2a** did not improve the reaction performance (entry 12). Careful monitoring revealed that the reaction required only 4 h to reach completion in MeCN (entry 13). Finally, decreasing the amount of **2a** to 1.5 equiv did not change the reaction yield (entry 14), but it did drop dramatically to 14% when we used 1.2 equiv of **2a** (entry 15).

Table 1. Optimization of Dihydroquinoline Synthesis[a]



1a **2a** **3a**

entry	**2a** (equiv)	PPh_3 (mol %)	solvent	concentration[b] (M)	time (h)	yield (%)
1	2.0	20	THF	0.1	17	28
2[c]	2.0	20	THF	0.1	17	28
3	2.0	20	THF	0.1	24	32
4	2.0	100	THF	0.1	24	0
5	2.0	20	THF	0.05	17	25
6	2.0	20	THF	0.2	17	67
7	2.0	20	THF	0.4	17	68
8	2.0	20	MeCN	0.2	17	71
9	2.0	20	MeCN	0.4	N/A[d]	N/A[d]
10	2.0	10	MeCN	0.2	17	75
11	2.0	5	MeCN	0.2	17	49
12	2.5	5	MeCN	0.2	17	47
13	2.0	10	MeCN	0.2	4	76
14	1.5	10	MeCN	0.2	4	76
15	1.2	10	MeCN	0.2	4	14

[a]Butynone **2a** was added in one portion to a solution of **1a** and PPh_3 in the indicated solvent. [b]Concentration of the aldehyde **1a**. [c]Addition of butynone **2a** over 2 h via syringe pump. [d]Not available.

The isolated dihydroquinoline adduct **3a** was unstable and readily decomposed at room temperature.[3a] Treating the vinylogous hemiaminal with acetyl chloride and pyridine resulted in the clean production of the stable quinoline **4a** in excellent yield (Scheme 3a). In this two-pot procedure, decomposition of the unstable dihydroquinoline **3a** during its isolation resulted in a lower yield of the quinoline product **4a**. Such loss could be avoided through a one-pot procedure to directly convert the unstable dihydroquinoline intermediate into the corresponding quinoline. The ideal reagent for such a procedure would necessarily contain a "chloride" to trap the tosyl group in the form of the byproduct TsCl; in addition, it should transform the OH group into a good leaving group. Hydrogen chloride met these requirements; simply quenching

dx.doi.org/10.1021/jo3015825 | J. Org. Chem. 2012, 77, 8257–8267

Scheme 3. (a) Quinoline Formation from Dihydroquinoline, (b) One-Pot Phosphine-Catalyzed Synthesis of Quinoline

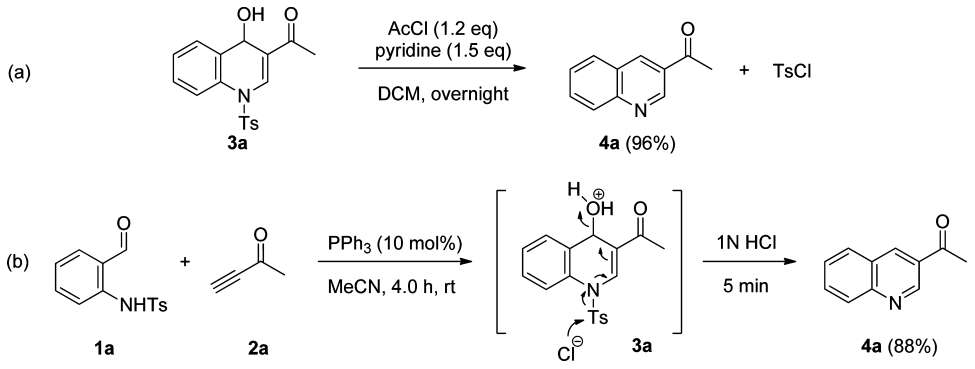
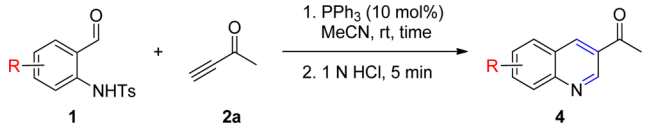
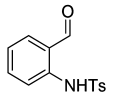
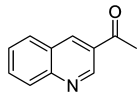
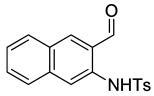
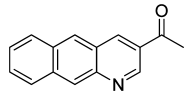
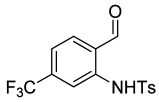
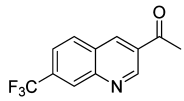
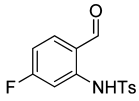
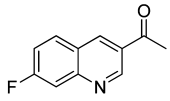
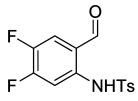
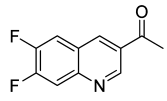
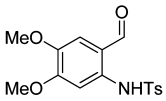
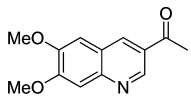
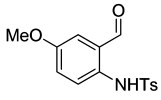
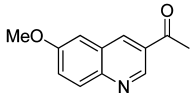


Table 2. One-Pot Phosphine-Catalyzed Syntheses of Substituted 3-Acetylquinolines[a]



entry	substrate		product		time (h)	yield (%)[b]
1		**1a**		**4a**	4	88
2		**1b**		**4b**	5	89
3		**1c**		**4c**	19	94
4		**1d**		**4d**	19	96
5		**1e**		**4e**	11	95
6		**1f**		**4f**	1.5	99
7		**1g**		**4g**	1.5	92

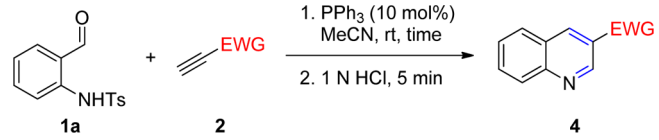
[a]**2a** (1.5 equiv) was added in one portion to a solution of **1** (0.2 M) and PPh_3 (10 mol %) in MeCN. [b]Isolated yield.

the reaction with 1 M aqueous HCl provided the quinoline **4a** in 88% yield together with TsCl as a byproduct (Scheme 3b). This higher yield for the isolated quinoline relative to that of the isolated dihydroquinoline confirmed the loss of the latter product through decomposition in the two-pot procedure.

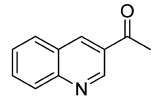
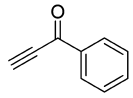
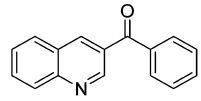
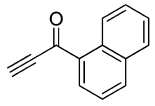
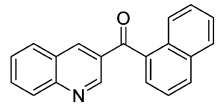
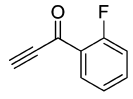
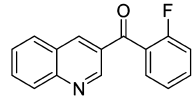
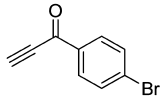
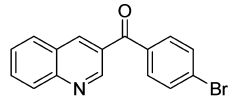
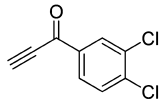
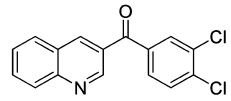
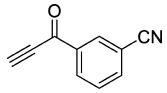
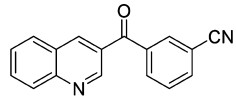
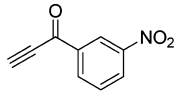
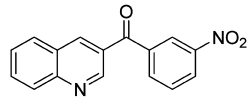
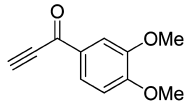
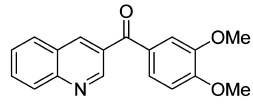
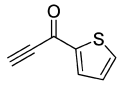
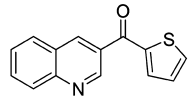
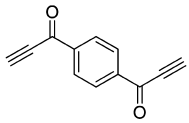
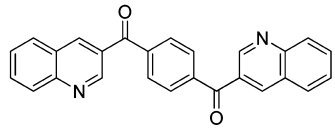
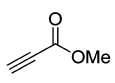
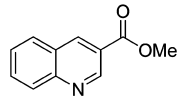
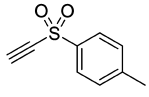
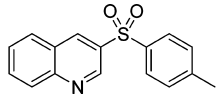
Having optimized the one-pot procedure for the synthesis of the 3-substituted quinoline, we further examined the scope of this reaction for the synthesis of 3-acetylquinolines (Table 2). Regardless of the electron-donating or -withdrawing ability of the substituents on the aminobenzaldehyde, the reactions were highly efficient, generating the desired quinolines in high yields. Nevertheless, the nature of the substituents had a significant impact on the rate of the reaction. The reaction of the nonsubstituted *N*-tosyl-2-aminobenzaldehyde (**1a**) reached completion within 4 h in 88% yield (entry 1). The electronically similar *N*-tosyl-3-amino-2-naphthaldehyde (**1b**) was converted into the quinoline **4b** in a comparable yield of 89% after a similar reaction time of 5 h (entry 2). The presence

dx.doi.org/10.1021/jo3015825 | J. Org. Chem. 2012, 77, 8257−8267

Table 3. One-Pot Phosphine-Catalyzed Syntheses of 3-Substituted Quinolines[a]



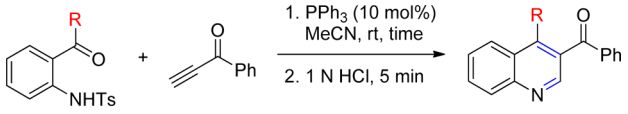
1a 2 4

entry	substrate		product		time (min)	yield (%)[b]
1		**2a**		**4a**	240	88
2		**2h**		**4h**	30	95
3		**2i**		**4i**	20	99
4		**2j**		**4j**	5	98
5		**2k**		**4k**	5	98
6		**2l**		**4l**	5	97
7		**2m**		**4m**	5	96
8		**2n**		**4n**	5	98
9		**2o**		**4o**	90	93
10		**2p**		**4p**	40	86
11[c]		**2q**		**4q**	5	63
12		**2r**		**4r**	600	61
13		**2s**		**4s**	5	30

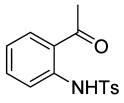
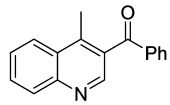
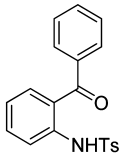
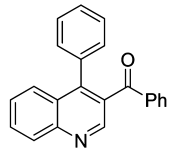
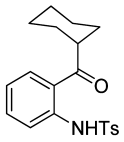
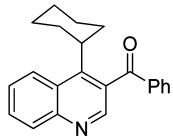
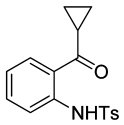
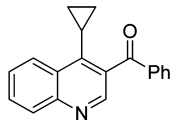
[a]**2** (1.5 equiv) was added in one portion to a solution of **1a** (0.2 M) and PPh_3 (10 mol %) in MeCN. [b]Isolated yield. [c]Diacetylene **2q** (0.10 mmol) was added to a solution of **1a** (0.21 mmol, 0.21 M) and PPh_3 (20 mol %) in MeCN.

dx.doi.org/10.1021/jo3015825 | J. Org. Chem. 2012, 77, 8257−8267

Table 4. One-Pot Phosphine-Catalyzed Syntheses of 3,4-Disubstituted Quinolines[a]



1 2b 4

entry	substrate		product		time (h)	yield (%)[b]
1		**1t**		**4t**	3.5	79
2		**1u**		**4u**	3.5	72
3		**1v**		**4v**	6.5	75
4		**1w**		**4w**	2.5	67

[a]**2b** (1.5 equiv) was added in one portion to a solution of **1** (0.2 M) and PPh_3 (10 mol %) in MeCN. [b]Isolated yield.

of electron-withdrawing groups significantly slowed the rates of the reactions (entries 3−5), whereas electron-donating groups accelerated them (entries 6 and 7). In general, the presence of a substituent, regardless of its electronic nature, had a positive impact on the yield of the reaction (entry 1 vs entries 2−7).

The successful syntheses of the 3-acetylquinolines in Table 2 encouraged us to expand the scope of the reaction to include other 3-substituted quinolines (Table 3). In general, the reaction was highly efficient for acetylenic ketones but much less efficient for other activated alkynes (entries 1−10 vs entries 12 and 13). We obtained lower yields for the reactions performed with methyl propiolate or an acetylenic sulfone, due to formation of the corresponding simple Michael adducts with the aldehyde functionality intact (entries 12 and 13). With regard to the acetylenic ketone, the reactions of aryl acetylenyl ketones were faster and provided higher yields than those of alkyl acetylenyl ketones (entry 1 vs entries 2−9). The electronic nature of the aryl group of the acetylenic ketone greatly impacted the reaction rate and yield. With electron-deficient aryl groups, the reactions required only a few minutes to reach completion in excellent yields (entry 2 vs entries 3−8 and 11). In contrast, electron-rich aryl groups prolonged the reaction and resulted in excellent but lower yields (entry 2 vs entries 9 and 10). We also examined the versatility of the reaction when using a multifunctional acetylenic ketone, namely a bis(acetylenic ketone); here, the reaction proceeded smoothly to form the bisquinoline product in good yield (entry 11).

We further expanded the scope of the reaction to include less-reactive *o*-aminophenones as partners for the syntheses of 3,4-disubstituted quinolines. The reactions afforded the desired products, albeit in lower yields after longer reaction times (Table 3, entry 2 vs Table 4). Longer reaction times were expected because of the lower reactivity of ketones relative to corresponding aldehydes. Among the selected *o*-aminophenones, those with larger R groups required the longest reaction times (entry 3 vs entries 1, 2 and 4), although the size of the R group had only a minor impact on the reaction yield (entries 1−4).

MECHANISTIC DISCUSSION

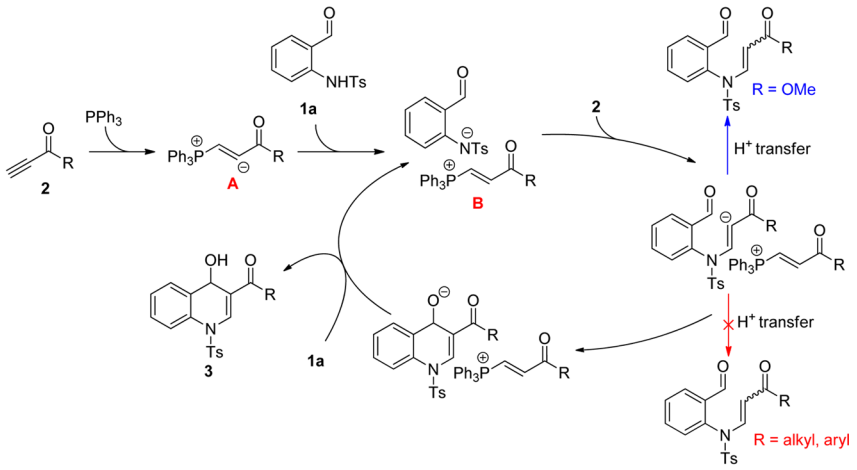
Scheme 4 outlines three possible mechanistic scenarios. Mechanism 1 involves a general base catalysis. Nucleophilic addition of the free phosphine to the activated alkyne results in the phosphonium allenolate **A**, which acts as a base to activate the pronucleophile through deprotonation, resulting in a subsequent general base-catalyzed Michael/aldol reaction. Mechanism 2 is based on a nucleophilic phosphine catalysis, in which the phosphine is consumed and regenerated along the catalytic cycle; the ion pair **B**, which is also generated in mechanism 1, is presumably associated in a sufficiently tight manner to enforce the nucleophilic addition within the ion pair.[9] Mechanism 3 is also based on a nucleophilic phosphine catalysis, where the aldol addition occurs immediately after the formation of the phosphonium allenolate **A**; hence, the ion pair **B** is not formed.

Because we isolated the Michael adduct together with the quinoline product in the reaction of methyl propiolate (Table 3, entry 12),[11] we speculate that mechanism 3 was most unlikely to operate. As indicated in Table 5, the reaction

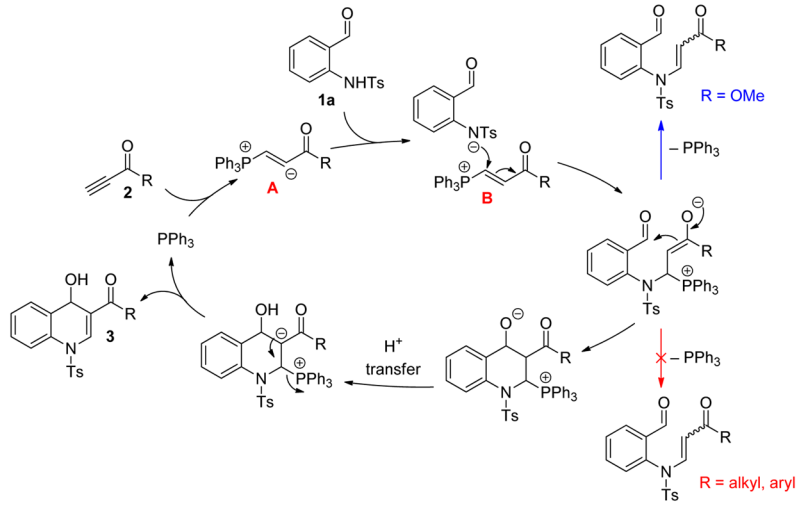
dx.doi.org/10.1021/jo3015825 | J. Org. Chem. 2012, 77, 8257−8267

Scheme 4. Possible Mechanistic Schemes for Phosphine-Catalyzed Dihydroquinoline Formation

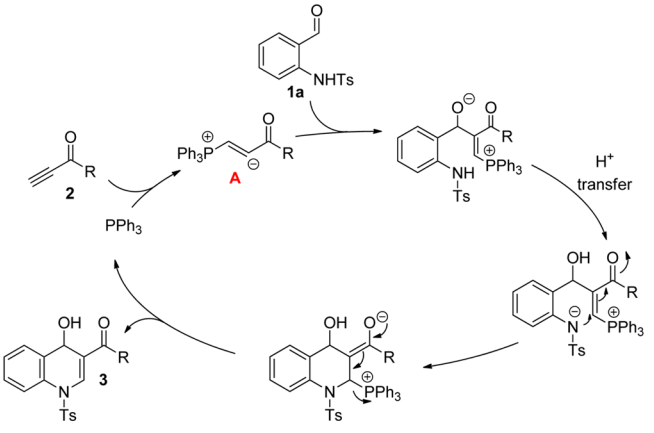
(a) Mechanism 1: Michael/Aldol tandem reaction



(b) Mechanism 2: Michael/Morita–Baylis–Hillman tandem reaction



(c) Mechanism 3: Aldol/Michael tandem reaction

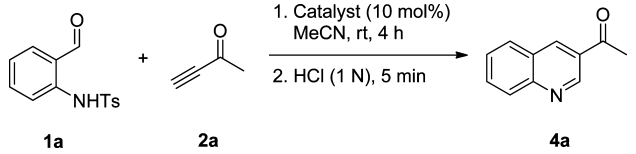


proceeded to form the quinoline product in the presence of a catalytic amount of a non-nucleophilic base. This result supports the operation of the general base catalysis mechanism in this reaction.

In the hopes of seeing reaction intermediates that could help to identify the true mechanistic pathway out of the three possibilities discussed above, we used NMR spectroscopy to monitor the reaction between **1a** and **2a** in the presence of 10 mol % PPh_3 in CD_3CN; unfortunately, no intermediates were evident at any time during the course of the reaction. The ^1H NMR spectra of the reaction mixture revealed that the signal for the NH unit of reactant **1a** disappeared within 10 min (Figure 1C). Apparently, the reaction was initiated rapidly in MeCN with partial deprotonation of the NH group; fast proton exchange made the NH proton undetectable, on the time scale of ^1H NMR spectroscopy, at 10.83 ppm (the presence of *N*-

dx.doi.org/10.1021/jo3015825 | J. Org. Chem. 2012, 77, 8257–8267

Table 5. Non-Nucleophilic Base Catalysis for Dihydroquinoline Synthesis



1a **2a** **4a**

entry	catalyst	yield (%)[a]
1[b]	K_2CO_3	69
2[b]	Cs_2CO_3	71
3	1 M aq NaOH	58

[a]Isolated yield. [b]Heterogeneous reaction mixture.

tosylaminobenzaldehyde **1a** was verified through TLC analysis during the reaction period). At the same time, two new signals, corresponding to protons H^a and H^b of the dihydroquinoline adduct, were growing (Figures 1C–F). Because of rapid proton exchange, the proton of the OH group of the dihydroquinoline product was also undetectable in the ^1H NMR spectra recorded throughout the course of the reaction. In general, only the starting materials and the final dihydroquinoline products were evident (i.e., no intermediates were observed) at any time during the reactions monitored using ^1H NMR spectroscopy.

CONCLUSION

We have developed an efficient one-pot procedure for the syntheses of 3-substituted and 3,4-disubstituted quinolines from the reactions of activated acetylenes with *N*-tosyl-2-amino-

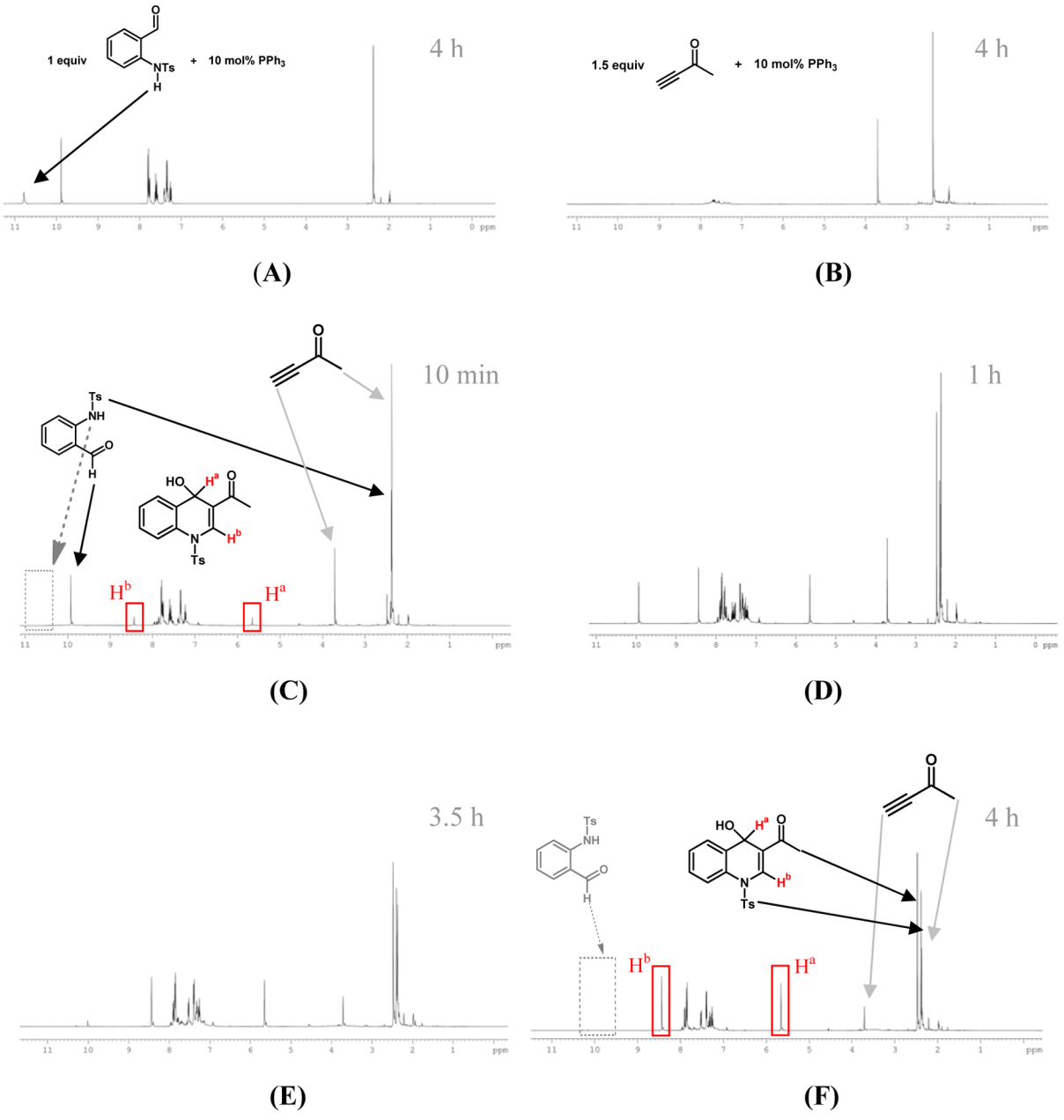


Figure 1. ^1H NMR spectra revealing the formation of the dihydroquinoline **3a**. (A, B) Control experiments performed without (A) 3-butyn-2-one (**2a**) or (B) *N*-tosyl-2-aminobenzaldehyde (**1a**) in the reaction mixture; spectra recorded after 4 h. (C–F) Spectra of the reaction proper after (C) 10 min, (D) 1 h, (E) 3.5 h, and (F) 4 h.

dx.doi.org/10.1021/jo3015825 | J. Org. Chem. 2012, 77, 8257–8267

benzaldehydes and *N*-tosyl-2-aminobenzophenones, respectively. This approach provides a convenient and direct route toward 3-substituted quinolines, which are challenging to prepare using other methods. The reaction conditions are mild, and many different substituents can be introduced without compromising yields.

EXPERIMENTAL SECTION

General Information. All reactions were performed in dry solvents under an Ar atmosphere and anhydrous conditions, unless otherwise indicated. DCM, THF, and MeCN were freshly distilled over CaH_2 prior to use. Anhydrous DMSO was used as received from a commercial source. All other reagents were used as received from commercial sources. Reactions were monitored through thin layer chromatography (TLC) on 0.25-mm SiliCycle silica gel plates and visualized under UV light and with permanganate or 2,4-dinitrophenylhydrazine (DNP) staining. Flash column chromatography (FCC) was performed using SiliCycle Silica-P Flash silica gel (60-Å pore size, 40−63 μm). IR spectra were recorded using a Jasco FT-IR 4100 spectrometer. NMR spectra of the dihydroquinoline **3a** were obtained using Bruker Avance-500 instruments, calibrated to residual THF-d_8 as the internal reference (1.73 and 3.58 ppm for ^{1}H NMR spectra; 25.4 and 67.6 ppm for ^{13}C NMR spectra). NMR spectra of the quinolines **4** were recorded using Bruker Avance-500 instruments, calibrated to $CD(H)Cl_3$ as the internal reference (7.26 and 77.0 ppm for ^{1}H and ^{13}C NMR spectra, respectively). ^{1}H NMR spectral data are reported in terms of chemical shift (δ, ppm), multiplicity, coupling constant (Hz), and integration. ^{13}C NMR spectral data are reported in terms of chemical shift (δ, ppm) and multiplicity, with the coupling constant (Hz) in the case of J_{CF} coupling. The following abbreviations indicate the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. High resolution mass spectra were recorded using a Waters LCT Premier XE time-of-flight instrument controlled by MassLynx 4.1 software. Samples were infused using direct loop injection from a Waters Acquity UPLC into the multi-mode ionization source. The lock mass standard for accurate mass determination was leucine enkephalin (Sigma L9133).

General Procedure for the Syntheses of Substrates 1. The *N*-tosylbenzaldehydes **1a−g** were prepared from the corresponding anthranilic acids in three steps without purification of any intermediates.[12] The *N*-tosyl-*o*-aminophenones **1t** and **1u** were prepared directly from the corresponding *o*-aminophenones through a single tosylation step.[13] The *N*-tosyl-*o*-aminophenones **1v** and **1w** were prepared from the corresponding 2-aminobenzonitriles in two steps, without purification of any intermediates.[14]

Syntheses of Substrates 2. The activated acetylene **2** were prepared in two steps, without purification of any intermediates, according to reported procedures.[15]

General Procedure for the Syntheses of Quinolines. *o*-Aminobenzaldehyde (**1**, 0.2 mmol), PPh_3 (5.3 mg, 10 mol %), and MeCN (1 mL) were added sequentially to a flame-dried flask (10 mL); unless otherwise noted, the mixture was stirred until complete dissolution occurred. The activated acetylene **2** (0.3 mmol) was added in one portion, and then the mixture was stirred under Ar at room temperature. Upon completion of the reaction, 1 M aqueous HCl (1 mL) was added, and then the mixture was stirred for 5 min before saturated aqueous $NaHCO_3$ (1 mL) was added to neutralize the mixture. The mixture was poured into a separatory funnel along with DCM (10 mL) and saturated aqueous $NaHCO_3$ (10 mL). The aqueous phase was separated and extracted with DCM (2 mL). The combined organic phases were dried (Na_2SO_4) and concentrated in vacuo; the residue was purified through flash column chromatography [ethyl acetate (EtOAc)/hexanes (Hex), 3:7, unless specified otherwise] to afford the desired quinoline product.

*1-(1-Tosyl-1,4-dihydroquinolin-3-yl)ethanone (**3a**).* To a flame-dried flask (10 mL) were sequentially added *N*-tosyl 2-aminobenzaldehyde (**1a**) (0.2 mmol), PPh_3 (5.3 mg, 10 mol %), and MeCN (1 mL). The mixture was stirred until complete dissolution, and then 3-butyn-2-one (**2**) (23.5 μL, 0.3 mmol) was added in one portion. The mixture was stirred under argon at room temperature; upon completion of the reaction (4.0−4.5 h), the mixture was concentrated in vacuo and purified through flash column chromatography (gradient EtOAc/Hex, 3:7 to 1L1) to furnish a slightly yellow solid (52.1 mg, 76% yield): IR (film) ν_{max} 3391, 3088, 3050, 3006, 2923, 1645, 1632, 1597, 1566, 1485, 1456, 1343, 1210, 1160, 1088, 1017, 1009 cm^{-1}; ^{1}H NMR (500 MHz, THF-d_8) δ 7.81 (d, J = 8.1 Hz, 1H), 7.41−7.37 (m, 4H), 7.32 (s, 1H), 7.21 (t, J = 7.7 Hz, 1H), 7.15 (d, J = 8.2 Hz, 2H), 6.81 (d, J = 6.1 Hz, 1H), 5.85 (d, J = 6.1 Hz, 1H), 2.32 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (125 MHz, THF-d_8) δ 194.2, 143.3, 137.0, 135.0, 134.2, 132.2, 130.0, 128.9, 128.8, 126.5, 125.6, 124.8, 124.6, 73.3, 24.1, 20.2; HRMS (ESI-TOF) m/z [M − OH]$^+$ Calcd for $C_{18}H_{16}NO_3S$ 326.0851, found 326.0847.

*1-(Quinolin-3-yl)ethanone (**4a**).*[16] 30.1 mg, 88% yield; slightly yellow solid: mp 98−99 °C; IR (film) ν_{max} 3065, 3009, 2920, 1681, 1615, 1587, 1571, 1493, 1371 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.42 (s, 1H), 8.69 (s, 1H), 8.15 (d, J = 8.5 Hz, 1H), 7.93 (d, J = 8.0 Hz, 1H), 7.83 (t, J = 7.5 Hz, 1H), 7.62 (t, J = 7.5 Hz, 1H), 2.73 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.5, 149.5, 149.0, 137.3, 131.9, 129.22, 129.19, 129.1, 127.5, 126.7, 26.7; HRMS (ESI-TOF) m/z [M + H]$^+$ Calcd for $C_{11}H_{10}NO$ 172.0762, found 172.0762.

*1-(Benzo[g]quinolin-3-yl)ethanone (**4b**).* 39.5 mg, 89% yield; bright yellow solid: mp 150−152 °C; IR (film) ν_{max} 3046, 2998, 2922, 1676, 1612, 1532, 1352, 1215 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.47 (s, 1H), 8.84 (s, 1H), 8.70 (s, 1H), 8.51 (s, 1H), 8.10 (d, J = 8.5 Hz, 1H), 8.06 (d, J = 8.5 Hz, 1H), 7.62−7.55 (m, 2H), 2.76 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.5, 149.5, 149.0, 137.3, 131.9, 129.22, 129.19, 129.1, 127.5, 126.7, 26.7; HRMS (ESI-TOF) m/z [M + H]$^+$ Calcd for $C_{15}H_{12}NO$ 222.0919, found 222.0921.

*1-[7-(Trifluoromethyl)quinolin-3-yl]ethanone (**4c**).* 44.8 mg, 94% yield; white crystalline solid: mp 126−127 °C; IR (film) ν_{max} 3059, 3020, 2929, 1689, 1594, 1464, 1124 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.50 (s, 1H), 8.75 (s, 1H), 8.45 (s, 1H), 8.08 (d, J = 8.5 Hz, 1H), 7.80 (d, J = 8.5 Hz, 1H), 2.77 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.1, 150.4, 148.7, 136.8, 133.3 (q, J = 32.9 Hz), 130.5, 130.4, 128.3, 127.2 (q, J = 4.4 Hz), 123.5 (q, J = 271.0 Hz), 123.1 (q, J = 4.5 Hz), 26.8; HRMS (ESI-TOF) m/z [M + H]$^+$ Calcd for $C_{12}H_9F_3NO$ 240.0636, found 240.0632.

*1-(7-Fluoroquinolin-3-yl)ethanone (**4d**).* 36.4 mg, 96%; white solid: mp 116−118 °C; IR (film) ν_{max} 3051, 2923, 1670, 1619, 1602, 1579, 1274, 1193 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.42 (s, 1H), 8.70 (s, 1H), 7.95 (dd, J = 8.9, 5.1 Hz, 1H), 7.77 (dd, J = 9.8, 2.3 Hz, 1H), 7.42 (dt, J = 8.7, 2.5, 1H), 2.73 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.2, 164.5 (d, J = 254.8 Hz), 150.9 (d, J = 12.7 Hz), 150.2, 140.0, 131.5 (d, J = 10.5 Hz), 128.8, 123.8, 118.2 (d, J = 25.7 Hz), 113.3 (d, J = 20.7 Hz), 26.7; HRMS (ESI-TOF) m/z [M + H]$^+$ Calcd for $C_{11}H_9FNO$ 190.0668, found 190.0670.

*1-(6,7-Difluoroquinolin-3-yl)ethanone (**4e**).* 39.5 mg, 95% yield; white solid: mp 151−153 °C; IR (film) ν_{max} 3061, 2923, 1682, 1595, 1505, 1475, 1347, 1253, 1234 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.39 (s, 1H), 8.65 (s, 1H), 8.45 (s, 1H), 7.90 (dd, J = 7.7, 7.7 Hz, 1H), 7.68 (dd, J = 8.3, 8.3 Hz, 1H), 2.74 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.0, 153.7 (dd, J = 257.0, 17.8 Hz), 150.6 (dd, J = 257.0, 17.8 Hz), 147.1 (d, J = 11.2 Hz), 136.2, 129.3, 123.8 (d, J = 7.1 Hz), 115.9 (d, J = 17.2 Hz), 114.3 (d, J = 17.2 Hz), 26.7; HRMS (ESI-TOF) m/z [M + H]$^+$ Calcd for $C_{11}H_8F_2NO$ 208.0574, found 208.0584.

*1-(6,7-Dimethoxyquinolin-3-yl)ethanone (**4f**).*[17] EtOAc/Hex, 1:1. 45.7 mg, 99% yield; white solid: mp 160−163 °C; IR (film) ν_{max} 3008, 2960, 2925, 2831, 1667, 1597, 1504, 1438, 1427, 1228, 1144, 1003 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.24 (s, 1H), 8.56 (s, 1H), 7.46 (s, 1H), 7.14 (s, 1H), 4.06 (s, 3H), 4.03 (s, 3H), 2.71 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.6, 154.4, 150.4, 147.4, 147.3, 135.0, 127.9, 122.4, 107.8, 106.0, 56.2, 56.0, 26.6; HRMS (ESI-TOF) m/z [M + H]$^+$ Calcd for $C_{13}H_{14}NO_3$ 232.0974, found 232.0964.

*1-(6-Methoxyquinolin-3-yl)ethanone (**4g**).* 37.1 mg, 92% yield; light-yellow solid: mp 122−124 °C; IR (film) ν_{max} 2956, 2923, 2852, 1682, 1619, 1595, 1503, 1368, 1227, 1023 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.25 (s, 1H), 8.57 (s, 1H), 8.02 (d, J = 9.0 Hz, 1H), 7.45

dx.doi.org/10.1021/jo3015825 | J. Org. Chem. 2012, 77, 8257−8267

(dd, J = 9.0, 2.5 Hz, 1H), 7.14 (d, J = 2.5 Hz, 1H), 3.93 (s, 3H), 2.71 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.8, 158.3, 146.7, 146.0, 135.8, 130.6, 129.4, 127.9, 127.8, 124.8, 55.5, 26.8; HRMS (ESI-TOF) m/z [M + H]$^+$ Calcd for $C_{12}H_{12}NO_2$ 202.0868, found 202.0870.

*Phenyl(quinolin-3-yl)methanone (**4h**).*[7] 44.2 mg, 95% yield; crystalline yellow solid: mp 73−75 °C; IR (film) ν_{max} 3052, 1647, 1616, 1597, 1571, 1287, 1243 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.33 (s, 1H), 8.56 (s, 1H), 8.20 (d, J = 8.0 Hz, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.88−7.86 (m, 3H), 7.69−7.63 (m, 2H), 7.58−7.48 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.8, 150.3, 149.4, 138.7, 136.9, 133.0, 131.8, 129.97, 129.95, 129.4, 129.1, 128.6, 127.5, 126.5; HRMS (ESI-TOF) m/z [M + H]$^+$ Calcd for $C_{16}H_{12}NO$ 234.0919, found 234.0915.

*Naphth-1-yl(quinolin-3-yl)methanone (**4i**).*[7] 56.3 mg, 99% yield; pale-yellow oil: IR (film) ν_{max} 3051, 1652, 1616, 1589, 1568, 1493, 1286, 1237, 1186 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.43 (s, 1H), 8.54 (s, 1H), 8.21−8.19 (m, 2H), 8.08 (d, J = 8.2 Hz, 1H), 7.96 (d, J = 8.2 Hz, 1H), 7.87−7.84 (m, 2H), 7.66 (d, J = 7.1 Hz, 1H), 7.62−7.53 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.3, 150.4, 149.7, 139.5, 135.2, 133.8, 132.0, 130.8, 130.7, 129.4, 129.3, 128.5, 128.4, 127.6, 127.5, 126.7, 126.6, 125.4, 124.3; HRMS (ESI-TOF) m/z [M + H]$^+$ Calcd for $C_{20}H_{14}NO$ 284.1075, found 284.1072.

*2-Fluorophenyl(quinolin-3-yl)methanone (**4j**).* 49.2 mg, 98% yield; light-yellow solid: mp 84−86 °C; IR (film) ν_{max} 3086, 1664, 1610, 1595, 1568, 1448, 1296, 1213 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.33 (s, 1H), 8.54 (s, 1H), 8.16 (d, J = 8.8 Hz, 1H), 7.90 (d, J = 7.9 Hz, 1H), 7.84 (t, J = 7.8 Hz, 1H), 7.66 (d, J = 14.1 Hz, 1H), 7.62−7.59 (m, 2H), 7.33 (t, J = 7.9 Hz, 1H), 7.20 (t, J = 8.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 191.7, 160.1 (d, J = 253.6 Hz), 149.7, 138.9, 133.9 (d, J = 8.4 Hz), 132.1, 130.9 (d, J = 2.7 Hz), 129.9, 129.4 (d, J = 10.1 Hz), 127.5, 126.6, 126.0 (d, J = 14.4 Hz), 124.6 (d, J = 3.8 Hz), 116.4 (d, J = 21.8 Hz); HRMS (ESI-TOF) m/z [M + H]$^+$ Calcd for $C_{16}H_{11}FNO$ 252.0825, found 252.0829.

*4-Bromophenyl(quinolin-3-yl)methanone (**4k**).* 61.2 mg, 98% yield; white crystalline solid: mp 115−117 °C; IR (film) ν_{max} 3090, 3056, 1645, 1618, 1584, 1566, 1491, 1366, 1231, 1168, 1069 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.30 (s, 1H), 8.53 (s, 1H), 8.20 (d, J = 8.1 Hz, 1H), 7.92 (d, J = 8.1 Hz, 1H), 7.87 (t, J = 8.1 Hz, 1H), 7.74 (d, J = 8.5 Hz, 2H), 7.69 (d, J = 8.5 Hz, 2H), 7.65 (t, J = 8.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.7, 150.0, 149.5, 138.6, 135.7, 131.94, 131.92, 131.4, 129.6, 129.5, 129.1, 128.2, 127.6, 126.4; HRMS (ESI-TOF) m/z [M + H]$^+$ Calcd for $C_{16}H_{11}BrNO$ 312.0024, found 312.0013.

*3,4-Dichlorophenyl(quinolin-3-yl)methanone (**4l**).* 58.4 mg, 97% yield; light-yellow solid: mp 112−113 °C; IR (film) ν_{max} 3076, 1637, 1617, 1577, 1385, 1293, 1238 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.28 (d, J = 1.9 Hz, 1H), 8.52 (d, J = 1.9 Hz, 1H), 8.19 (d, J = 7.9 Hz, 1H), 7.95−7.92 (m, 2H), 7.87 (ddd, J = 8.5, 7.0, 1.3 Hz, 1H), 7.69−7.61 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.4, 149.8, 149.6, 138.7, 136.5, 133.4, 132.1, 131.6, 130.7, 129.5, 129.12, 129.10, 128.9, 127.8, 126.4; HRMS (ESI-TOF) m/z [M + H]$^+$ Calcd for $C_{16}H_{10}Cl_2NO$ 302.0139, found 302.0135.

*3-(Quinoline-3-carbonyl)benzonitrile (**4m**).* 49.5 mg, 96% yield; off-white crystalline solid: mp 105−107 °C; IR (film) ν_{max} 3067, 2227, 1653, 1616, 1596, 1567, 1291, 1179 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.30 (d, J = 2.7 Hz, 1H), 8.53 (d, J = 2.7 Hz, 1H), 8.21 (d, J = 10.6 Hz, 1H), 8.14 (s, 1H), 8.09 (dt, J = 9.8, 1.9 Hz, 1H), 7.95−7.92 (m, 2H), 7.89 (t, J = 9.7 Hz, 1H), 7.69 (q, J = 10.1 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.6, 149.74, 149.66, 138.9, 137.9, 135.8, 133.7, 133.2, 132.4, 129.6, 129.5, 129.2, 128.7, 127.9, 126.3, 117.6, 113.2; HRMS (ESI-TOF) m/z [M + H]$^+$ Calcd for $C_{17}H_{11}N_2O$ 259.0871, found 259.0882.

*3-Nitrophenyl(quinolin-3-yl)methanone (**4n**).* 54.6 mg, 98% yield; white solid: mp 138−140 °C; IR (film) ν_{max} 3086, 1642, 1612, 1527, 1491, 1346, 1285 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.31 (s, 1H), 8.69 (s, 1H), 8.56 (s, 1H), 8.50 (d, J = 8.5 Hz, 1H), 8.20 (t, J = 7.3 Hz, 2H), 7.94 (d, J = 8.5 Hz, 1H), 7.90 (t, J = 7.3 Hz, 1H), 7.77 (t, J = 7.3 Hz, 1H), 7.67 (t, J = 7.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.4, 149.71, 149.70, 148.2, 138.9, 138.3, 135.3, 132.4, 129.9, 129.5, 129.2, 128.7, 127.9, 127.2, 126.4, 124.5; HRMS (ESI-TOF) m/z [M + H]$^+$ Calcd for $C_{16}H_{11}N_2O_3$ 279.0770, found 279.0776.

*3,4-Dimethoxyphenyl(quinolin-3-yl)methanone (**4o**).* 54.6 mg, 93% yield; white solid: mp 93−95 °C; IR (film) ν_{max} 3042, 2995, 2934, 1637, 1592, 1580, 1513, 1418, 1295, 1264, 1247, 1228, 1143, 1113, 1020 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.28 (d, J = 1.3 Hz, 1H), 8.54 (d, J = 1.3 Hz, 1H), 8.20 (d, J = 8.4 Hz, 1H), 7.93 (d, J = 8.1 Hz, 1H), 7.85 (t, J = 8.2 Hz, 1H), 7.65 (t, J = 8.2 Hz, 1H), 7.55 (s, 1H), 7.42 (d, J = 8.1 Hz, 1H), 6.94 (d, J = 8.4 Hz, 1H), 3.99 (s, 3H), 3.97 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.1, 150.4, 148.7, 136.8, 131.9, 129.22, 129.19, 129.1, 127.5, 126.7, 26.7; HRMS (ESI-TOF) m/z [M + H]$^+$ Calcd for $C_{18}H_{16}NO_3$ 294.1130, found 294.1130.

*Quinolin-3-yl(thien-2-yl)methanone (**4p**).*[7] 41.1 mg, 86% yield; white solid: mp 89−91 °C; IR (film) ν_{max} 3102, 3065, 1629, 1617, 1588, 1517, 1492, 1410, 1366, 1292, 1251, 1062 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.33 (s, 1H), 8.64 (s, 1H), 8.18 (d, J = 8.9 Hz, 1H), 7.93 (d, J = 8.9 Hz, 1H), 7.84 (t, J = 7.2 Hz, 1H), 7.79 (d, J = 5.0 Hz, 1H), 7.70 (d, J = 5.0 Hz, 1H), 7.64 (t, J = 7.5 Hz, 1H), 7.21 (t, J = 5.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 186.1, 149.5, 149.3, 143.1, 137.7, 135.01, 134.99, 131.7, 130.6, 129.4, 129.0, 128.3, 127.6, 126.6; HRMS (ESI-TOF) m/z [M + H]$^+$ Calcd for $C_{14}H_{10}NOS$ 240.0483, found 240.0494.

*1,4-Phenylenebis(quinolin-3-ylmethanone) (**4q**).* Synthesized from *o*-aminobenzaldehyde **1** (57.8 mg, 0.21 mmol), PPh_3 (5.3 mg, 20 mol %), and the activated bis-acetylene **2q** (18.2 mg, 0.1 mmol) in MeCN (1 mL); gradient EtOAc/Hex, from 3:7 to 1:1. 24.5 mg, 63% yield; pale-yellow powder: mp 237−239 °C; IR (film) ν_{max} 3023, 1641, 1614, 1595, 1571, 1366, 1290, 1246, 1122 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.38 (s, 2H), 8.61 (s, 2H), 8.22 (d, J = 8.2 Hz, 2H), 8.03 (s, 4H), 7.96 (d, J = 8.2 Hz, 2H), 7.89 (t, J = 8.2 Hz, 2H), 7.68 (t, J = 8.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.0, 150.0, 149.6, 140.4, 139.1, 132.2, 130.0, 129.5, 129.22, 129.18, 127.8, 126.5; HRMS (ESI-TOF) m/z [M + H]$^+$ Calcd for $C_{26}H_{17}N_2O_2$ 389.1290, found 389.1291.

*Methyl Quinoline-3-carboxylate (**4r**).*[18] 22.7 mg, 61/% yield; white crystalline solid: mp 69−70 °C; IR (film) ν_{max} 3056, 2948, 2924, 2849, 1714, 1618, 1572, 1433, 1367, 1290, 1240, 1193, 1100 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.44 (s, 1H), 8.84 (s, 1H), 8.16 (d, J = 7.9 Hz, 1H), 7.93 (d, J = 7.9 Hz, 1H), 7.83 (t, J = 7.9 Hz, 1H), 7.62 (t, J = 7.9 Hz, 1H), 4.01 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.7, 149.9, 149.7, 138.7, 131.8, 129.4, 129.0, 127.3, 126.7, 122.9, 52.4; HRMS (ESI-TOF) m/z [M + H]$^+$ Calcd for $C_{11}H_{10}NO_2$ 188.0712, found 188.0709.

*Quinolin-3-yl(tosyl)methanone (**4s**).*[19] 17.0 mg, 30% yield; yellow crystalline solid: mp 165−170 °C; IR (film) ν_{max} 3068, 3056, 2925, 2851, 1616, 1593, 1585, 1497, 1312, 1304, 1290, 1153, 1140, 1091 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.25 (d, J = 1.7 Hz, 1H), 8.79 (d, J = 1.8 Hz, 1H), 8.14 (d, J = 8.5 Hz, 1H), 7.95 (d, J = 8.5 Hz, 1H), 7.90 (d, J = 8.2 Hz, 2H), 7.86 (t, J = 8.4 Hz, 3H), 7.67 (t, J = 8.4 Hz, 1H), 7.32 (d, J = 8.3 Hz, 2H), 2.39 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.2, 147.0, 144.8, 137.9, 136.5, 135.0, 132.5, 130.1, 129.5, 129.1, 128.2, 127.8, 126.3, 21.5; HRMS (ESI-TOF) m/z [M + H]$^+$ Calcd for $C_{16}H_{14}NO_2S$ 284.0745, found 284.0753.

*4-Methylquinolin-3-yl(phenyl)methanone (**4t**).*[7] EtOAc/Hex, 1:5. 40.3 mg, 82% yield; yellow crystalline solid: mp 82−86 °C; IR (film) ν_{max} 3059, 3030, 2918, 1658, 1645, 1581, 1494, 1449, 1248, 1161 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.82 (s, 1H), 8.17 (d, J = 8.3 Hz, 1H), 8.12 (d, J = 8.5 Hz, 1H), 7.85−7.78 (m, 3H), 7.68−7.61 (m, 2H), 7.49 (t, J = 7.8 Hz, 2H), 2.67 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.9, 148.5, 148.0, 143.5, 137.4, 133.8, 131.8, 130.3, 130.1, 130.0, 128.7, 127.5, 127.2, 124.3, 15.8; HRMS (ESI-TOF) m/z [M + H]$^+$ Calcd for $C_{17}H_{14}NO$ 248.1075, found 248.1064.

*Phenyl(4-phenylquinolin-3-yl)methanone (**4u**).*[7] EtOAc/Hex, 1:5. 44.6 mg, 72% yield; yellow crystalline solid: mp 108−110 °C; IR (film) ν_{max} 3062, 1654, 1570, 1486, 1324 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.00 (s, 1H), 8.24 (d, J = 8.5 Hz, 1H), 7.83−7.78 (m, 2H), 7.63−7.61 (m, 2H), 7.57−7.54 (m, 1H), 7.46−7.42 (m, 1H), 7.30−7.25 (m, 7H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.7, 148.8, 148.4, 146.9, 137.3, 134.8, 133.1, 131.7, 130.4, 130.0, 129.7, 129.6, 128.4,

dx.doi.org/10.1021/jo3015825 | J. Org. Chem. 2012, 77, 8257−8267

128.14, 128.12, 127.4, 126.7, 126.3; HRMS (ESI-TOF) m/z $[M + H]^+$ Calcd for $C_{22}H_{16}NO$ 310.1232, found 310.1230.

*4-Cyclohexylquinolin-3-yl(phenyl)methanone (**4v**).* 47.5 mg, 75% yield; pale-yellow oil: IR (film) ν_{max} 3066, 2927, 2853, 1665, 1577, 1498, 1448, 1282, 1241 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.64 (s, 1H), 8.34 (br s, 1H), 8.16 (d, J = 8.4 Hz, 1H), 7.85 (d, J = 6.3 Hz, 2H), 7.75 (t, J = 7.1 Hz, 1H), 7.61 (q, J = 7.3 Hz, 2H), 7.46 (t, J = 7.3 Hz, 2H), 3.25 (br s, 1H), 1.97 (br s, 2H), 1.85−1.77 (m, 4H), 1.26 (br s, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.2, 150.7, 148.7, 148.1, 137.6, 133.8, 132.0, 130.7, 130.1, 129.6, 128.9, 128.6, 126.7, 126.6, 32.0, 27.0, 25.7; HRMS (ESI-TOF) m/z $[M + H]^+$ Calcd for $C_{22}H_{22}NO$ 316.1701, found 316.1699.

*4-Cyclopropylquinolin-3-yl(phenyl)methanone (**4w**).* 36.6 mg, 67% yield; pale-yellow oil: IR (film) ν_{max} 3064, 3005, 2922, 1654, 1596, 1567, 1499, 1447, 1322, 1279, 1241, 1226, 1170 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.83 (s, 1H), 8.51 (d, J = 8.5 Hz, 1H), 8.17 (d, J = 8.5 Hz, 1H), 7.85−7.79 (m, 3H), 7.68−7.66 (m, 1H), 7.65−7.59 (m, 1H), 7.59−7.46 (m, 2H), 2.11−2.08 (m, 1H), 0.95−0.93 (m, 2H), 0.59−0.57 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.2, 148.9, 148.5, 147.4, 138.0, 133.4, 132.7, 130.3, 130.0, 129.6, 128.6, 128.3, 127.1, 125.5, 12.8, 8.2; HRMS (ESI-TOF) m/z $[M + H]^+$ Calcd for $C_{19}H_{16}NO$ 274.1232, found 274.1230.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

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

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Financial support was provided by the NIH (R01GM071779 and P41GM081282). This material is based upon work supported by the National Science Foundation under Equipment Grant No. CHE-1048804.

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