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Gold-Catalyzed Ammonium Acetate Assisted Cascade Cyclization of 2-Alkynylarylketones

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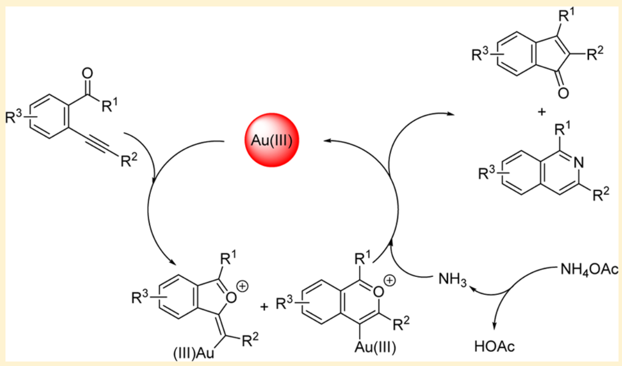
S *Supporting Information*

ABSTRACT: An ammonium acetate assisted gold-catalyzed cascade cyclization reaction of 2-alkynylarylketones is described. Under the reported conditions, a gold-catalyzed intramolecular cyclization of 2-alkynylarylketones takes place through two competing reaction mechanisms—a 5-*exo-dig* or a 6-*endo-dig* cyclization—leading to two regioisomeric intermediates: isobenzofuranium or isobenzopyrylium. In the presence of ammonium acetate, the two intermediate compounds undergo further rearrangement to 2,3-disubstituted indenones and 1,3-disubstituted isoquinolines, respectively. While both reaction pathways proceed via a cyclization−rearrangement cascade, the gold-mediated 5-*exo-dig* process is especially notable, as it provides a novel cyclization protocol of 2-alkynylarylketones.



■ INTRODUCTION

The Lewis acid induced intramolecular electrophilic cyclization of *o*-alkynylarylcarbonyl compounds has proven to be a versatile synthetic approach to a variety of biologically interesting heterocycles and carbocycles.[1,2] Among the *o*-alkynylarylcarbonyl compounds, *o*-alkynylarylaldehydes have shown great versatility, displaying high reactivity as substrates for cyclization reactions.[3] In comparison to the many electrophilic cyclization reactions explored for *o*-alkynylarylaldehydes, examples of cyclization reactions involving *o*-alkynylarylketones are relatively rare,[4] possibly due to their lower chemical reactivity than the aldehydes. The cyclizations of *o*-alkynylarylketones are usually explored as an extension of the reaction scope of analogous *o*-alkynylarylaldehydes. In general, the known cyclization processes of *o*-alkynylarylaldehydes and -ketones share the same isobenzopyrylium intermediate, which either reacts with a nucleophile to furnish isochromene derivatives[3a,b,5] (Scheme 1, path a) or undergoes a cycloaddition with an alkene/alkyne moiety to generate polycyclic compounds (Scheme 1, path b).[6] Besides the two major reaction pathways, a few examples have demonstrated that, in the presence of a nitrogen nucleophile, such as ammonia,[7] ammonium acetate,[8] or primary amines,[9] intramolecular cyclizations of *o*-alkynylarylaldehydes and -ketones lead to the formation of isoquinoline derivatives (Scheme 1, path c). Although the two *o*-alkynylarylcarbonyl substrates often show similar chemical reactivity and lead to the same derivatives, it is known that *o*-alkynylarylaldehydes preferentially undergo 6-*endo-dig* cyclizations to form isobenzopyrylium intermediates, whereas *o*-alkynylarylketones often undergo 5-*exo-dig* cyclizations to form isobenzofuraniums, under similar reaction conditions. While the reactivity of isobenzopyrylium intermediates generated from the cyclization of *o*-alkynylarylcarbonyl compounds has been explored in numerous processes, such as nucleophilic additions[5] and cycloadditions,[6] the reactivity of isobenzofuranium intermediates generated in these electrophilic cyclization reactions has not yet been widely elucidated.[10] Most of the known reactions of isobenzofuranium intermediates are limited to simple nucleophilic additions, which exclusively lead to isobenzofuran derivatives (Scheme 1, path d).[11]

We previously developed a one-pot synthesis of isoquinolines by a palladium-catalyzed sequential coupling−imination−annulation reaction,[8a] involving a key mechanistic step—the electrophilic cyclization of *o*-alkynylarylaldehydes in the presence of *in situ* generated ammonia. When we attempted to expand the substrate scope of this synthetic protocol to *o*-alkynylarylketones, we encountered limited success, and the desired isoquinolines were only obtained in low yields (<20%). The low chemical reactivity observed for *o*-alkynylarylketones in our previous work prompted us to further explore their reactivity in the electrophilic cyclization reactions. We hereby report our recent progress on this topic: an ammonium acetate-assisted gold-catalyzed electrophilic cyclization of *o*-alkynylarylketones, through a cascade cyclization−rearrangement process, leading to the formation of indenones and isoquinolines (Scheme 1, path e).

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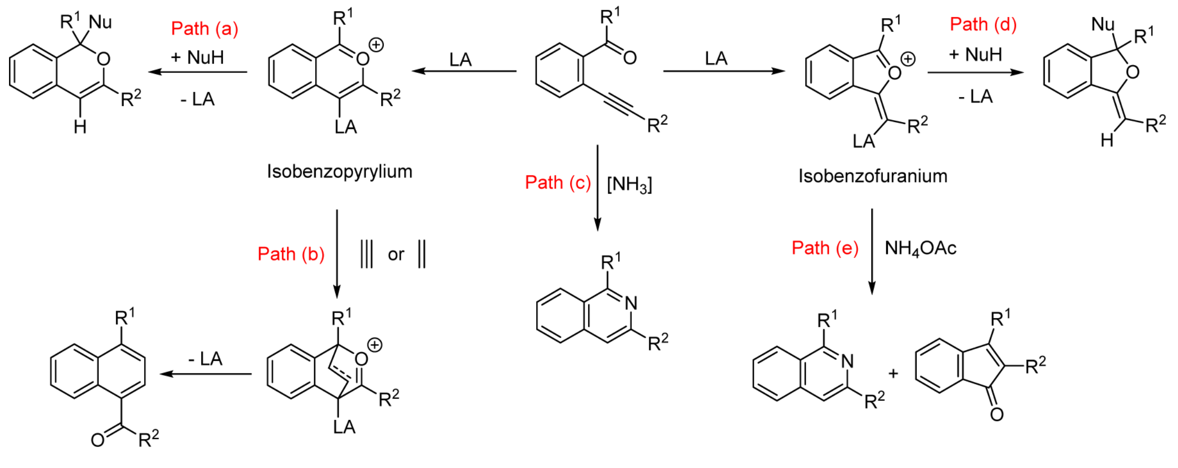
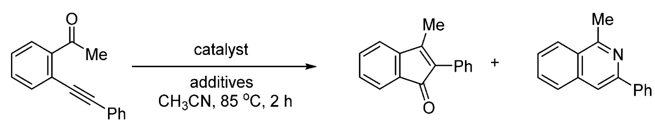
Scheme 1. Intramolecular Cyclization Reactions of *o*-Alkynylarylaldehydes and -ketones



* LA = Lewis acid

Table 1. Optimization of Reaction Conditions for the Cyclization of *o*-Alkynylarylketones[a]



1a 2a 3a

entry	catalyst (mol %)	additive (equiv)	yield (%)[b] 2a, 3a
1[c]	$NaAuCl_4{\cdot}2H_2O/AgSbF_6$ (6/6)	–	–, –
2[d]	$NaAuCl_4{\cdot}2H_2O/AgSbF_6$ (6/6)	NH_4OAc (1 equiv)	48, 10
3	$NaAuCl_4{\cdot}2H_2O/AgSbF_6$ (6/6)	NH_4OAc (1 equiv), pyridine *N*-oxide (2 equiv)	53, 15
4	$NaAuCl_4{\cdot}2H_2O/AgSbF_6$ (6/6)	$(NH_4)_2CO_3$ (1 equiv), pyridine *N*-oxide (2 equiv)	50, 14
5	$NaAuCl_4{\cdot}2H_2O/AgSbF_6$ (6/6)	HCO_2NH_4 (1 equiv), pyridine *N*-oxide (2 equiv)	43, 13
6	$NaAuCl_4{\cdot}2H_2O/AgSbF_6$ (6/6)	L-Proline (1 equiv), pyridine *N*-oxide (2 equiv)	51, –
7	$NaAuCl_4{\cdot}2H_2O/AgSbF_6$ (6/6)	NH_4OAc (1 equiv), 4-methoxypyridine *N*-oxide (2 equiv)	59, 18
8	$NaAuCl_4{\cdot}2H_2O/AgSbF_6$ (6/6)	NH_4OAc (1 equiv), 4-nitropyridine *N*-oxide (2 equiv)	41, 12
9	$NaAuCl_4{\cdot}2H_2O/AgSbF_6$ (6/6)	NH_4OAc (1 equiv), 2,6-dichloropyridine *N*-oxide (2 equiv)	37, 12
10	$NaAuCl_4{\cdot}2H_2O/AgSbF_6$ (6/6)	NH_4OAc (1 equiv), quinoline *N*-oxide (2 equiv)	56, 15
11	$NaAuCl_4{\cdot}2H_2O/AgSbF_6$ (6/6)	NH_4OAc (1 equiv), diphenylsulfoxide (2 equiv)	47, 20
12	$NaAuCl_4{\cdot}2H_2O/AgSbF_6$ (6/6)	NH_4OAc (1.5 equiv), 4-methoxypyridine *N*-oxide (2 equiv)	55, 20
13	$NaAuCl_4{\cdot}2H_2O/AgSbF_6$ (6/6)	NH_4OAc (1 equiv), 4-methoxypyridine *N*-oxide (1.2 equiv)	69, 19
14	$NaAuCl_4{\cdot}2H_2O$ (12)	NH_4OAc (1 equiv), 4-methoxypyridine *N*-oxide (1.2 equiv)	46, 19
15	$AgSbF_6$ (12)	NH_4OAc (1 equiv), 4-methoxypyridine *N*-oxide (1.2 equiv)	–, 74

[a]General procedure: The catalyst, additives, substrate **1a** (110.2 mg, 0.5 mmol), and CH_3CN (4 mL) were added to a 4-dram vial. The reaction mixture was purged with argon, sealed, and stirred at 85 °C for 2 h. [b]Isolated yields after column chromatography. [c]Reaction was stopped after 8 h. [d]Reaction was stopped after 4 h, and 30% of **1a** was recovered.

RESULTS AND DISCUSSION

Our initial study focused on the cyclization reaction of the model substrate 1-(2-(phenylethynyl)phenyl)ethan-1-one (**1a**). In the presence of 6 mol % of both $NaAuCl_4{\cdot}2H_2O$ and $AgSbF_6$, reaction of **1a** led to partial decomposition and no useful product was obtained (Table 1, entry 1). During the course of studying this reaction, we found significant additive effects in this cyclization. In the presence of 1 equiv of ammonium acetate (NH_4OAc), indenone **2a** was obtained in 48% yield together with 10% of isoquinoline **3a** after 4 h in a 70% conversion (Table 1, entry 2). A longer reaction time did not improve the chemical yields but caused partial decomposition of the products. Further investigation showed that in the presence of 2 equiv of pyridine *N*-oxide the reaction was completed in 2 h and the chemical yields of indenone **2a** and isoquinoline **3a** were enhanced to 53% and 15%, respectively (Table 1, entry 3). Other ammonium salts such as ammonium carbonate ($(NH_4)_2CO_3$) and ammonium formate (HCO_2NH_4) were also tested (Table 1, entries 4 and 5); however, both produced slightly inferior results compared to NH_4OAc. When L-proline was employed in this reaction to replace NH_4OAc, indenone **2a** was isolated as the sole product, although only in moderate yield (51%; Table 1, entry 6). Further investigation of additives, including several pyridine *N*-oxide derivatives and diphenyl sulfoxide (Table 1, entries 7−11), showed that the highest yields of the cyclization products were produced in the presence of 4-methoxypyridine *N*-oxide (Table 1, entry 7). No enhancement of chemical yields was observed, when the loading of NH_4OAc was increased to 1.5 equiv (Table 1, entry 12). When the loading of 4-methoxypyridine *N*-oxide was reduced to 1.2 equiv, the chemical yields of **2a** and **3a** were further raised to 69% and 19% (Table 1, entry 13). When $NaAuCl_4{\cdot}2H_2O$ was used as the sole catalyst, the yield of **2a**

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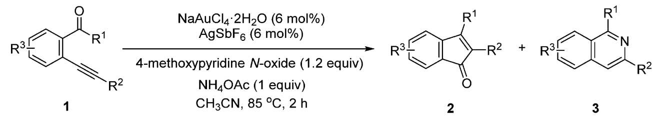
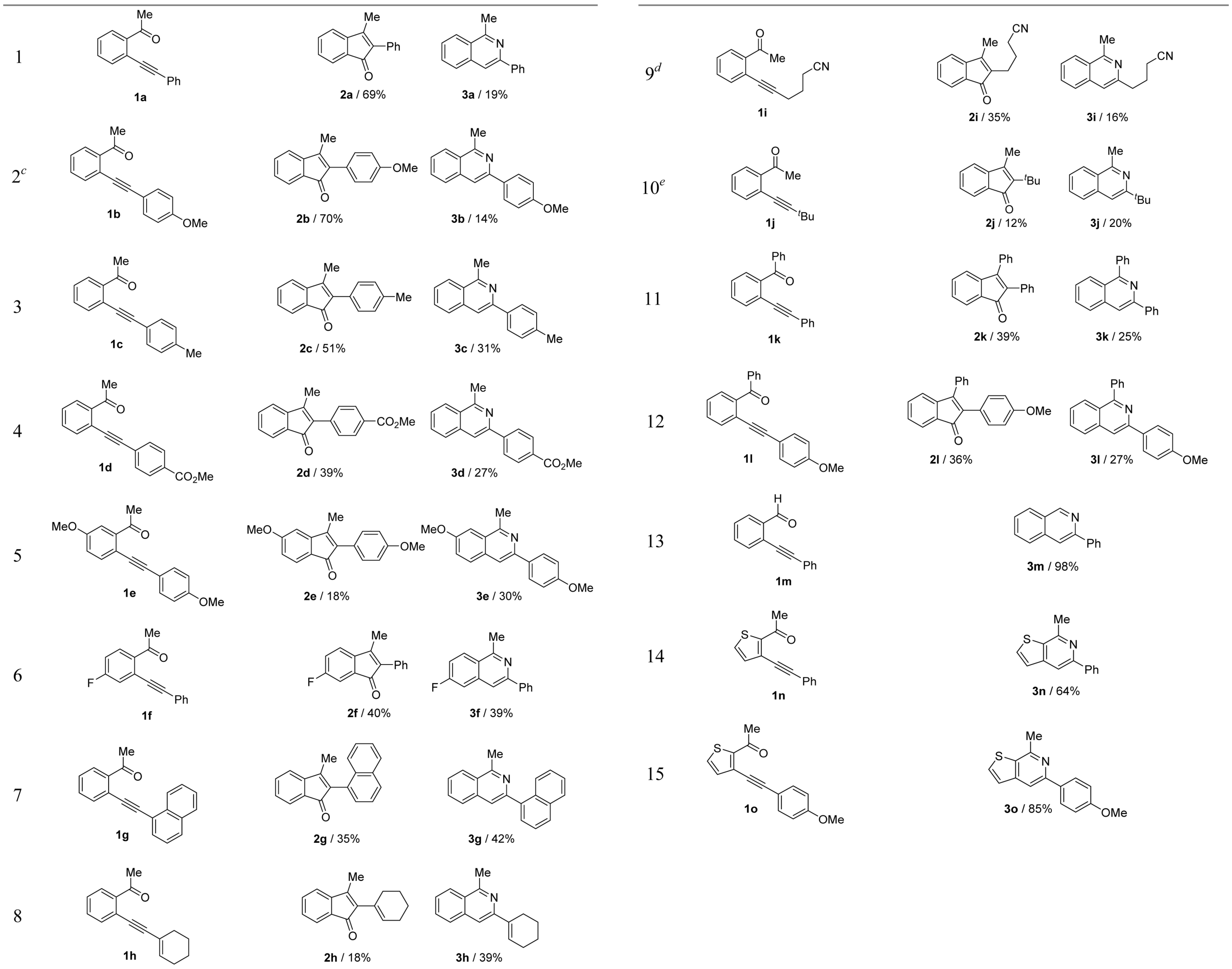
Table 2. Gold-Catalyzed Cyclization of *o*-Alkynylarylketones and -aldehydes[a]





entry	substrate 1	product 2 & 3 / yield[b]	
1	1a	2a / 69%	3a / 19%
2[c]	1b	2b / 70%	3b / 14%
3	1c	2c / 51%	3c / 31%
4	1d	2d / 39%	3d / 27%
5	1e	2e / 18%	3e / 30%
6	1f	2f / 40%	3f / 39%
7	1g	2g / 35%	3g / 42%
8	1h	2h / 18%	3h / 39%
9[d]	1i	2i / 35%	3i / 16%
10[e]	1j	2j / 12%	3j / 20%
11	1k	2k / 39%	3k / 25%
12	1l	2l / 36%	3l / 27%
13	1m		3m / 98%
14	1n		3n / 64%
15	1o		3o / 85%

[a]See the Experimental Section for the general procedure. [b]Isolated yields after column chromatography. [c]When L-proline was employed to replace NH_4OAc, indenone **2b** was isolated as the sole product in 29% yield. [d]When L-proline was employed to replace NH_4OAc, indenone **2i** was isolated as the sole product in 30% yield. [e]The reaction was stopped after 8 h, and 60% of starting material **1j** was recovered.

decreased to 46% while **3a** was obtained in the same yield (Table 1, entry 14). On the other hand, **3a** was obtained as the only product in 74% yield when $AgSbF_6$ was used as the sole catalyst (Table 1, entry 15). Considering the formation of **2a** involving an unprecedented cyclization−rearrangement cascade reaction of *o*-alkynylarylketones, the conditions listed in entry 13 in Table 1 were chosen to be tested with other substrates.

A variety of 2-alkynylarylketones, including those with aryl, alkenyl, and alkyl groups at the distal position of the alkyne triple bond, were then subjected to the optimized reaction conditions (Table 2, entries 1−10). Based on these results, electron-donating and -withdrawing groups are found to be compatible on both the distal and proximal phenyl rings, relative to the alkyne triple bond (Table 2, entries 2 to 6), although lower yields for indenones are obtained when an electron-withdrawing substituent such as an ester group is present at the *para*-position of the distal phenyl ring (Table 2, entry 4) or when an electron-donating substituent such as a methoxy group is present at the *para*-position of the proximal phenyl ring (Table 2, entry 5). Additionally, the introduction of a sterically hindered *α*-naphthyl group at the distal position of the triple bond leads to a lower chemical yield for indenone (35%) but an increased yield of isoquinoline (42%; Table 2, entry 7). Alkenyl and alkyl moieties at the distal position of the triple bond are also compatible, but likewise lower the yield of the indenone products (Table 2, entries 8−10). When a sterically hindered *tert*-butyl group is present, a low conversion of the starting material (40%) is observed during the cyclization, even after an elongated reaction time (Table 2, entry 10).

Aside from acetophenone substrates, several other species were also investigated to further elucidate the regioselectivity of

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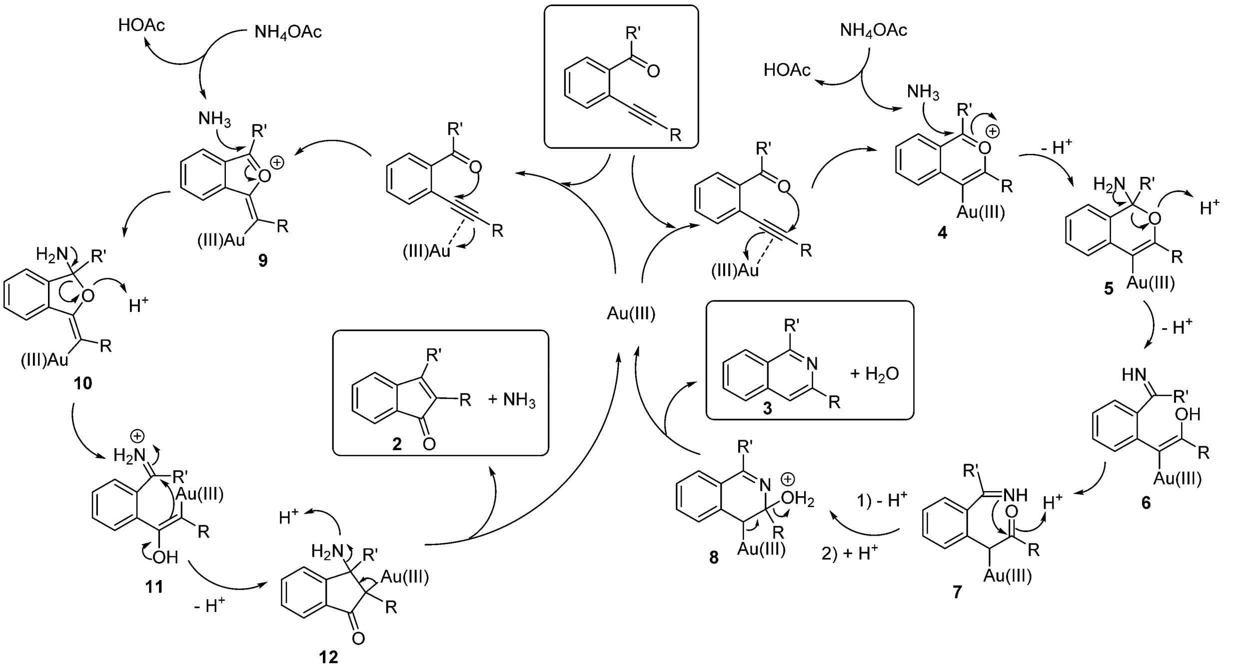
Scheme 2. Proposed Mechanism for Gold-Catalyzed Cyclization of *o*-Alkynylarylketones



the cyclization process. As with acetophenone, benzophenone moieties lead to both the indenone and isoquinoline products (Table 2, entries 11 and 12). However, the cyclization of the benzaldehyde substrate occurs only via a 6-*endo-dig* route, leading regiospecifically to isoquinoline (Table 2, entry 13). Likewise, the cyclization of 1-(3-(arylethynyl)thiophen-2-yl)-ethan-1-ones, which has the ketone and alkynyl moieties at the *ortho*-positions of the 5-membered heterocyclic ring system, proceeds exclusively via a 6-*endo-dig* cyclization, affording only thieno[2,3-*c*]pyridines (Table 2, entries 14 and 15).

The reaction presumably begins with a gold-catalyzed intramolecular electrophilic cyclization, proceeding via one of two possible reaction pathways—a 6-*endo-dig* or 5-*exo-dig* cyclization (Scheme 2). When a 6-*endo-dig* cyclization takes place, the isobenzopyrylium intermediate **4** forms. The nucleophilic addition of ammonia to **4** leads to the isochromene intermediate **5**. After protonation of the oxygen atom of isochromene **5**, the carbon−oxygen bond dissociates to form enol **6**, which subsequently tautomerizes to ketone **7**. An intramolecular nucleophilic addition of the imino group to the ketone carbonyl group forms cyclized intermediate **8**. Following dehydration, the final isoquinoline product is produced, together with the regenerated catalyst. Alternatively, when a 5-*exo-dig* cyclization takes place, the isobenzofuranium intermediate **9** forms. The nucleophilic addition of ammonia to **9** leads to the isobenzofuran intermediate **10**. After protonation of the oxygen atom of isobenzofuran **10**, the carbon−oxygen bond is cleaved to form enol **11**, which subsequently cyclizes via an intramolecular nucleophilic addition to the imino group to form indanone intermediate **12**. After elimination of ammonia, the indenone is produced together with the regenerated catalyst. In both cases the role of ammonium acetate is to trap the oxonium intermediates (**4** and **9**) and drive the reaction in the forward direction. Our results showed that both $NaAuCl_4$ and $AgSbF_6$ were effective catalysts for the cyclization of 2-alkynylarylketones though they displayed different regioselectivity. $AgSbF_6$ induces a regiospecific 6-*endo-dig* cyclization (Table 1, entry 15), while $NaAuCl_4$ leads to the formation of a mixture of 6-*endo-dig* and 5-*exo-dig* cyclization products (Table 1, entry 14). In the current reaction protocol, $AgSbF_6$ presumably activates the gold catalyst by abstracting the chloride ions,[12] and the combination of $NaAuCl_4$ and $AgSbF_6$ provides a superior result compared to solely $NaAuCl_4$ as the catalyst (Table 1, entries 13 and 14). While the specific role of 4-methoxypyridine *N*-oxide is unclear, it is hypothesized to function as an accelerant that stabilizes the gold(III) catalyst, thus increasing the turnover number of both cyclization processes.[13] We also cannot rule out the possibility that 4-methoxypyridine *N*-oxide plays the role as a buffer to maintain an optimal pK_a value of the reaction medium for the cascade cyclization.[14]

■ CONCLUSION

An ammonium acetate assisted gold-catalyzed cascade cyclization of 2-alkynylarylketones is described. The cyclization process is initiated by one of two competing reactions—a 5-*exo-dig* or a 6-*endo-dig* cyclization—of the carbonyl group with the alkyne triple bond, leading to isobenzofuranium or isobenzopyrylium intermediates, respectively. The two intermediates tandemly undergo an ammonium acetate assisted rearrangement and a subsequent cyclization to generate two different species: indenone and isoquinoline. The methodology reported herein is notable as it describes the first documented example of an isobenzofuranium intermediate undergoing a novel cascade reaction. Further exploration into the processes controlling the regioselectivity of this cascade and into the chemical reactivity of the isobenzofuranium intermediates is currently underway in our laboratory and will be reported in due course.

■ EXPERIMENTAL SECTION

General Information. All reactions were carried out in sealed 4-/6-dram vials, unless otherwise indicated. All commercially available chemicals were used as received without further purification, unless otherwise noted. All ^{1}H and ^{13}C NMR spectra were recorded at 500 or

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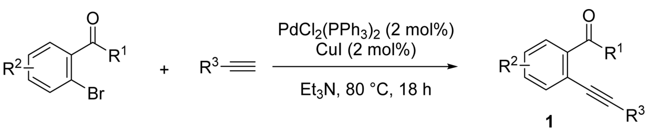
400 MHz and 125 or 100 MHz, respectively, using $CDCl_3$ as the solvent. The chemical shifts of all ^1H and ^{13}C NMR spectra are referenced to the residual signal of $CDCl_3$ (δ 7.26 ppm for the ^1H NMR spectra and δ 77.23 ppm for the ^{13}C NMR spectra). High resolution mass analysis was carried out on a high resolution mass spectrometer using electrospray ionization (ESI) mode with a time-of-flight (TOF) mass analyzer. Samples were dissolved in methylene chloride and methanol and analyzed via flow injection into the mass spectrometer at a flow rate of 200 μL/min. The mobile phase was 90:10 methanol/water, with 0.1% formic acid. The mass spectrometer was operated in positive ion mode, and the melting points are uncorrected.

The 2-alkynylarylketone/2-alkynylarylaldehyde materials (**1**) were prepared by Sonogashira coupling[15] of 2-bromoarylketone/2-bromoarylaldehyde with terminal alkynes, except compounds **1c**, **1d**, **1g**, and **1q**. 1-(2-Ethynylphenyl)ethanone (**1q**) was prepared from 1-(2-((trimethylsilyl)ethynyl)phenyl)ethan-1-one (**1p**) via a cesium fluoride mediated desilylation reaction. Compounds **1c**, **1d**, and **1g** were prepared by Sonogashira coupling of **1q** with aryl iodides.

General Procedure for the Preparation of 2-Alkynylarylketones and Aldehydes (1). A 6-dram vial was charged with 2-



bromoarylketone (2.0 mmol), a terminal alkyne (2.2 mmol), $Pd(PPh_3)_2Cl_2$ (28.1 mg, 0.04 mmol), CuI (7.6 mg, 0.04 mmol), and Et_3N (14 mL). The vial was then purged with argon and sealed. The reaction mixture was stirred at 80 °C for 18 h, until the disappearance of starting material was observed, as monitored by thin layer chromatography. The reaction mixture was diluted with diethyl ether (40 mL) and washed with brine (40 mL), and the aqueous phase was then extracted with diethyl ether (2 × 20 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated using a rotary evaporator under reduced pressure (20 mmHg); the resulting residue was purified by flash column chromatography on silica gel (eluent: hexane/ethyl acetate).

1-(2-(Phenylethynyl)phenyl)ethanone (1a). This product was obtained as a light brown oil (286.4 mg, 65% yield); ^1H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, J = 7.9 Hz, 1H), 7.63 (d, J = 7.6 Hz, 1H), 7.54−7.57 (m, 2H), 7.47 (t, J = 7.5 Hz, 1H), 7.36−7.41 (m, 4H), 2.80 (s, 3H). The ^1H NMR spectral data are in good agreement with the literature data.[16]

1-(2-((4-Methoxyphenyl)ethynyl)phenyl)ethanone (1b). This product was obtained as a light brown oil (160.2 mg, 32% yield); ^1H NMR (500 MHz, $CDCl_3$) δ 7.75 (dd, J = 7.8, 1.0 Hz, 1H), 7.61 (dd, J = 7.7, 0.6 Hz, 1H), 7.45−7.51 (m, 3H), 7.38 (dt, J = 7.7, 1.0 Hz, 1H), 6.90 (d, J = 8.9 Hz, 2H), 3.84 (s, 3H), 2.80 (s, 3H). The ^1H NMR spectral data are in good agreement with the literature data.[17]

1-(5-Methoxy-2-((4-methoxyphenyl)ethynyl)phenyl)ethanone (1e). This product was obtained as a light brown oil (229.9 mg, 41% yield); ^1H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, J = 8.6 Hz, 1H), 7.44−7.47 (m, 2H), 7.26 (d, J = 2.8 Hz, 1H), 7.01 (dd, J = 8.6, 2.7 Hz, 1H), 6.87−6.90 (m, 2H), 3.86 (s, 3H), 3.83 (s, 3H), 2.82 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.8, 160.0, 159.4, 142.1, 135.3, 133.0, 118.3, 115.4, 114.6, 114.3, 113.1, 94.1, 87.4, 55.7, 55.5, 30.5; IR (neat, cm^{-1}) ν 2922, 1715, 1697, 1595, 1509, 1490, 1455, 1379, 1208, 1083, 1025, 853, 829, 755, 712, 696; HRMS (ESI) calcd for $C_{18}H_{17}O_3$ $(M + H)^+$ 281.1172; found 281.1175.

1-(4-Fluoro-2-(phenylethynyl)phenyl)ethanone (1f). This product was obtained as a light yellow oil (333.6 mg, 70% yield); ^1H NMR (500 MHz, $CDCl_3$) δ 7.82 (dd, J = 8.8, 5.9 Hz, 1H), 7.53−7.57 (m, 2H), 7.37−7.39 (m, 3H), 7.31 (dd, J = 9.1, 2.4 Hz, 1H), 7.07−7.11 (m, 1H), 2.78 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.7, 164.1 (d, J_{C-F} = 250.9 Hz), 136.9 (d, J_{C-F} = 3.0 Hz), 131.83, 131.75, 129.3, 128.7, 124.6 (d, J_{C-F} = 10.4 Hz), 122.5, 120.6 (d, J_{C-F} = 23.2 Hz), 115.9 (d, J_{C-F} = 21.5 Hz), 96.4, 87.7 (d, J_{C-F} = 2.6 Hz), 30.1; IR (neat, cm^{-1}) ν 2970, 1735, 1683, 1595, 1558, 1490, 1447, 1418, 1364, 1266, 1228, 1216, 1098, 1066, 1024, 925, 877, 826, 756, 688; HRMS (ESI) calcd for $C_{16}H_{12}FO$ $(M + H)^+$ 239.0867. Found: 239.0868.

1-(2-(Cyclohex-1-en-1-ylethynyl)phenyl)ethanone (1h). This product was obtained as a light brown oil (152.5 mg, 34% yield); ^1H NMR (500 MHz, $CDCl_3$) δ 7.70 (dd, J = 7.9, 1.1 Hz, 1H), 7.50 (d, J = 7.9, 1.2 Hz, 1H), 7.41 (dt, J = 7.3, 1.2 Hz, 1H), 7.33 (dt, J = 7.7, 1.3 Hz, 1H), 6.24−6.26 (m, 1H), 2.74 (s, 3H), 2.22−2.25 (m, 2H), 2.14−2.18 (m, 2H), 1.66−1.71 (m, 2H), 1.60−1.65 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.0, 140.8, 136.4, 133.9, 131.4, 128.8, 127.9, 122.5, 120.8, 97.4, 86.2, 30.3, 29.0, 26.0, 22.4, 21.6; IR (neat, cm^{-1}) ν 2925, 1696, 1587, 1464, 1426, 1355, 1281, 1239, 1091, 1025, 958, 756; HRMS (ESI) calcd for $C_{16}H_{17}O$ $(M + H)^+$ 225.1274; found 225.1275.

6-(2-Acetylphenyl)hex-5-ynenitrile (1i). This product was obtained as a yellow oil (169.0 mg, 40% yield); ^1H NMR: (400 MHz, $CDCl_3$) δ 7.66 (dd, J = 7.7, 1.0 Hz, 1H), 7.48 (dd, J = 7.6, 1.0 Hz, 1H), 7.40 (td, J = 7.6, 1.5 Hz, 1H), 7.34 (td, J = 7.6, 1.4 Hz, 1H), 2.60−2.65 (m, 5H), 2.41−2.50 (m, 2H), 1.93−1.99 (m, 2H). The ^1H NMR spectral data are in good agreement with the literature data.[18]

1-(2-(3,3-Dimethylbut-1-yn-1-yl)phenyl)ethan-1-one (1j). This product was obtained as yellow oil (280.4 mg, 70% yield); ^1H NMR: (400 MHz, $CDCl_3$) δ 7.64 (dd, J = 7.8, 1.0 Hz, 1H), 7.44 (dd, J = 7.7, 0.9 Hz, 1H), 7.35 (td, J = 7.6, 1.5 Hz, 1H), 7.28 (td, J = 7.6, 1.4 Hz, 1H), 2.71 (s, 3H), 1.32 (s, 9H). The ^1H NMR spectral data are in good agreement with the literature data.[19]

Phenyl(2-(phenylethynyl)phenyl)methanone (1k). This product was obtained as a light yellow oil (254.1 mg, 45% yield); ^1H NMR (500 MHz, $CDCl_3$) δ 7.88−7.90 (m, 2H), 7.62 (dd, J = 7.3, 1.1 Hz, 1H), 7.57−7.60 (m, 1H), 7.51−7.55 (m, 2H), 7.44−7.50 (m, 3H), 7.18−7.25 (m, 3H), 7.03−7.05 (m, 2H). The ^1H NMR spectral data are in good agreement with the literature data.[20]

(2-((4-Methoxyphenyl)ethynyl)phenyl) (Phenyl)methanone (1l). This product was obtained as a light brown oil (324.9 mg, 52% yield); ^1H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, J = 7.3 Hz, 2H), 7.57−7.60 (m, 2H), 7.41−7.53 (m, 5H), 6.97 (d, J = 8.8 Hz, 2H), 6.73 (d, J = 8.7 Hz, 2H), 3.76 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.4, 159.9, 141.4, 137.5, 133.3, 133.1, 132.5, 130.5, 130.4, 128.9, 128.5, 128.0, 122.4, 114.8, 113.9, 95.5, 86.5, 55.4; IR (neat, cm^{-1}) ν 2932, 2834, 2216, 1735, 1665, 1605, 1594, 1510, 1465, 1449, 1436, 1365, 1316, 1289, 1250, 1178, 1149, 1091, 1026, 960, 936, 880, 830, 805, 788, 770; HRMS (ESI) calcd for $C_{22}H_{17}O_2$ $(M + H)^+$ 313.1223; found 313.1226.

2-(Phenylethynyl)benzaldehyde (1m). This product was obtained as a light brown oil (325.9 mg, 79% yield); ^1H NMR (500 MHz, $CDCl_3$) δ 10.66 (s, 1H), 7.96 (d, J = 7.6 Hz, 1H), 7.66 (d, J = 7.6 Hz, 1H), 7.61 (d, J = 7.2 Hz, 1H), 7.57−7.59 (m, 2H), 7.47 (t, J = 7.5 Hz, 1H), 7.39−7.41 (m, 3H). The ^1H NMR spectral data are in good agreement with the literature data.[21]

1-(3-(Phenylethynyl)thiophen-2-yl)ethanone (1n). This product was obtained as a yellow solid (353.0 mg, 78% yield): mp = 45.5−46.8 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.53−7.75 (m, 3H), 7.38−7.39 (m, 3H), 7.23 (d, J = 5.0 Hz, 1H), 2.83 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 191.3, 145.8, 133.0, 132.1, 131.6, 129.3, 128.8, 125.6, 122.5, 96.9, 84.8, 29.2; IR (neat, cm^{-1}) ν 3079, 2205, 1738, 1648, 1595, 1517, 1485, 1442, 1405, 1379, 1293, 1243, 1216, 1098, 1070, 1043, 1018, 992, 920, 846, 755; HRMS (ESI) calcd for $C_{14}H_{11}OS$ $(M + H)^+$ 227.0525; found 227.0529.

1-(3-((4-Methoxyphenyl)ethynyl)thiophen-2-yl)ethanone (1o). This product was obtained as a light yellow solid (256.3 mg, 50% yield): mp = 97.2−98.8 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, J = 4.9 Hz, 1H), 7.47−7.49 (m, 2H), 7.21 (d, J = 5.1 Hz, 1H), 6.90−6.92 (m, 2H), 3.85 (s, 3H), 2.83 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 191.4, 160.5, 145.2, 133.2, 132.9, 132.1, 126.1, 114.6, 114.4, 97.2, 83.8, 55.6, 29.2; IR (neat, cm^{-1}) ν 2915, 2839, 2200, 1638, 1601, 1519, 1497, 1405, 1384, 1291, 1242, 1176, 1161, 1111, 1027, 991, 921, 850, 835, 811, 747; HRMS (ESI) calcd for $C_{15}H_{13}O_2S$ $(M + H)^+$ 257.0631; found 257.0633.

1-(2-((Trimethylsilyl)ethynyl)phenyl)ethan-1-one (1p). This product was obtained as a light yellow oil (341.8 mg, 79% yield); ^1H NMR (500 MHz, $CDCl_3$) δ 7.68 (dd, J = 7.6, 1.4 Hz, 1H), 7.55

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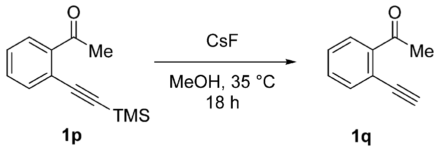
J. Org. Chem. 2015, 80, 11360−11368

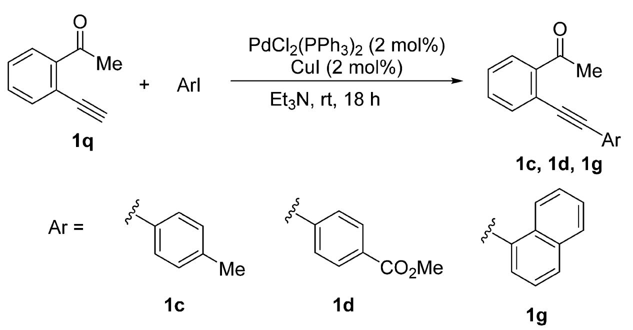
(dd, J = 7.6, 1.3 Hz, 1H), 7.42 (dt, J = 7.6, 1.6 Hz, 1H), 7.37 (dt, J = 7.6, 1.4 Hz, 1H), 2.74 (s, 3H), 0.26 (s, 9H). The ^{1}H NMR spectral data are in good agreement with the literature data.[22]

Procedure for the Preparation of 1-(2-Ethynylphenyl)-ethanone (1q). A 6-dram vial was charged with 1-(2-



((trimethylsilyl)ethynyl)phenyl)ethanone (**1p**, 432.8 mg, 2.0 mmol), CsF (455.7 mg, 3.0 mmol), and methanol (12 mL). The reaction mixture was stirred at 35 °C for 18 h, until the disappearance of the starting material as monitored by thin layer chromatography. Methanol was removed using a rotary evaporator, under reduced pressure (20 mmHg). The residue was dissolved in diethyl ether (30 mL) and washed with brine (30 mL). The aqueous phase was extracted with diethyl ether (20 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated using a rotary evaporator, under reduced pressure (20 mmHg). The residue was purified by flash column chromatography on silica gel (eluent: hexanes/ethyl acetate), to afford a light yellow oil (181.7 mg, 63% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, J = 7.8 Hz, 1H), 7.60 (d, J = 7.5 Hz, 1H), 7.41–7.47 (m, 2H), 3.39 (s, 1H), 2.72 (s, 3H). The ^{1}H NMR spectral data are in good agreement with the literature data.[22]

General Procedure for the Preparation of 2-Alkynylaryl-ketones (1c, 1d, 1g). A 6-dram vial was charged with 1-(2-



ethynylphenyl)ethanone (**1q**, 144.2 mg, 1.0 mmol), an aryl iodide (1.1 mmol), $Pd(PPh_3)_2Cl_2$ (14.0 mg, 0.02 mmol), CuI (3.8 mg, 0.02 mmol), and Et_3N (7 mL). The vial was then purged with argon and sealed. The reaction mixture was stirred at room temperature for 18 h, until the disappearance of starting material was observed, as monitored by thin layer chromatography. The reaction mixture was diluted with diethyl ether (40 mL) and washed with brine (40 mL), and the aqueous phase was then extracted with diethyl ether (2 × 20 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated using a rotary evaporator, under reduced pressure (20 mmHg). The resulting residue was purified by flash column chromatography on silica gel (eluent: hexanes/ethyl acetate).

1-(2-(*p*-Tolylethynyl)phenyl)ethanone (1c). This product was obtained as a light brown oil (142.9 mg, 61% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (dd, J = 7.8, 1.3 Hz, 1H), 7.62 (dd, J = 7.7, 1.1 Hz, 1H), 7.44–7.49 (m, 3H), 7.39 (dt, J = 7.5, 1.2 Hz, 1H), 7.18 (d, J = 7.9 Hz, 2H), 2.80 (s, 3H), 2.38 (s, 3H). The ^{1}H NMR spectral data are in good agreement with the literature data.[17]

Methyl 4-((2-Acetylphenyl)ethynyl)benzoate (1d). This product was obtained as a yellow solid (200.4 mg, 72% yield): mp = 118.3–119.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03–8.05 (m, 2H), 7.78 (d, J = 7.8 Hz, 1H), 7.66 (d, J = 7.6 Hz, 1H), 7.62 (d, J = 8.0 Hz, 2H), 7.51 (t, J = 7.5 Hz, 1H), 7.44 (t, J = 7.6 Hz, 1H), 3.94 (s, 3H), 2.78 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.2, 166.7, 140.9, 134.3, 131.69, 131.67, 130.1, 129.8, 129.1, 129.0, 127.8, 121.3, 94.0, 91.5, 52.5, 30.0; IR (neat, cm^{-1}) ν 2924, 1719, 1684, 1431, 1407, 1365, 1275, 1217, 1104, 1017, 931, 876, 823, 796, 762, 729, 697; HRMS (ESI) calcd for $C_{18}H_{15}O_3$ $(M + H)^+$ 279.1016; found 279.1019.

1-(2-(Naphthalen-1-ylethynyl)phenyl)ethanone (1g). This product was obtained as a yellow solid (183.8 mg, 68% yield): mp = 92.1–93.2 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.52 (d, J = 8.3 Hz, 1H), 7.88 (d, J = 8.2 Hz, 2H), 7.77–7.82 (m, 3H), 7.64 (dt, J = 8.2, 1.2 Hz, 1H), 7.52–7.57 (m, 2H), 7.43–7.50 (m, 2H), 2.83 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.4, 140.7, 134.4, 133.5, 133.4, 131.6, 130.9, 129.5, 129.1, 128.5, 127.3, 126.8, 126.4, 125.5, 122.1, 120.8, 93.4, 30.1 (fewer ^{13}C signals were observed due to signal overlapping); IR (neat, cm^{-1}) ν 3056, 2201, 1734, 1682, 1589, 1540, 1506, 1478, 1436, 1354, 1290, 1268, 1243, 1162, 1014, 956, 879, 802, 768; HRMS (ESI) calcd for $C_{20}H_{15}O$; $(M + H)^+$ 271.1117; found 271.1120.

General Procedure for the Gold-Catalyzed Intramolecular Cyclization of 2-Alkynylarylketones and -aldehydes. A 4-dram vial was charged with $NaAuCl_4 \cdot 2H_2O$ (11.9 mg, 0.03 mmol), $AgSbF_6$ (10.3 mg, 0.03 mmol), NH_4OAc (38.5 mg, 0.5 mmol), 4-methoxypyridine *N*-oxide (75.1 mg, 0.6 mmol), 2-alkynylarylketone (**1**, 0.5 mmol), and acetonitrile (4 mL). The vial was purged with argon and sealed. The reaction mixture was stirred at 85 °C for 2 h. After cooling to room temperature, the resulting mixture was diluted with diethyl ether (15 mL) and washed with brine (15 mL). The aqueous phase was extracted with diethyl ether (2 × 10 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated using a rotary evaporator, under reduced pressure (20 mmHg). The residue was purified by flash column chromatography on silica gel (eluent: hexanes/ethyl acetate).

3-Methyl-2-phenyl-1*H*-inden-1-one (2a). This compound was obtained as a light brown oil (76.0 mg, 69% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, J = 6.9 Hz, 1H), 7.41–7.46 (m, 5H), 7.34–7.36 (m, 1H), 7.25–7.28 (m, 1H), 7.17 (d, J = 7.2 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.7, 154.9, 146.1, 133.8, 133.6, 131.3, 130.6, 129.7, 129.1, 128.5, 127.9, 122.3, 119.6, 12.8; HRMS (ESI) calcd for $C_{16}H_{13}O$ $(M + H)^+$ 221.0961; found 221.0961. The ^{1}H and ^{13}C NMR spectral data are in good agreement with the literature data.[23]

1-Methyl-3-phenylisoquinoline (3a). This compound was obtained as a light yellow oil (20.8 mg, 19% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (dd, J = 8.2, 1.3 Hz, 3H), 7.93 (s, 1H), 7.86 (d, J = 8.2 Hz, 1H), 7.68 (dt, J = 6.8, 1.1 Hz, 1H), 7.56–7.59 (m, 1H), 7.49–7.52 (m, 2H), 7.40 (tt, J = 7.4, 1.8 Hz, 1H), 3.05 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.8, 150.2, 140.0, 136.9, 130.3, 128.9, 128.5, 127.8, 127.2, 127.0, 126.8, 125.9, 115.5, 22.9; HRMS (ESI) calcd for $C_{16}H_{14}N$ $(M + H)^+$ 220.1121; found 220.1119. The ^{1}H and ^{13}C NMR spectral data are in good agreement with the literature data.[24]

2-(4-Methoxyphenyl)-3-methyl-1*H*-inden-1-one (2b). This compound was obtained as an orange solid (87.6 mg, 70% yield): mp = 106.6–107.4 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, J = 7.0 Hz, 1H), 7.41 (td, J = 7.7, 1.0 Hz, 1H), 7.37–7.39 (m, 2H), 7.25 (t, J = 7.3 Hz, 1H), 7.15 (d, J = 7.2 Hz, 1H), 6.98 (dd, J = 6.9, 1.9 Hz, 2H), 3.85 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.1, 159.3, 153.6, 146.3, 133.8, 133.1, 131.0, 130.6, 128.8, 123.7, 122.2, 119.4, 114.0, 55.5, 12.8; IR (neat, cm^{-1}) ν 2919, 2849, 1707, 1611, 1591, 1508, 1547, 1378, 1247, 1176, 1113, 1080, 1024, 1004, 861, 822, 795, 758; HRMS (ESI) calcd for $C_{17}H_{15}O_2$ $(M + H)^+$ 251.1067; found 251.1068.

3-(4-Methoxyphenyl)-1-methylisoquinoline (3b). This compound was obtained as a beige solid (17.5 mg, 14% yield): mp = 56.1–57.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08–8.11 (m, 3H), 7.84 (s, 1H), 7.82 (d, J = 8.2 Hz, 1H), 7.63–7.66 (m, 1H), 7.52–7.55 (m, 1H), 7.02–7.05 (m, 2H), 3.88 (s, 3H), 3.03 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.1, 158.6, 149.9, 137.0, 132.7, 130.1, 128.4, 127.6, 126.6, 126.4, 125.8, 114.30, 114.28, 55.6, 22.9; HRMS (ESI) calcd for $C_{17}H_{16}NO$ $(M + H)^+$ 250.1226; found 250.1227. The ^{1}H and ^{13}C NMR spectral data are in good agreement with the literature data.[25]

3-Methyl-2-(*p*-tolyl)-1*H*-inden-1-one (2c). The product was obtained as a beige solid (59.8 mg, 51% yield): mp = 80.3–82.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, J = 7.2 Hz, 1H), 7.40 (dt, J = 7.6, 1.0 Hz, 1H), 7.31–7.33 (m, 2H), 7.23–7.26 (m, 3H), 7.14 (d, J =

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J. Org. Chem. 2015, 80, 11360–11368

7.2 Hz, 1H), 2.39 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.9, 154.3, 146.2, 137.8, 133.8, 133.6, 130.6, 129.6, 129.2, 129.0, 128.4, 122.3, 119.5, 21.6, 12.8; IR (neat, cm^{-1}) ν 2922, 2852, 1716, 1635, 1540, 1418, 1375, 1324, 1265, 1216, 1204, 1165, 1114, 1066, 1015, 926, 861, 806, 760; HRMS (ESI) calcd for $C_{17}H_{15}O$ $(M + H)^+$ 235.1117; found 235.1118.

1-Methyl-3-(*p*-tolyl)isoquinoline (3c). This compound was obtained as a yellow solid (36.2 mg, 31% yield): mp = 83.2−84.8 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (dd, *J* = 8.5, 0.8 Hz, 1H), 8.04 (dd, *J* = 6.5, 1.6 Hz, 2H), 7.89 (s, 1H), 7.84 (d, *J* = 8.2 Hz, 1H), 7.64−7.67 (m, 1H), 7.54−7.57 (m, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 3.04 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.7, 150.2, 138.4, 137.2, 137.0, 130.2, 129.7, 127.7, 127.0, 126.8, 126.6, 125.8, 114.9, 22.9, 21.5; HRMS (ESI) calcd for $C_{17}H_{16}N$ $(M + H)^+$ 234.1277; found 234.1276. The ^{1}H and ^{13}C NMR spectral data are in good agreement with the literature data.[26]

Methyl 4-(3-Methyl-1-oxo-1*H*-inden-2-yl)benzoate (2d). This compound was obtained as a yellow solid (54.3 mg, 39% yield): mp = 158.9−159.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (d, *J* = 8.4 Hz, 2H), 7.49−7.51 (m, 3H), 7.44 (dt, *J* = 7.6, 0.9 Hz, 1H), 7.29 (t, *J* = 7.4 Hz, 1H), 7.20 (d, *J* = 7.2 Hz, 1H), 3.93 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.0, 167.1, 156.4, 145.7, 136.1, 134.0, 132.6, 130.5, 129.7, 129.5, 129.2, 122.5, 120.0, 52.4, 13.0 (fewer ^{13}C signals were observed due to signal overlapping); IR (neat, cm^{-1}) ν 2923, 2851, 1716, 1705, 1609, 1591, 1507, 1456, 1428, 1408, 1279, 1190, 1106, 1081, 1028, 1004, 969, 946, 884, 867, 847, 820, 761, 754; HRMS (ESI) calcd for $C_{18}H_{15}O_3$ $(M + H)^+$ 279.1016; found 279.1018.

Methyl 4-(1-Methylisoquinolin-3-yl)benzoate (3d). This compound was obtained as a white solid (37.4 mg, 27% yield): mp = 125.1−126.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (dt, *J* = 8.7, 1.9 Hz, 2H), 8.17 (t, *J* = 1.6 Hz, 1H), 8.14−8.16 (m, 2H), 8.01 (s, 1H), 7.89 (d, *J* = 8.5 Hz, 1H), 7.69−7.72 (m, 1H), 7.60−7.63 (m, 1H), 3.96 (s, 3H), 3.05 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.3, 159.1, 148.8, 144.3, 136.7, 130.5, 130.3, 129.8, 128.0, 127.6, 127.1, 127.0, 125.9, 116.4, 52.4, 22.9; IR (neat, cm^{-1}) ν 2922, 2852, 1738, 1711, 1617, 1565, 1456, 1443, 1414, 1383, 1364, 1332, 1317, 1272, 1230, 1217, 1103, 1015, 960, 902, 889, 863, 852, 824, 785; HRMS (ESI) calcd for $C_{18}H_{16}NO_2$ $(M + H)^+$ 278.1176; found 278.1178.

5-Methoxy-2-(4-methoxyphenyl)-3-methyl-1*H*-inden-1-one (2e). This compound was obtained as a pink solid (25.2 mg, 18% yield): mp = 119.3−120.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.1 Hz, 1H), 7.37−7.39 (m, 2H), 6.97−6.98 (m, 2H), 6.70 (d, *J* = 2.2 Hz, 1H), 6.62 (dd, *J* = 7.7, 2.2 Hz, 1H), 3.88 (s, 3H), 3.84 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.9, 164.9, 159.3, 151.1, 149.1, 134.5, 131.0, 124.1, 123.9, 123.4, 114.0, 109.9, 108.6, 55.9, 55.5, 12.6; IR (neat, cm^{-1}) ν 2915, 2848, 1700, 1662, 1653, 1594, 1576, 1507, 1473, 1457, 1437, 1306, 1289, 1251, 1180, 1115, 1070, 1023, 1001, 829, 799, 780; HRMS (ESI) calcd for $C_{18}H_{16}NaO_3$ $(M + Na)^+$ 303.0992; found 303.0991.

7-Methoxy-3-(4-methoxyphenyl)-1-methylisoquinoline (3e). This compound was obtained as an orange solid (41.9 mg, 30% yield): mp = 130.5−132.2 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05−8.06 (m, 2H), 7.78 (s, 1H), 7.74 (d, *J* = 8.8 Hz, 1H), 7.29−7.33 (m, 2H), 7.01−7.03 (m, 2H), 3.96 (s, 3H), 3.87 (s, 3H), 2.98 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.9, 158.0, 156.9, 148.3, 132.9, 132.5, 129.2, 128.1, 127.3, 122.9, 114.3, 114.2, 103.7, 55.63, 55.55, 23.0; IR (neat, cm^{-1}) ν 2914, 2849, 1593, 1569, 1511, 1308, 1283, 1247, 1233, 1218, 1175, 1069, 1030, 876, 824, 817, 779, 752; HRMS (ESI) calcd for $C_{18}H_{18}NO_2$ $(M + H)^+$ 280.1332; found 280.1335.

6-Fluoro-3-methyl-2-phenyl-1*H*-inden-1-one (2f). This compound was obtained as a beige solid (47.7 mg, 40% yield): mp = 105.7−107.8 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43−7.46 (m, 2H), 7.39−7.41 (m, 2H), 7.34−7.37 (m, 1H), 7.21 (dd, *J* = 7.1, 2.4 Hz, 1H), 7.10−7.13 (m, 1H), 7.07 (dt, *J* = 8.8, 2.4 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.0, 163.9 (d, J_{C-F} = 250.5 Hz), 155.1, 141.4 (d, J_{C-F} = 3.6 Hz), 134.0 (d, $_{JC-F}$ = 4.6 Hz), 133.0 (d, J_{C-F} = 7.4 Hz), 131.1, 129.6, 128.6, 128.0, 120.7 (d, J_{C-F} = 7.8 Hz), 119.0 (d, J_{C-F} = 22.2 Hz), 111.1 (d, J_{C-F} = 24.7 Hz), 13.0; IR (neat, cm^{-1}) ν 3061, 2927, 1703, 1618, 1604, 1473, 1428, 1373, 1355, 1330, 1309, 1271, 1220, 1203, 1098, 1076, 1027, 1013, 887, 839, 813, 793, 769; HRMS (ESI) calcd for $C_{16}H_{12}FO$ $(M + H)^+$ 239.0867; found 239.0871.

6-Fluoro-1-methyl-3-phenylisoquinoline (3f). The product was obtained as a brown oil (46.3 mg, 39% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11−8.14 (m, 3H), 7.85 (s, 1H), 7.51 (t, *J* = 7.8 Hz, 2H), 7.40−7.45 (m, 2H), 7.31 (dt, *J* = 8.8, 2.5 Hz, 1H), 3.02 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.3 (d, J_{C-F} = 251.9 Hz), 158.7, 151.2, 139.6, 138.6 (d, J_{C-F} = 10.4 Hz), 129.0, 128.9 (d, J_{C-F} = 10.6 Hz), 128.8, 127.2, 124.0, 117.1 (d, J_{C-F} = 25.0 Hz), 115.0 (d, J_{C-F} = 5.0 Hz), 110.9 (d, J_{C-F} = 20.4 Hz), 23.0; IR (neat, cm^{-1}) ν 3062, 1716, 1625, 1601, 1570, 1443, 1362, 1268, 1225, 1215, 1135, 1027, 964, 882, 815, 775, 758; HRMS (ESI) calcd for $C_{16}H_{13}FN$ $(M + H)^+$ 238.1027; found 238.1031.

3-Methyl-2-(naphthalen-1-yl)-1*H*-inden-1-one (2g). This product was obtained as a red solid (47.3 mg, 35% yield): mp = 100.4−102.2 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (t, *J* = 6.9 Hz, 2H), 7.70 (d, *J* = 8.2 Hz, 1H), 7.53−7.56 (m, 2H), 7.43−7.51 (m, 3H), 7.31−7.35 (m, 2H), 7.23 (d, *J* = 7.2 Hz, 1H), 2.11 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.7, 157.6, 145.9, 134.2, 133.9, 133.8, 132.3, 130.9, 129.3, 129.2, 128.8, 128.7, 128.3, 126.2, 126.1, 125.5, 122.5, 119.7, 13.2 (fewer ^{13}C signals were observed due to signal overlapping); IR (neat, cm^{-1}) ν 3055, 2922, 285, 1701, 1596, 1459, 1378, 1314, 1171, 1085, 1026, 879, 807, 798; HRMS (ESI) calcd for $C_{20}H_{15}O$ $(M + H)^+$ 271.1117; found 271.1114.

1-Methyl-3-(naphthalen-1-yl)isoquinoline (3g). This product was obtained as a beige solid (56.6 mg, 42% yield): mp = 86.5−88.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.4 Hz, 1H), 8.13 (d, *J* = 8.5 Hz, 1H), 7.92 (d, *J* = 8.4 Hz, 2H), 7.88 (d, *J* = 8.1 Hz, 1H), 7.79 (s, 1H), 7.69−7.75 (m, 2H), 7.64−7.67 (m, 1H), 7.57−7.60 (m, 1H), 7.51 (dt, *J* = 6.8, 1.0 Hz, 1H), 7.45−7.48 (m, 1H), 3.09 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.6, 151.8, 139.1, 136.6, 134.2, 131.8, 130.4, 128.7, 128.5, 127.9, 127.7, 127.3, 126.5, 126.4, 126.2, 126.0, 125.9, 125.6, 120.2, 22.8; IR (neat, cm^{-1}) ν 3056, 2221, 1763, 1696, 1618, 1564, 1390, 1358, 1325, 1260, 1213, 1160, 1147, 1018, 964, 903, 890, 873, 855, 804, 776; HRMS (ESI) calcd for $C_{20}H_{16}N$ $(M + H)^+$ 270.1277; found 270.1278.

2-(Cyclohex-1-en-1-yl)-3-methyl-1*H*-inden-1-one (2h). This product was obtained as a light brown oil (20.2 mg, 18% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33−7.38 (m, 2H), 7.18 (t, *J* = 7.4 Hz, 1H), 7.05 (d, *J* = 6.7 Hz, 1H), 5.74−5.76 (m, 1H), 2.25−2.26 (m, 2H), 2.18−2.20 (m, 2H), 2.18 (s, 3H), 1.70−1.73 (m, 2H), 1.65−1.68 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.6, 153.2, 146.4, 136.7, 133.5, 130.8, 130.0, 129.8, 128.5, 121.9, 119.2, 28.3, 25.7, 22.9, 22.2, 12.7; IR (neat, cm^{-1}) ν 2930, 2855, 2430, 2360, 2017, 1704, 1612, 1590, 1170, 759; HRMS (ESI) calcd for $C_{16}H_{17}O$ $(M + H)^+$ 225.1274; found 225.1275.

3-(Cyclohex-1-en-1-yl)-1-methylisoquinoline (3h). This product was obtained as a brown oil (43.6 mg, 39% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (dd, *J* = 8.2, 0.7 Hz, 1H), 7.76 (d, *J* = 8.1 Hz, 1H), 7.60−7.63 (m, 1H), 7.48−7.52 (m, 1H), 7.44 (s, 1H), 7.06−7.07 (m, 1H), 2.96 (s, 3H), 2.55−2.58 (m, 2H), 2.31−2.34 (m, 2H), 1.83−1.87 (m, 2H), 1.69−1.74 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.8, 151.2, 136.9, 135.8, 130.0, 128.3, 127.7, 126.6, 126.3, 125.8, 113.1, 26.23, 26.19, 23.2, 22.9, 22.5; HRMS (ESI) calcd for $C_{16}H_{18}N$ $(M + H)^+$ 224.1434; found 224.1430. The ^{1}H and ^{13}C NMR spectral data are in good agreement with the literature data.[27]

4-(3-Methyl-1-oxo-1*H*-inden-2-yl)butanenitrile (2i). This product was obtained as an orange oil (37.0 mg, 35% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32−7.35 (m, 2H), 7.17 (td, *J* = 7.1, 0.7 Hz, 1H), 7.04 (dd, *J* = 6.9, 1.0 Hz, 1H), 2.42 (t, *J* = 7.4 Hz, 2H), 2.33 (t, *J* = 7.1 Hz, 2H), 2.15 (s, 3H), 1.85 (p, *J* = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.8, 155.8, 145.8, 133.6, 132.3, 130.6, 128.7, 121.8, 119.6, 119.2, 24.6, 21.8, 16.8, 11.7; IR (neat, cm^{-1}) ν 2937, 2245, 1701, 1701, 1628, 1608, 1593, 1455, 1427, 1384, 1148, 1084, 987, 918, 755; HRMS (ESI) calcd for $C_{14}H_{14}NO$ $(M + H)^+$ 212.1070; found 212.1074.

4-(1-Methylisoquinolin-3-yl)butanenitrile (3i). This product was obtained as a brown oil (16.8 mg, 16% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.5 Hz, 1H), 7.74 (d, *J* = 8.3 Hz, 1H),

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J. Org. Chem. 2015, 80, 11360−11368

7.65 (t, *J* = 7.2 Hz, 1H), 7.55 (t, *J* = 7.9 Hz, 1H), 7.36 (s, 1H), 3.02 (t, *J* = 7.2 Hz, 2H), 2.93 (s, 3H), 2.39 (t, *J* = 7.0 Hz, 2H), 2.14−2.22 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 151.5, 136.6, 130.4, 127.0, 126.8, 126.3, 125.8, 119.9, 117.7, 36.5, 25.5, 22.5, 16.7; IR (neat, cm^{-1}) ν 2939, 2245, 1717, 1617, 1592, 1568, 1496, 1432, 1390, 1365, 1331, 1216, 1023, 954, 899, 828, 785; HRMS (ESI) calcd for $C_{14}H_{15}N_2$ (M + H)$^+$ 211.1230; found 211.1240.

2-(*tert*-Butyl)-3-methyl-1*H*-inden-1-one (2j). This product was obtained as a yellow solid (12.0 mg, 12% yield): mp = 57.0−58.0 °C; ^{1}H NMR (500 MHz; $CDCl_3$) δ 7.32−7.35 (m, 2H), 7.16 (td, *J* = 7.4, 0.6 Hz, 1H), 7.04−7.06 (m, 1H), 2.29 (s, 3H), 1.36 (s, 9H); ^{13}C NMR (125 MHz; $CDCl_3$) δ 198.8, 151.2, 147.1, 140.3, 133.4, 130.7, 128.3, 121.4, 118.6, 34.1, 30.7, 13.4; HRMS (ESI) calcd for $C_{14}H_{17}O$ (M + H)$^+$ 201.1274; found 201.1276. The ^{1}H and ^{13}C NMR spectral data are in good agreement with the literature data.[28]

3-(*tert*-Butyl)-1-methylisoquinoline (3j). This product was obtained as a yellow oil (20.0 mg, 20% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.4 Hz, 1H), 7.75 (d, *J* = 8.2 Hz, 1H), 7.60 (td, *J* = 7.6, 0.8 Hz, 1H), 7.50 (td, *J* = 7.6, 1.2 Hz, 1H), 7.44 (s, 1H), 2.95 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.0, 157.4, 136.7, 129.6, 127.4, 126.1, 125.8, 125.6, 112.8, 37.1, 30.4, 22.8; IR (neat, cm^{-1}) ν 2953, 2863, 1738, 1624, 1571, 1480, 1442, 1388, 1355, 1329, 1216, 1203, 1155, 928, 877, 847, 785; HRMS (ESI) calcd for $C_{14}H_{18}N$ (M + H)$^+$ 200.1434; found 200.1434.

2,3-Diphenyl-1*H*-inden-1-one (2k). This product was obtained as a red solid (55.1 mg, 39% yield): mp = 150.0−152.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (d, *J* = 6.7 Hz, 1H), 7.36−7.42 (m, 6H), 7.25−7.30 (m, 6H), 7.15 (d, *J* = 7.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.8, 155.5, 145.4, 133.7, 132.9, 132.6, 130.93, 130.91, 130.2, 129.5, 129.2, 129.0, 128.7, 128.3, 127.9, 123.2, 121.5; HRMS (ESI) calcd for $C_{21}H_{15}O$ (M + H)$^+$ 283.1117; found 283.1120. The ^{1}H and ^{13}C NMR spectral data are in good agreement with the literature data.[29]

1,3-Diphenylisoquinoline (3k). This product was obtained as an orange solid (35.2 mg, 25% yield): mp = 76.0−77.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21−8.23 (m, 2H), 8.13 (dd, *J* = 8.5, 0.7 Hz, 1H), 8.08 (s, 1H), 7.941 (d, *J* = 8.2 Hz, 1H), 7.81−7.83 (m, 2H), 7.69 (ddd, *J* = 8.1, 6.9, 1.1 Hz, 1H), 7.48−7.59 (m, 6H), 7.42 (dm, *J* = 7.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 150.4, 140.1, 139.8, 138.0, 130.4, 130.3, 128.9, 128.8, 128.7, 128.5, 127.8, 127.7, 127.3, 127.1, 126.0, 115.9; HRMS (ESI) calcd for $C_{21}H_{16}N$ (M + H)$^+$ 282.1277; found 282.1274. The ^{1}H and ^{13}C NMR spectral data are in good agreement with the literature data.[30]

2-(4-Methoxyphenyl)-3-phenyl-1*H*-inden-1-one (2l). This compound was obtained as a red solid (56.2 mg, 36% yield): mp = 117.0−117.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.0 Hz, 1H), 7.37−7.42 (m, 5H), 7.34 (dt, *J* = 7.4, 1.0 Hz, 1H), 7.21−7.24 (m, 3H), 7.10 (d, *J* = 7.1 Hz, 1H), 6.78−6.80 (m, 2H), 3.77 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.2, 159.4, 154.0, 145.7, 133.6, 133.2, 132.0, 131.5, 130.9, 129.3, 129.0, 128.9, 128.7, 123.2, 123.1, 121.2, 113.8, 55.4; HRMS (ESI) calcd for $C_{22}H_{17}O_2$ (M + H)$^+$ 313.1223; found 313.1228. The ^{1}H and ^{13}C NMR spectral data are in good agreement with the literature data.[31]

3-(4-Methoxyphenyl)-1-phenylisoquinoline (3l). This compound was obtained as a yellow solid (42.0 mg, 27% yield): mp = 113.0−115.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17−8.19 (m, 2H), 8.11 (d, *J* = 8.6 Hz, 1H), 8.00 (s, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.81−7.83 (m, 2H), 7.65−7.68 (m, 1H), 7.55−7.58 (m, 2H), 7.46−7.53 (m, 2H), 7.02−7.04 (m, 2H), 3.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.4, 160.3, 150.1, 140.1, 138.1, 132.4, 130.4, 130.2, 128.7, 128.48, 128.46, 127.7, 127.5, 126.7, 125.6, 114.8, 114.3, 55.6; IR (neat, cm^{-1}) ν 3057, 2921, 2221, 1763, 1712, 1604, 1561, 1512, 1437, 1387, 1336, 1285, 1247, 1170, 1159, 1142, 1023, 976, 828, 806, 769; HRMS (ESI) calcd for $C_{22}H_{18}NO$ (M + H)$^+$ 312.1383; found 312.1384.

3-Phenylisoquinoline (3m). This product was obtained as a light red solid (100.6 mg, 98% yield): mp = 103.1−104.2 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.35 (s, 1H), 8.13−8.15 (m, 2H), 8.07 (s, 1H), 7.98 (d, *J* = 8.3 Hz, 1H), 7.86 (d, *J* = 8.1 Hz, 1H), 7.69 (t, *J* = 8.3 Hz, 1H), 7.58 (t, *J* = 7.7 Hz, 1H), 7.51−7.54 (m, 2H), 7.41−7.45 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.6, 151.4, 139.8, 136.8, 130.7, 129.0, 128.7, 127.9, 127.7, 127.23, 127.17, 127.07, 116.7; HRMS (ESI) calcd for $C_{15}H_{12}N$ (M + H)$^+$ 206.0964; found 206.0964. The ^{1}H and ^{13}C NMR spectral data are in good agreement with the literature data.[30]

7-Methyl-5-phenylthieno[2,3-*c*]pyridine (3n). This product was obtained as a yellow oil (72.1 mg, 64% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (d, *J* = 7.4 Hz, 2H), 7.95 (s, 1H), 7.65 (d, *J* = 5.4 Hz, 1H), 7.49 (t, *J* = 7.3 Hz, 2H), 7.39−7.42 (m, 2H), 2.89 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.7, 152.0, 146.1, 140.2, 134.4, 131.4, 128.9, 128.4, 127.3, 124.2, 112.7, 23.9; IR (neat, cm^{-1}) ν 3058, 1575, 1545, 1480, 1439, 1392, 1377, 1348, 1117, 1086, 1065, 1032, 862, 820, 772; HRMS (ESI) calcd for $C_{14}H_{12}NS$ (M + H)$^+$ 226.0685; found 226.0687.

5-(4-Methoxyphenyl)-7-methylthieno[2,3-*c*]pyridine (3o). This product was obtained as a yellow solid (108.5 mg, 85% yield): mp = 82.1−83.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, *J* = 9.0 Hz, 2H), 7.89 (s, 1H), 7.65 (d, *J* = 5.5 Hz, 1H), 7.39 (d, *J* = 5.1 Hz, 1H), 7.01 (d, *J* = 8.7 Hz, 2H), 3.87 (s, 3H), 2.86 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.1, 152.6, 151.8, 146.2, 133.8, 132.9, 131.4, 128.5, 124.2, 114.3, 111.9, 55.6, 24.0; IR (neat, cm^{-1}) ν 1650, 1605, 1575, 1545, 1515, 1387, 1300, 1280, 1250, 1180, 1035, 830; HRMS (ESI) calcd for $C_{15}H_{14}NOS$ (M + H)$^+$ 256.0791; found 256.0795.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01939.

Copies of ^{1}H and ^{13}C NMR spectra for the new compounds. (PDF)

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Notes

The authors declare no competing financial interest.

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