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Coupling Radical Homoallylic Expansions with C−C Fragmentations for the Synthesis of Heteroaromatics: Quinolines from Reactions of *o*-Alkenylarylisonitriles with Aryl, Alkyl, and Perfluoroalkyl Radicals

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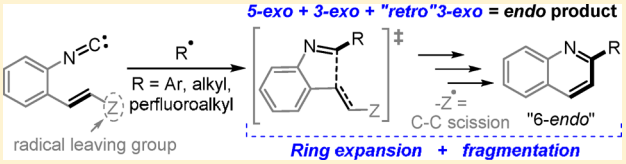
Supporting Information

ABSTRACT: Selective addition of radicals to isonitriles can be harnessed for initiating reaction cascades designed to overcome the stereoelectronic restrictions on homoallylic ring expansion in alkyne reactions and to develop a new general route for the preparation of N-heteroaromatics. This method utilizes alkenes as synthetic equivalents of alkynes by coupling homoallylic ring expansion to yield the formal "6-*endo*" products with aromatization via stereoelectronically assisted C−C bond scission. Computational analysis of the homoallyic expansion potential energy surface reveals that the indirect 5-exo/3-exo/retro-3-exo path is faster than the direct 6-endo-trig closure, revealing the general exo-preference for the cyclization processes.



INTRODUCTION

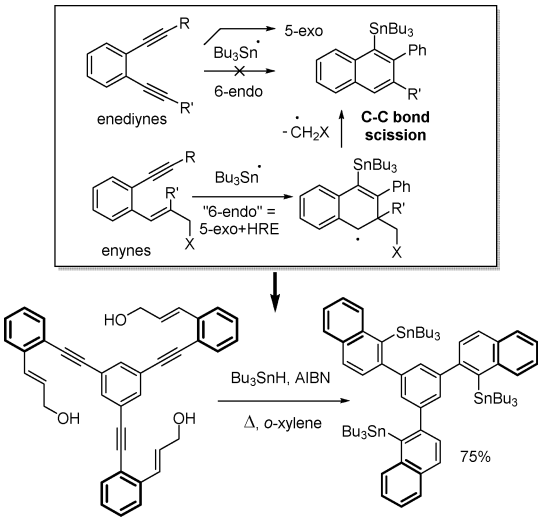
Alkynes are attractive starting materials for the preparation of carbon-rich conjugated molecules.[1] In particular, the 6-*endo*-dig cyclizations of alkynes open atom-economical access to functionalized polycyclic aromatic hydrocarbons (PAHs). However, the radical version of this alkyne cyclization is plagued by selectivity problems. Instead of the desired 6-*endo*-dig product, the reaction often favors a five-membered ring formation via the stereoelectronically preferred 5-*exo*-dig path.[2] We have recently established a combination of 5-*exo*-trig cyclization of enynes with homoallylic ring expansion (HRE) and C−C fragmentation as an indirect but efficient way to six-membered aromatic compounds that are inaccessible from the 6-*endo*-dig cyclization of related bis-alkynes (Scheme 1).[3]

This process, where alkenes are used as synthetic analogues of alkynes, takes advantage of the greater stereoelectronic flexibility of alkyl radicals derived from alkenes in order to bypass the inefficient HRE of vinyl radicals derived from alkynes. In the alkyne route, the HRE process stalls because the vinyl radical in the *exo*-dig product is constrained to orthogonality relative to the target π−system (Scheme 2, left).[4] In contrast, the HRE in the 5-*exo*-trig radical products that form from the alkene precursors can undergo conversion into the *endo*-products (Scheme 2, right).[5] The C−C fragmentation adjusts the oxidation state of the six-membered product of enyne cyclizations, rendering it fully aromatic.

Two conditions are important for the success of this transformation where alkenes serve as synthetic equivalents of alkynes in order to bypass the unreliable *endo*-dig cyclization. First, the 5-*exo*-trig product should be capable of fast 3-*exo*-trig cyclization into a relatively strained intermediate. Second, the C-Z bond should be sufficiently strong to be compatible with the radical conditions, but the final C-Z bond scission should be faster than intramolecular quenching of the nonaromatic six-membered intermediate in order to complete the crossover to the formal 6-*endo*-dig product.

The solution to the second problem was identified based on our earlier work on the design of radical leaving groups.[4a]

Scheme 1. Application of Alkenes as Alkyne Equivalents in Radical Cascades Terminated by Fragmentation



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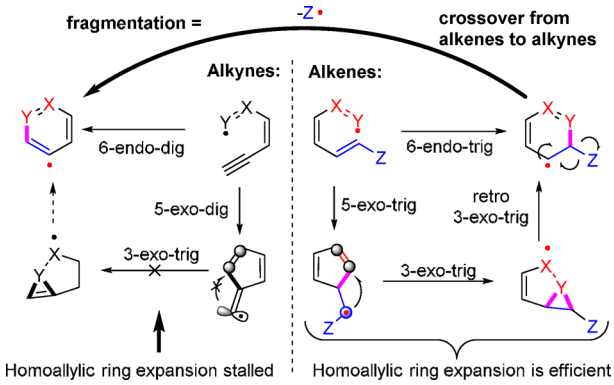
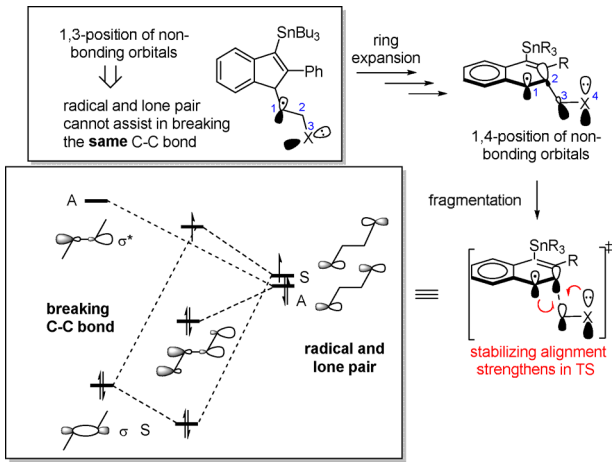
Scheme 2. Left: Stereoelectronic Restriction on the 5-*exo*-Dig → 6-*endo*-Dig Homoallylic Ring Expansion (HRE) and Right: "Recycling" 5-*exo*-Trig Products into 6-*endo*-Trig Products via Homoallylic Ring Expansion[a]



[a]Z = CH_2Ph, CH_2OR.

Although the choice of the relatively strong C−C bond as the "weak link" may seem surprising, it prevents the premature fragmentation and decreases the probability of undesired side-reactions. Only when the evolution of the radical cascade places the radical center at the γ-atom relative to a lone pair or a Ph group, the C−C fragmentation becomes sufficiently fast due to the activation of three-electron through-bond (TB) orbital interactions via the breaking bond (Scheme 3).[4a] These interactions facilitate the C−C bond scission that furnishes the final cascade product.

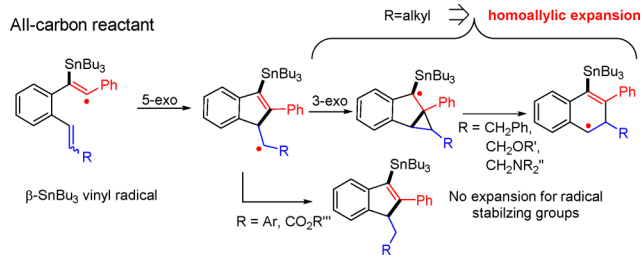
Scheme 3. Activation of the Stabilizing Through-Bond Interactions in the C−C Bond Fragmentation of the Properly Substituted 6-*endo* Products of Enyne Cyclizations



On the other hand, the 5-*exo*-trig/HRE sequence is not general because it is sensitive to the nature of reactants and can be interrupted at different stages. In particular, the HRE step is stopped and the 5-*exo*-trig products can be obtained in high yield when the *exo*-cyclic radical is stabilized by a conjugating substituent (Scheme 4).

We were interested in expanding this approach to the preparation of N-heterocyclic aromatic systems.[6] In recent years, much work has been devoted to developing methods for the construction of N-heterocyles[7] including examples of cascades of *o*-alkynylarylisonitriles.[8] These transformations

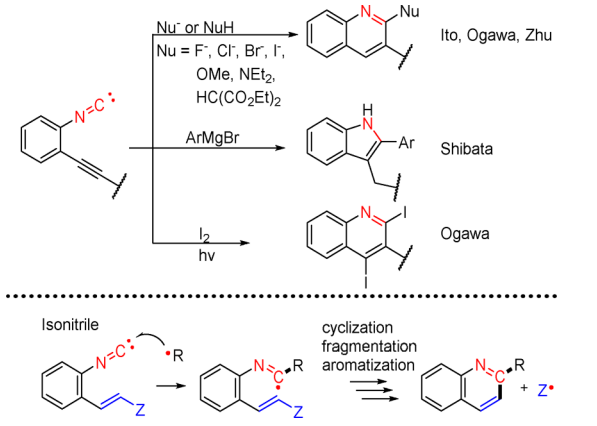
Scheme 4. Homoallylic Ring Expansion Can Be Stopped by Stabilization of the 5-*exo*-Product



included a variety of mechanistic approaches, such as nucleophile promoted,[8a−d] photochemical,[8e] and cycloaromatization[9] routes.

In particular, we envisioned the use of isonitriles in an analogous reaction of vinyl radicals. Reactions of isonitriles with radicals are well-known to be selective and provide a vinyl (iminoyl) radical intermediate that seems to be well-suited for the cyclization/fragmentation cascade (Scheme 5).[10] However,

Scheme 5. Top: Representation of the Impact of Cyclization Partners on 5-*exo*/6-*endo* Selectivity in Alkynylisonitrile Products and Bottom: Condensed Mechanism for Radical Addition/Cyclization Cascade Using Alkenes as Equivalents to Alkynes



the subsequent selectivity in the reaction of such radicals in *o*-alkynylarylisonitrile systems (e.g., the ratio of 5-*exo* vs 6-*endo* products) using $HSnBu_3$/AIBN was found to be highly sensitive to the alkyne substitution.[8f,g]

These observations motivated us to design an alternative isonitrile substrate that can use "alkenes as alkyne" equivalents as a potential approach to control the 5-*exo* and 6-*endo* competition.

However, the earlier work by Fukuyama suggests that the initial 5-*exo*-products do not undergo the ring expansion even for alkyl substituted alkenes (where, otherwise, the 5-*exo* products were not deactivated by resonance stabilization).[11a] Furthermore, the selectivity for the alkyl substituted substrates of this type agrees with the formation of the 5-*exo* products reported later by Studer in radical trifluoromethylations terminated by deprotonation/electron transfer.[12a] The goal of this article is to understand whether this reluctance toward HRE is general in these systems and, if not, to develop a robust system for efficient cascade reactions (Scheme 6).

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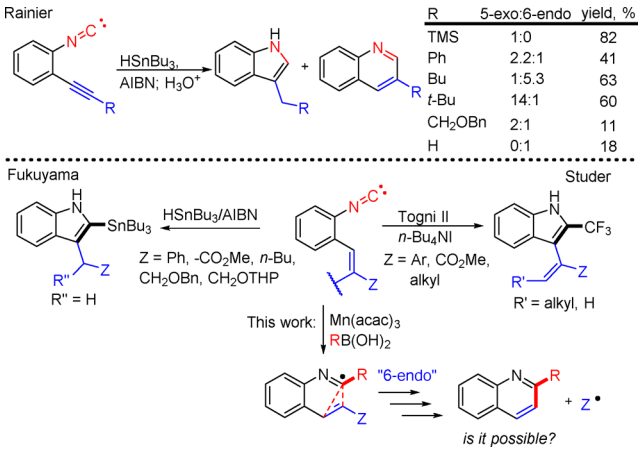
Scheme 6. Literature Precedents in Radical Cyclizations[a]



[a]Top: *o*-alkynyl arylisonitriles. Bottom: *o*-alkenyl arylisonitriles.

This work combines experiments and computations for understanding mechanistic details of the N-heterocycle synthesis based on radical 5-*exo*/expansion/fragmentation cascade of *o*-alkenyl arylisonitriles. This methodology overcomes issues of low 6-*endo*-dig selectivity normally associated with radical cyclizations.

RESULTS AND DISCUSSION

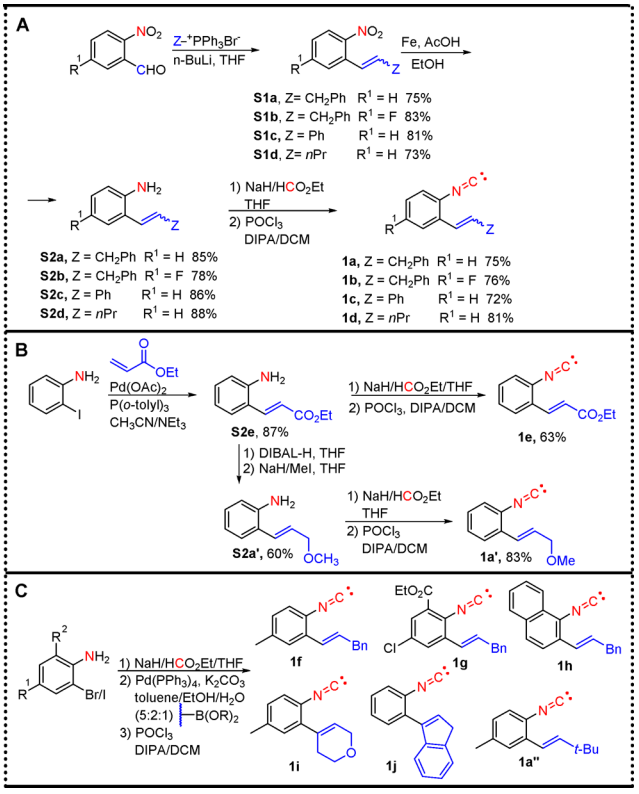
Synthesis of Cyclization Precursors. We have developed convenient routes to the diverse array of cyclization substrates from a wide selection of inexpensive and readily available *o*-substituted aldehydes/halides (depicted in Scheme 7). The reliable Wittig,[13] Heck,[14] and Suzuki[15] reactions can be used to install the alkene functionality in good yields. For the Suzuki/Heck pathways the corresponding E-isomer isonitriles were prepared in two steps, Pd-catalyzed coupling of alkenes with 2-haloformamides, followed by formamide → isonitrile conversion. The Wittig reactions of 2-nitrobenzaldehydes afford the desired isonitriles in moderate to good yields via a sequence of: nitro group reduction, amine formylation, and subsequent dehydration. Wittig route provided a mixture of cis/trans isomers in moderate to good yields.

The parent isonitrile **1a** was used as a test substrate for investigating the scope of radical sources that can induce the cyclization/expansion/fragmentation cascades.

Our initial studies turned to Sn-centered radicals that can be conveniently generated via the radical chain process from a suitable tin hydride precursor and allows the installation of valuable Sn-functionality in the final product.[16] However, earlier literature precedents were discouraging.[11] In particular, a thorough study of Fukuyama has shown that the 5-*exo* indole products are formed in the reactions of $HSnBu_3$/AIBN with *o*-alkenylarylisonitriles, even when Z = CH_2OR (Scheme 6). Indeed, we have reproduced this literature report and observed only the 5-*exo*-product formation from the CH_2OR-substituted substrate **1a′** in the $HSnBu_3$/AIBN-mediated reaction. This result drastically contrasts our observation of efficient ring-expansion/fragmentation cascade in the analogous all-carbon systems.[4]

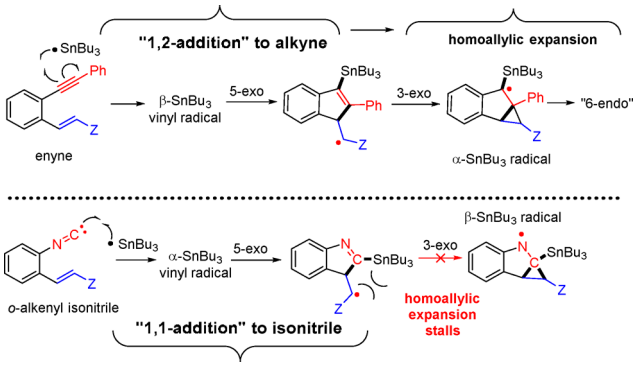
We suspected that the variation in selectivity may stem from the difference in the position of Bu_3Sn-group relative to the radical center in the two types of vinyl radicals.[17] The Bu_3Sn addition to enynes forms a β-Sn-substituted radical where bulky

Scheme 7. Synthesis of *o*-alkenyl isocyanide substrates via routes that utilize Wittig (A), Heck (B) and Suzuki (C) Coupling Reactions To Install the Alkenyl Group onto the *o*-Amino-Substituted Aromatic Core



−$SnBu_3$ moiety is placed away from the point of the new bond formation in the subsequent 3-*exo*-step. (Scheme 8, below).

Scheme 8. Top: All Carbon System Allows for HRE Process with Using AIBN/$HSnBu_3$ and Bottom: α-$SnBu_3$ Prevents HRE in Isonitrile System



This radical readily undergoes the HRE process because the 3-*exo*-cyclization TS is not sterically hindered. In contrast, isonitriles act as a "1,1-synthon" in radical additions, to form an α-Sn-substituted iminoyl radical. Consequently, the initial product of the 5-*exo* cyclization of isonitrile has the bulky $SnBu_3$-group directly at the radical carbon involved in the initiation of subsequent HRE. The increased steric hindrance should slow the 3-*exo*-step of sequence, explaining why the HRE cascade stops and only the indole products are observed (Scheme 8, below).

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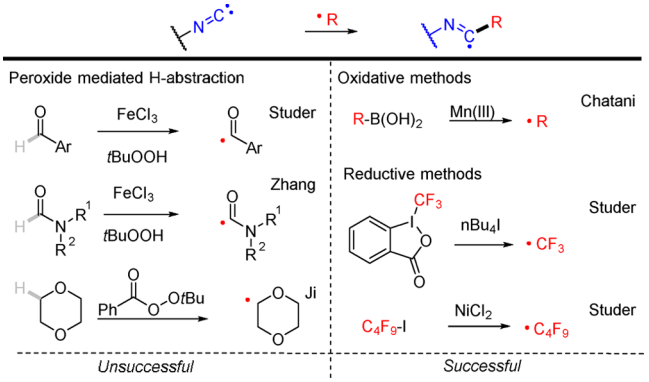
Many radical species are known to add to isonitriles.[10−12] However, much of this work relies on an H-abstraction step (often with peroxides) to generate the desired radical source (Scheme 9, left).[18] In the literature cases, this step would often

Scheme 9. Examples of Radical Additions To Isonitriles[a]

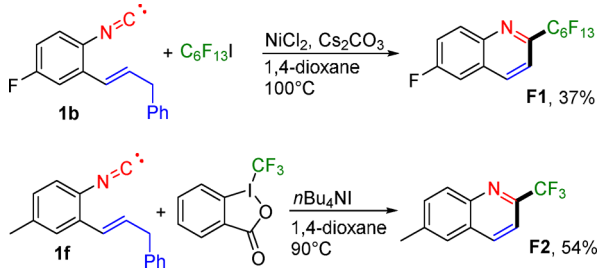


[a](Left): Unsuccessful approaches based on C−H abstraction by peroxides. (Right): Successful oxidative and reductive methods.

be compatible with the subsequent transformations. Unfortunately, the "benzallylic" C−H bonds in our alkenes are sufficiently weak (BDE: ∼ 84 kcal/mol)[19] to undergo competing H-abstraction even when such activated C−H bond substrates as aldehydes, formamides, and ethers were used.[20] Consequently, our exploratory attempts to initiate the cyclization/fragmentation cascades via C−H abstraction from the above substrates resulted in complex mixtures.

On the other hand, iodoperfluorocarbons can be successfully used as radical precursors under initiation conditions reported by Studer and co-workers (Scheme 9).[12a,21] For example, the reaction of **1b** with perfluorohexyl iodide, yielded solely F1 as the product. In a similar manner, reaction of isonitrile **1f** with the Togni II reagent initiated the desired cascade with fragmentation/aromatization cascade to yield F2 (Scheme 10).

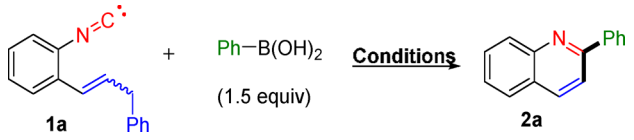
Scheme 10. Perfluoro Radicals Successfully Induce Addition/Cyclization/Fragmentation Cascade of *o*-Alkenylarylisonitriles



In search of other general protocols that did not rely on H-abstraction to generate radicals (Scheme 9),[12,21,22] we turned to organoboron reagents that increasingly gain popularity as radical precursors.[23,24] We were also interested in testing whether the oxidative activation of boronic acids by a mild oxidant can offer advantages for the manipulation of the oxidation state of reacting species (i.e., radicals vs cations). Furthermore, the synthetic utility of this methodology is enhanced by the wide variety of commercially available boronic acids.

To our delight, in the presence of $Mn(acac)_3$ and phenyl boronic acid, substrate **1a** underwent the selective 6-*endo* cyclization/fragmentation cascade.[25,26] Table 1 outlines the

Table 1. Optimization of Reaction Conditions[a]



entry	oxidant	equiv	solvent	temp ∘C	yield %[b]
1	$Mn(acac)_3$	1	C_7H_8	90	17
2	$Mn(acac)_3$	2	C_7H_8	90	64
3	$Mn(acac)_3$	3	C_7H_8	90	86
5	$Mn(acac)_3$	3	C_7H_8	reflux	82
6	$Mn(acac)_3$	3	C_7H_8	rt	0
7	$Mn(acac)_3$	3	C_7H_8	50	59
8	$Mn(OAc)_3•2H_2O$	3	C_7H_8	90	67
9	$Mn(OAc)_2$	3	C_7H_8	90	0
10	$Cu(OAc)_2$	3	C_7H_8	90	0
11	$AgNO_3/Na_2S_2O_8$	0.2/3	DCM/H_2O	90	0
12	$Mn(acac)_3$	3	MeCN	reflux	79
13	$Mn(acac)_3$	3	C_6H_6	reflux	84
14	$Mn(acac)_3$	3	DMF	90	trace

[a]Reaction conditions: isocyanide (0.1 mmol), boronic acid (1.5 equiv), specified amount of oxidant in 3 mL of solvent. Reactions were stirred for 4 h, with exception of r.t. reaction that was allowed to react for 24 h. [b]NMR yield based on **1a**.

screening process that leads to the optimized conditions (entry 3) which yielded exclusively the quinoline **2a** in 86% yield. Slight excess (1.5 equiv) of boronic acid was needed, presumably to compensate for the side reactions, such as radical dimerization.[27] Elevated temperatures are required for full conversion (entries 3, 6, 7). $Mn(acac)_3$ outperformed other oxidants during the screening process and was chosen for further studies. The optimized conditions were used to study the substituent scope and limitation for the new transformation.

The scope of the reaction, in terms of both boronic acids and isonitriles, is quite broad, opening access to a variety of quinolines in good yields. Both donor and acceptor functional groups were tolerated (Table 2). The products were characterized via a combination of spectroscopic techniques and, in the case of product **2s**, via X-ray analysis. Successful formation of compound **2g** suggests that alkyl boronic acids are compatible with the reaction as well. The only exception was the alkenyl boronic acid that did not give product **2r** under the above conditions and yielded instead to a complex mixture of products unstable on SiO_2.

More than 2-fold excess of the oxidant, required for achieving full conversion, hints at a further single electron transfer (SET) oxidation of intermediate radicals.[19,28] This possibility was suggested for the $Mn(III)/RB(OH)_2$-mediated cyclization of isocyanobiphenyls, where a SET oxidation by the second equivalent of Mn(III) was postulated to generate a cationic intermediate that aromatizes into phenanthridines via loss of a proton.[29,30]

Considering that the CH_2Ph-substituted substrate yielded excellent results, we proceeded to investigate the effect on the yield of substituents at the terminus of the alkene and the selectivity of the cyclization/expansion/fragmentation cascade (Table 1). The yields of desired quinoline products follow the

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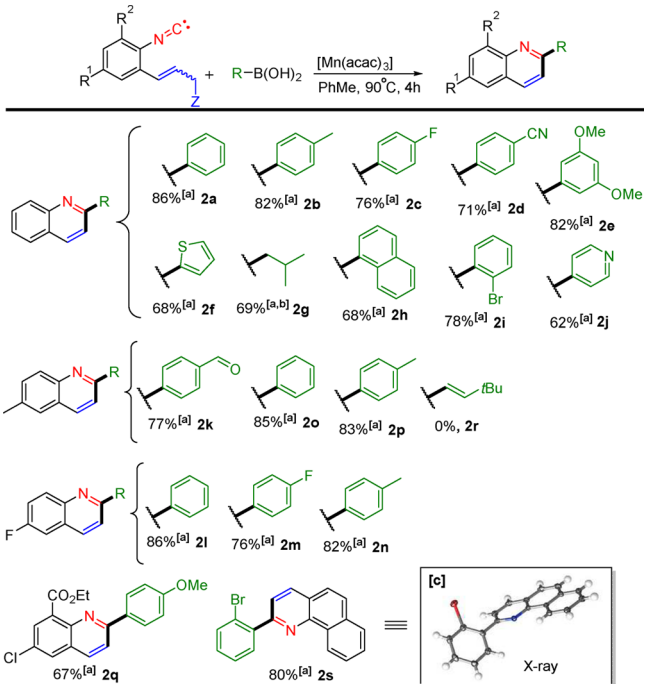
Table 2. Scope of Mn(III)-Mediated Transformations



[a]Yield of isolated product from starting materials. [b]3 equiv of boronic acid were used. [c]ORTEP drawing of **2s**; thermal ellipsoids are set at a 50% probability level.

trend of radical stability (benzyl > α-alkoxy > alkyl) for (Z: $-CH_2Ph$ = 86%; $-CH_2OMe$ = 69%; $-C(CH_3)_3$ = 19%). The dramatically lower quinoline yield for the fragmentation producing the *t*-Bu radical can also be attributed to the steric hindrance of the bulky *tert*-butyl group.

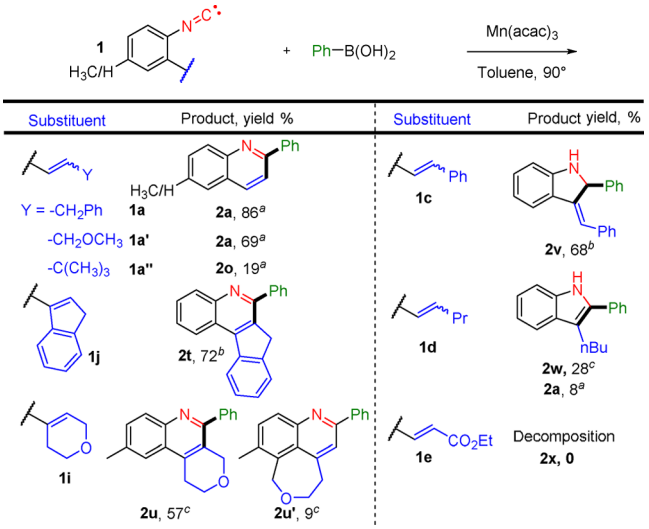
The effect of radical-stabilizing groups on regioselectivity was observed in the case of a phenyl substituted alkene **1c**, where exclusive 5-*exo* product formation was observed.[11,12,31] In this case, the radical formed upon initial 5-*exo* cyclization is stabilized by π-conjugation from the phenyl ring, which deactivates this species toward the HRE process.[32]

An intriguing result was observed for propyl substituted substrate, **1d**. The alkyl group should not interfere with the HRE of the 5-*exo* radical but is unable to provide stabilization in the fragmentation step. The overall mass-balance of this reaction is low. The 5-*exo* product **2w** was formed from **1d** in 28%, but the yield of the desired quinoline **2a** was even lower (8%, Table 3).

In parallel, we prepared two structurally constrained bicyclic substrates **1j** and **1i** (Table 3). Contrary to the formerly discussed results, the indene **1j** yielded only the 6-*endo* product, **2t**, without the C−C scission (proposed mechanism shown in Scheme 12). In the case of **1i**, a major (**2u**, 57%) and minor product (**2u′**, 9%) were observed as an inseparable mixture (proposed mechanism shown in Scheme 14).

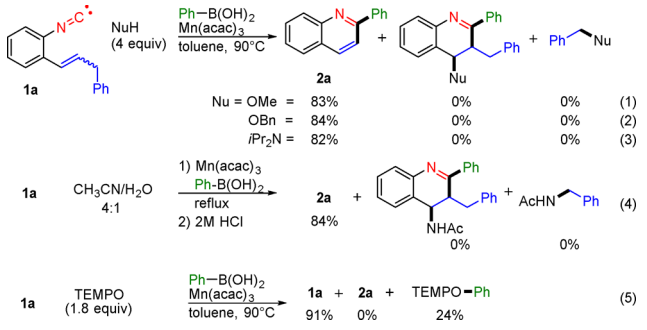
We have also considered the cationic mechanism for our system. However, additional experimental studies (as well as computations provided below) did not support the cationic pathway (Scheme 11). In particular, when we introduced nucleophilic species into the reaction (eqs 1, 2, and 3), we only observed the usual quinoline product, with only slightly reduced yields. It is known that the CH_3CN/H_2O mixture can trap benzylic carbocations to form, upon hydrolytic workup, the respective N-benzylacetamides.[33] When toluene

Table 3. Screening of Alkene Substituents[d]



[a]Isolated yield. [b]NMR yield based on starting material. [c]Yield of isolated major product with mixture of products. [d]Reaction conditions: isocyanide (0.1 mmol), boronic acid (1.5 equiv), $Mn(acac)_3$ (3 equiv), and toluene (3 mL) were heated at 90 °C for 4 h. Complete conversion was observed in all cases.

Scheme 11. Control Experiments for Evaluating the Relative Importance of Cationic and Radical Reaction Pathways



was replaced with a 4:1 mixture of CH_3CN/H_2O as the solvent (eq 4 below), only the quinoline product was observed in 84% after the hydrolytic workup. The same reaction in dry CH_3CN provided a similar yield (79%) of the same quinoline product.

Additionally, we conducted the reaction in the presence of 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO).[34] Under these conditions, we observed the formation of TEMPO-Ph as expected from successful trapping of the Ph radical.[35] Furthermore, the unreacted starting material was isolated in 91% (eq 5).

The available experimental results suggest the following mechanism (Scheme 12). The reaction begins with the formation of a carbon-centered radical in the reaction of Mn(III) and boronic acid.[36] The chemoselective addition of this radical to the arylisonitrile moiety generates the iminoyl radical **A1** capable of the reactions outlined in Scheme 12. The "6-*endo*" product **A2** formation was observed exclusively when an appropriate fragmenting group (i.e., CH_2Ph, $-CH_2OMe$) was installed. Potentially, the *endo*-product can be either produced directly or form via HRE of the 5-*exo*-trig radical **A3**.

The stereoelectronic factors in the C−C bond scission were probed via the reaction of the bicyclic substrates **1j** and **1i**. Both substrates yield solely the 6-*endo* products as outlined in

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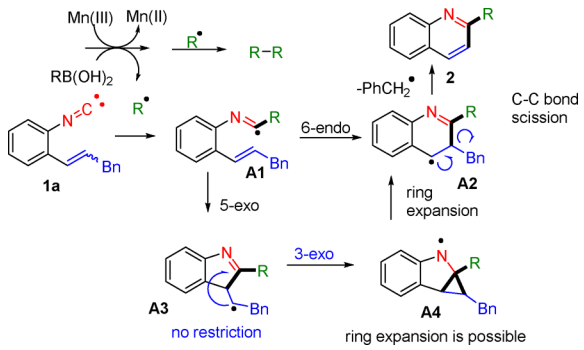
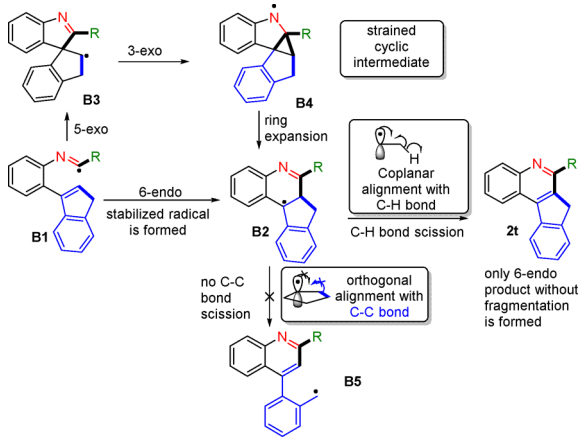
Scheme 12. Proposed Radical Pathway for 6-*endo* Product Formation

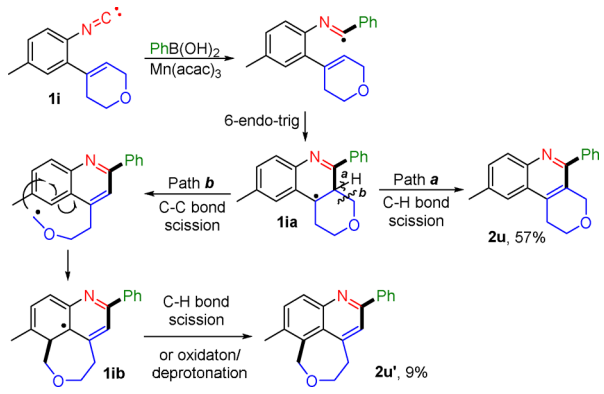


Scheme 13 and Scheme 14. However, the sequence of reaction steps for **1j** culminated in a C–H scission instead of the usual

Scheme 13. Radical Pathway for C–H Bond Cleavage in a Stereoelectronically Restricted Cycle



Scheme 14. Proposed Mechanism for Tethered Substrate Product Formation



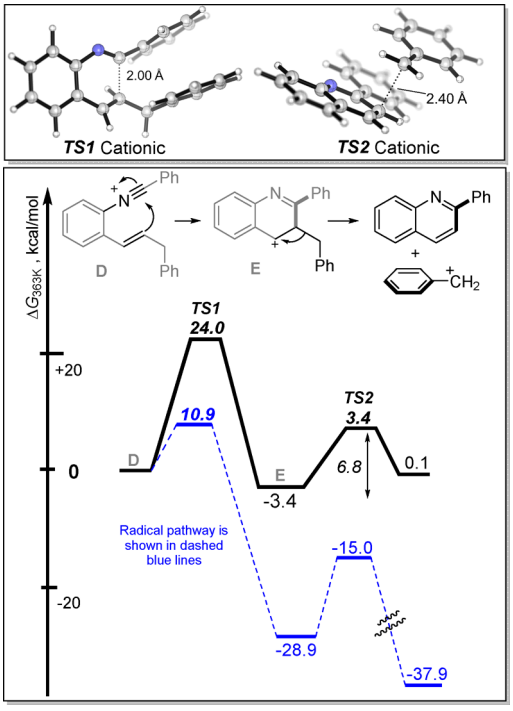
C–C fragmentation. We attribute the lack of C–C fragmentation to structural constraint that imposes the nearly perpendicular arrangement for the C–C bond and the radical orbital in **B2**. The same structural constraint aligns the benzylic C–H bond with the radical, facilitating the C–H bond scission at the expense of the C–C fragmentation.

On the other hand, the saturated cycle in the tetrahydropyrane containing substrate **1i** allows more flexibility in aligning the scissile C–C bond with the radical. Furthermore, the strategically positioned oxygen atom in this molecule can assist in the C–C fragmentation step by stabilizing the resulting radical. However, the ideal orbital alignment for this assistance is hampered by the cyclic constraints. Whereas compound **1i** produced exclusively the 6-*endo*-products, the fragmentation step was not selective. The major product, **2u** resulted from a C–H cleavage whereas the minor product, **2u′** was formed via the C–C bond scission. The latter path was continued by radical attack at the aromatic ring and subsequent rearomatization (a plausible mechanism is summarized in Scheme 14).

Calculations were carried with the Gaussian 09 software package,[37] using the M06-2X DFT functional[38] with the 6-311++G(d,p) basis set for all atoms. The implicit PCM[39] solvation model was used to simulate the effects of toluene throughout the reaction pathways. We also performed natural bond orbital[40] (NBO) analysis on key intermediates and transition states.

Cationic vs Radical. As the first step, we compared the energetics of radical and cationic pathways. In agreement with the experimental results discussed above, the cationic 6-*endo* cyclization/fragmentation sequence was found to be unlikely. Most notably, the barrier for 6-*endo* cyclization in the cationic pathway (Scheme 15, solid line) is 24 kcal/mol, much higher

Scheme 15. Gibbs Free Energy Diagram for the Cationic Pathway Shows that This an Unlikely Mechanism[a]



[a]Data for the respective radical mechanism are shown in blue and with a dashed line.

than the ~11 kcal/mol barrier for the radical process (Scheme 15, dashed line). Although both cationic and radical 6-*endo* cyclizations were found to be exergonic, the driving force for the cationic ring closure was significantly lower than for the radical cyclization (−3.4 vs −28.9 kcal/mol, respectively). The largest difference was observed for thermodynamics of the fragmentation steps: fragmentation for the cationic pathway is an uphill battle (+ 3.5 kcal/mol relative to the penultimate

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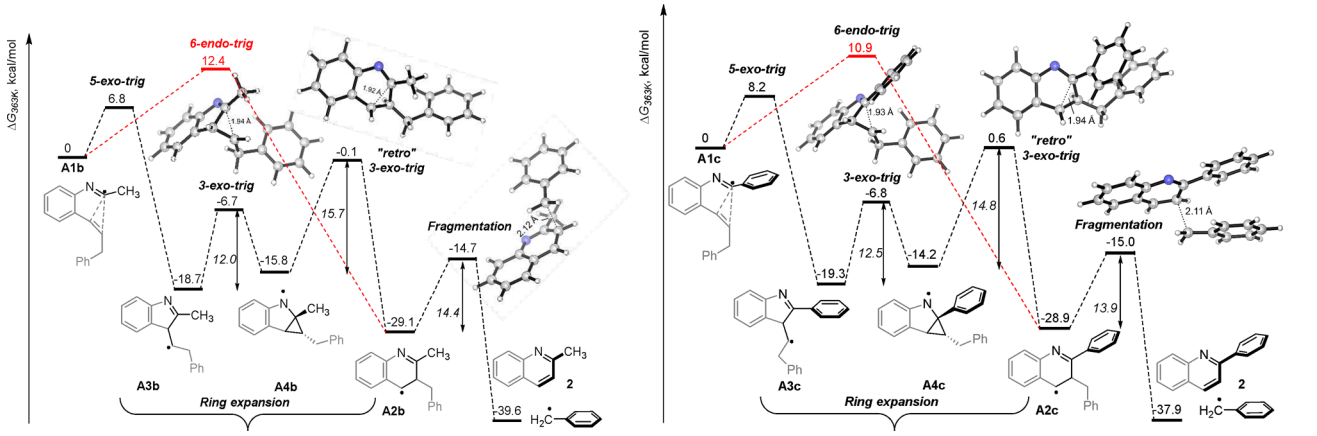
Scheme 16. Gibbs Free Energy Diagram for Full Radical Cascade Initiated by the Addition of Me and Ph Radicals, Including HRE, Direct 6-*endo* Path[a], and Fragmentation[b]



[a]Shown in red. [b]See SI for the other full cascade PESs.

intermediate) whereas the radical fragmentation is 11 kcal/mol exergonic. These results provide additional support to a radical mechanism for the observed cascade transformation.

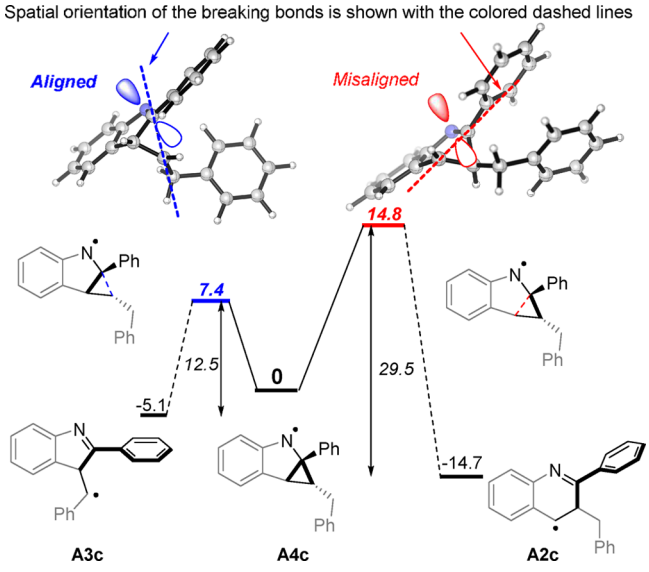
These results, along with an agreement with the experimental observations, give strong support to a radical mechanism for the observed cascade transformation. In the following section, we provide a general outline of the observed cascade.

Importance of HRE Path—Direct vs Indirect Pathways to the 6-Endo Product. The ring expansion cascade is relatively complex and involves a sequence of two fragmentations and two fragmentations. We plan to analyze the full details of substituent and structural effects on the interplay of the individual steps in a separate article. At the present stage, we will limit discussion to relative energies of the direct and indirect routes to the final products. The most important message is that, even though the tricyclic product of the 3-*exo*-trig cyclization **A4b**/**A4c** are slightly higher in energy than the 5-*exo*-product **A3b**/**A3c** (due to strain accumulation) and although the retro-3-*exo*-trig barrier for the conversion of **A4b**/**A4c** to the final 6-*endo* product **A2c** was relatively high (~14 kcal/mol relatively to **A4b**/**A4c**), the overall potential energy surface (PES) for the 5-*exo* → 6-*endo* HRE is much lower than the PES for the direct 6-*endo*-trig closure (Scheme 16).

Analysis of these calculated potential energy surfaces reiterates the importance of stereoelectronic concepts in the design of cyclization processes. Even though the direct 6-*endo* cyclization is not as disfavored as its 4-*endo* and 5-*endo* cousins, the combination of three *exo*-cyclizations (i.e., the 5-*exo*/homoallylic expansion) is still energetically preferred over the "direct" *endo* path to the six-membered product (Scheme 17). Avoiding the direct path in favor of a combination of indirect multistep route is reminiscent of the commonly encountered situation in catalysis when an unfavorable single-step transformation is accomplished in a more favorable way via a combination of elementary steps enabled by substrate/catalyst interactions.[41] This is a manifestation of the general *exo*-trig preference for cyclizations.[42]

Stereoelectronic Attenuation of Radical Clocks. Interestingly, the two 3-membered TS's in the cascade correspond to two alternative "radical-clock" ring openings of bicyclic radical **A4c**. A noteworthy feature in the competition between these reactions is that the barrier for the more exergonic of the two analogous processes is higher. This

Scheme 17. Stereoelectronic Attenuation of Radical Clocks by Alignment (or Lack of Thereof) with the Endocyclic π-System



difference reflects stereoelectronic factors involved in the C−C bond scission. Bicyclic restraints make orbital alignment different and hamper the C−C bond scission as illustrated by the TS geometries in Scheme 17. The more favorable TS has a much better overlap of the breaking C−C bond with the radical center at N.

Fragmentation Step. The final step of the cascade consists in a fragmentation that results in an aromatic product and a H_2C−X radical. Different X groups can stabilize this radical fragment by hyperconjugation (alkyl groups), *2c,3e* "half-bonds" (lone pair donor, such as MeO or NMe_2), or conjugation (phenyl group). Scheme 18A depicts the barriers and reaction energies for departure of various radicals. Since this reaction produces two products, it is expected for it to be an entropically driven process and therefore it benefits from higher temperatures. The greater the stabilization of the radical formed, the more exergonic is this step. As one would expect, the activation energy for such C−C scission also decreases as the fragmentations become more exergonic.

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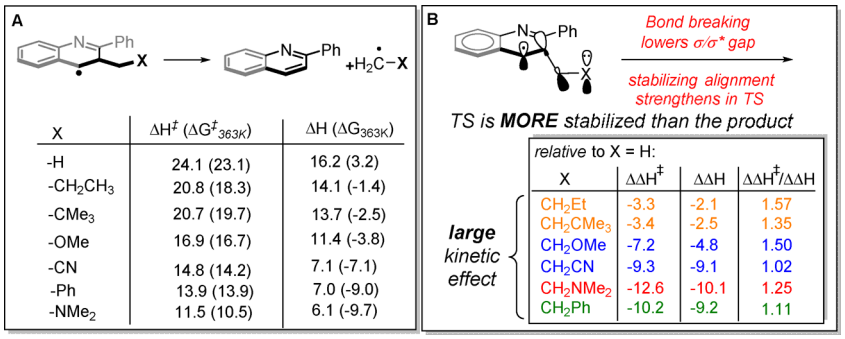
Scheme 18. Scope of Radical Leaving Groups and Relation between Kinetics and Thermodynamics of the C−C Scission[a]



X	$\Delta H^{\ddagger}$ ($\Delta G^{\ddagger}_{363K}$)	ΔH (ΔG_{363K})
-H	24.1 (23.1)	16.2 (3.2)
$-CH_2CH_3$	20.8 (18.3)	14.1 (-1.4)
$-CMe_3$	20.7 (19.7)	13.7 (-2.5)
-OMe	16.9 (16.7)	11.4 (-3.8)
-CN	14.8 (14.2)	7.1 (-7.1)
-Ph	13.9 (13.9)	7.0 (-9.0)
$-NMe_2$	11.5 (10.5)	6.1 (-9.7)

relative to X = H:

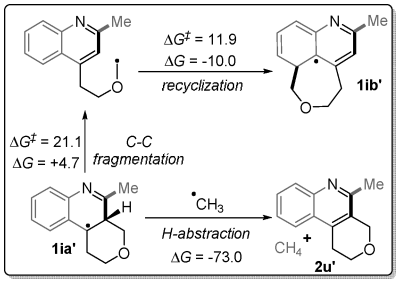
X	$\Delta\Delta H^{\ddagger}$	$\Delta\Delta H$	$\Delta\Delta H^{\ddagger}/\Delta\Delta H$
CH_2Et	-3.3	-2.1	1.57
CH_2CMe_3	-3.4	-2.5	1.35
CH_2OMe	-7.2	-4.8	1.50
CH_2CN	-9.3	-9.1	1.02
CH_2NMe_2	-12.6	-10.1	1.25
CH_2Ph	-10.2	-9.2	1.11

[a]Energies in kcal/mol.

The unique feature of these processes is that each substituent stabilizes TS more than the fully developed radical in product, as shown in Scheme 18B. The quantum mechanical rationale for this remarkable behavior is given in our earlier work.[4a] In short, through-bond interactions between the lone pair of X and the radical center are strengthened in the TS, producing large kinetic effects when compared to X = H, i.e., in absence of any stabilizing group.

On the other hand, bicyclic constraints make the barrier for C−CH_2(OR) bond scission much higher (~4 kcal/mol penalty in comparison to the C−CH_2OR in the acyclic case). Furthermore, because the former scission does not result in the formation of two separate molecules, the free energy of fragmentation is significantly less favorable and the overall process is endergonic (Scheme 19). Recyclization at the adjacent benzene ring has a calculated barrier of ~12 kcal/mol and, even though this attack should break aromaticity, the reaction is expected to be fairly exergonic (ΔG = −10 kcal/mol). The alternative pathway for this intermediate would consist on α-H abstraction by the radical source, coupled with aromatization of the pyridine core. This process is estimated to be extremely exergonic under our reaction conditions (ΔG = −73 kcal/mol). The results presented in Scheme 19 are in agreement with our experimental results.

Scheme 19. Effect of Bicyclic Constraints in the Fragmentation Step and Possible Capture of the Fragmented Radical[a]



[a]Energies in kcal/mol at 363 K.

CONCLUSIONS

This work presents a comprehensive study of radical cascades that transform *o*-alkenylarylisonitriles into substituted quinolines. Although cascades initiated by Bu_3Sn-addition to *o*-alkenylarylisonitriles stall at the 5-*exo*-trig state, the analogous reactions of aryl, alkyl, and perfluoroalkyl radicals to isonitriles lead to full homoallylic expansion cascade terminated by C−C scission and aromatization. The relative efficiency of the final C−C bond scission can be controlled stereoelectronically by introducing additional structural constraints. Use of an appropriate alkene partner allows for an efficient cyclization/fragmentation sequence that renders alkenes as synthetic equivalents to alkynes and provides a new approach to the *de novo* assembly of the substituted quinoline core.

EXPERIMENTAL SECTION

General Information. Unless otherwise described, all reactions were performed with standard Schlenk techniques or with a balloon to provide inert atmosphere. All ^{1}H NMR spectra were run in $CDCl_3$ on either 400 or 600 MHz spectrometer. All ^{13}C NMR were run in $CDCl_3$ on either 100 or 150 MHz spectrometer. Proton chemical shifts are given relative to the residual proton signal of $CDCl_3$ (7.26 ppm). Carbon chemical shifts were internally referenced to $CDCl_3$ (77.23 ppm) signal. Data are reported as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, spt = septet, m = multiplet), coupling constant (Hz), and integration. Infrared spectra (IR) were obtained on a PerkinElmer Lambda 950 or PerkinElmer Spectrum 100; absorptions are reported in reciprocal centimeters. An AccuTOF mass spectrometer analyzer was used to acquire high-resolution mass spectra (HRMS). Unless otherwise specified acetonitrile, toluene, and THF were obtained from a SPS-4 solvent purification system. Hexanes for column chromatography and preparatory thin layer chromatography were distilled prior to use. Dichloromethane and di-isopropylamine were distilled prior to use. All other solvents and chemicals were purchased from commercial suppliers and used as received without further purification.

Experimental Details. *General Procedure for Wittig Reaction.* To a solution of the desired Wittig salt (1.2 equiv) in anhydrous THF at −78 °C was added slowly *n*-BuLi (2.5 M in hexanes, 1.2 equiv). After 45 min, a solution of desired 2-nitrobenzaldehyde (1 equiv) in THF was added dropwise. The resulting solution was stirred for 1 h at −78 °C and then at room temperature for 12 h and quenched with saturated NH_4Cl solution. The aqueous phase was extracted with Et_2O (3 × 30 mL), and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The crude was purified by column chromatography(hexane) on silica gel affording the desired *o*-alkenylnitroarene.

1-Nitro-2-(3-phenylprop-1-enyl)benzene (**S1a**) was prepared following the general Wittig procedure as dark yellow oil (E:Z = 1:3, 75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12−8.05 (m, 3H), 7.96−7.90 (m, 1H), 7.65−7.58 (m, 4H), 7.58−7.55 (m, 1H), 7.50−7.19 (m, 27H), 6.98 (t, J = 10.4 Hz, 1H), 6.92 (d, J = 11.4 Hz, 3H), 6.39 (dt, J = 15.5, 7.0 Hz, 1H), 6.08 (dt, J = 11.4, 7.7 Hz, 3H), 3.64 (dd, J = 7.0, 1.0 Hz, 2H), 3.50 (dd, J = 7.7, 0.8 Hz, 6H). HRMS (ESI) m/z: $[M]^+$: Calcd for $C_{15}H_{13}NNaO_2$ 262.0844, Found: 262.0845. Spectral data match those previously reported.[26]

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4-Fluoro-1-nitro-2-(3-phenylprop-1-en-1-yl)benzene (**S1b**) was prepared following the general Wittig procedure as a light brown oil (E:Z = 1:3, 83%). R_f = 0.44 (hexanes/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (dd, J = 8.7, 5.1 Hz, 1H), 8.00 (dd, J = 9.1, 5.2 Hz, 1H), 6.37 (d, J = 15.5 Hz, 1H), 6.09 (dt, J = 11.4, 7.7 Hz, 1H), 3.62 (d, J = 6.7 Hz, 1H), 3.48 (d, J = 7.6 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.7, 163.2, 139.5, 136.2, 136.0, 135.9, 132.9, 128.8, 128.8, 128.8, 128.3, 127.8, 127.7, 126.7, 126.5, 126.2, 126.0, 118.7, 118.5, 115.3, 115.1, 39.6, 34.5. HRMS (ESI) m/z: $[M+Na]^+$: Calcd for $C_{15}H_{12}FNNaO_2$ 280.0742, Found: 280.0744. Spectral data match those previously reported.[26]

1-Nitro-2-styrylbenzene (**S1c**) was prepared following the general Wittig procedure to give 81% of the title compound (E:Z = 0.7:1) as a light brown oil. R_f = 0.44 (hexanes/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14−8.06 (m, 1H), 7.97 (dd, J = 8.1, 0.9 Hz, 1H), 7.78 (d, J = 7.5 Hz, 1H), 7.64−7.52 (m, 3H), 7.45−7.24 (m, 11H), 7.21−7.15 (m, 3H), 7.13−7.04 (m, 3H), 6.91 (d, J = 12.1 Hz, 1H), 6.78 (d, J = 12.1 Hz, 1H).^{13}C NMR (101 MHz, $CDCl_3$) δ 136.6, 136.0, 134.0, 134.0, 133.8, 133.8, 133.2, 133.2, 132.4, 132.0, 129.3, 129.0, 128.8, 128.7, 128.6, 128.4, 128.3, 128.2, 128.1, 127.7, 127.2, 126.6, 126.0, 124.9, 124.8, 123.7. HRMS (ESI) m/z: $[M]^+$: Calcd for $C_{14}H_{11}NO_2$ 225.0790, Found: 225.0801. Spectral data match those previously reported.[26]

1-Nitro-2-(pent-1-en-1-yl)benzene (**S 1d**) was prepared following the general Wittig procedure to give 73% of the title compound (E:Z = 1:2) as a light brown oil. R_f = 0.73 (hexanes/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (dd, J = 8.2, 1.0 Hz, 1H), 7.86−7.76 (m, 1H), 7.60−7.43 (m, 2H), 7.41−7.24 (m, 3H), 6.80 (d, J = 15.7 Hz, 1H), 6.66 (d, J = 11.6 Hz, 1H), 6.20 (dt, J = 15.6, 6.9 Hz, 1H), 5.78 (dt, J = 11.6, 7.5 Hz, 1H), 2.20 (qd, J = 7.3, 1.5 Hz, 1H), 2.03 (qd, J = 7.5, 1.7 Hz, 2H), 1.57−1.43 (m, 1H), 1.42−1.31 (m, 2H), 0.93 (t, J = 7.4 Hz, 2H), 0.83 (t, J = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.6, 134.5, 133.3, 132.8, 132.8, 132.6, 131.9, 128.3, 127.6, 127.3, 125.1, 125.0, 124.3, 124.3, 35.2, 30.4, 22.7, 22.2, 13.6, 13.6. HRMS (ESI) m/z: $[M]^+$: Calcd for $C_{11}H_{13}NO_2$ 191.0946, Found: 191.0942. Spectral data match those previously reported.[26]

General Procedure for Reduction of Nitro Group. To a solution of *o*-alkenylnitroarene (1 equiv) in absolute ethanol was added glacial acetic acid and iron powder (6 equiv). The mixture was heated to reflux. After 6 h, the crude mixture was cooled and filtered through a pad of Celite. The filtrate was concentrated *in vacuo*. Purification by flash chromatography on silica gel (hexanes:EtOAc) afforded desired *o*-alkenylaniline compounds.

2-(3-Phenylprop-1-en-1-yl)aniline (**S2a**) was prepared following general procedure for reduction of nitro group (**S1a**) yielding 1.1 g of a dark brown oil (E:Z = 1:3, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.04 (m, 31H), 6.81−6.69 (m, 7H), 6.67 (dd, J = 8.0, 1.0 Hz, 1H), 6.49 (d, J = 15.5 Hz, 1H), 6.44 (d, J = 11.1 Hz, 3H), 6.24 (dt, J = 15.5, 6.9 Hz, 1H), 5.99 (dt, J = 11.1, 7.5 Hz, 3H), 3.69 (s, 6H), 3.58 (d, J = 7.0 Hz, 3H), 3.52 (d, J = 7.5 Hz, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz) 144.8, 143.4, 136.2,133.4, 130.2, 129.8, 128.9, 128.8, 128.6, 126.9, 126.5, 123.0, 121.0, 120.5, 56.6, 35.5, 31.5, 21.6. HRMS (ESI) m/z: $[M]^+$: Calcd for $C_{15}H_{15}N$ 209.1250, Found: 209.1260 Spectral data match those previously reported.[26]

4-Fluoro-2-(3-phenylprop-1-en-1-yl)aniline (**S2b**) was prepared following general procedure for reduction of nitro group (**S1b**) to give 78% of the title compound (E:Z = 1:3) as a brown oil. R_f = 0.44 (hexanes/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 (dt, J = 9.5, 3.2 Hz, 1H), 6.67 (ddd, J = 8.4, 4.8, 1.4 Hz, 1H), 6.64−6.58 (m, 1H), 6.45 (d, J = 15.2 Hz, 1H), 6.40 (d, J = 11.4 Hz, 1H), 6.32−6.20 (m, 1H), 6.09−5.96 (m, 1H), 3.52 (d, J = 7.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.1, 154.8, 140.4, 133.8, 132.4, 128.8, 128.7, 128.7, 128.7, 1n28.5, 128.5, 126.4, 126.3, 126.1, 125.3, 124.0, 123.9, 116.2, 116.1, 115.9, 114.9, 114.7, 39.7, 34.8. HRMS (ESI) m/z: $[M]^+$: Calcd for $C_{15}H_{15}FN$ 228.1188, Found: 228.1199. Spectral data match those previously reported.[26]

2-Styrylaniline (**S2c**) was prepared following general procedure for reduction of nitro group (**S1c**) to give 86% of the title compound (E:Z = 0.7:1) as a dark oil. R_f = 0.44 (hexanes/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (dd, J = 8.1, 0.9 Hz, 1H), 7.64−7.58 (m, 1H), 7.54 (t, J = 7.6 Hz, 2H), 7.45 (dd, J = 7.7, 1.6 Hz, 2H), 7.41−7.25 (m, 6H), 7.18 (d, J = 16.1 Hz, 1H), 7.01 (t, J = 7.5 Hz, 1H), 6.92−6.85 (m, 1H), 6.85−6.78 (m, 3H), 6.68 (d, J = 12.1 Hz, 1H), 3.84 (s, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.0, 143.7, 137.5, 136.6, 131.5, 130.0, 129.5, 128.7, 128.7, 128.7, 128.6, 128.6, 128.4, 128.2, 127.5, 127.4, 127.1, 126.4, 126.4, 124.2, 123.6, 123.0, 119.0, 118.3, 116.2, 115.4. HRMS (ESI) m/z: $[M]^+$: Calcd for $C_{14}H_{14}N$ 196.1126, Found: 196.1141. Spectral data match those previously reported.[26]

2-(Pent-1-en-1-yl)aniline (**S 2d**) was prepared following general procedure for reduction of nitro group (**S 1d**) to give 88% of the title compound (E:Z = 1:2) as a light brown oil. R_f = 0.44 (hexanes/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.28 (m, 1H), 7.21−7.04 (m, 1H), 6.90−6.65 (m, 1H), 6.54−6.42 (m, 1H), 6.35 (d, J = 11.3 Hz, 1H), 6.14 (dtd, J = 9.1, 6.9, 2.2 Hz, 1H), 5.85 (dtd, J = 9.5, 7.4, 2.1 Hz, 1H), 3.71 (s, 1H), 2.38−2.05 (m, 1H), 1.66−1.40 (m, 1H), 1.21−0.85 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.0, 143.4, 134.8, 133.1, 129.8, 128.0, 127.9, 127.4, 125.5, 125.0, 124.5, 123.4, 119.0, 118.0, 116.0, 115.6, 115.1, 35.6, 30.7, 23.0, 22.7, 13.9, 13.8. HRMS (ESI) m/z: $[M]^+$: Calcd for $C_{11}H_{16}N$ 162.1282, Found: 162.1295. Spectral data match those previously reported.[26]

General Procedure for Formamide Preparation. A solution of *o*-alkenylaniline (1 equiv) and ethyl formate (8 equiv) in anhydrous THF was added dropwise to a suspension of NaH (60% in mineral oil, 2.2 equiv) in anhydrous THF at 0 °C. Upon complete addition the mixture was stirred at room temperature for 24 h, then the reaction was quenched with cold water. The solvents were removed under reduced pressure, and the residue was dissolved in ethyl acetate/water (5/1). The aqueous phase was extracted with ethyl acetate (3 × 20 mL), the combined organic extracts were dried over anhydrous Na_2SO_4 and evaporated. The residue was washed thoroughly with hexane (3 × 30 mL) and dried *in vacuo* to yield the desired formylamine, which was used in the following step without further purification.

General Procedure for Suzuki Reactions. To a solution of boronic acid (1.5 equiv), $Pd(PPh_3)_4$ (10 mol%) and K_2CO_3 (4 equiv) in toluene, absolute ethanol, and water (5:2:1) was added N-(2-halophenyl)formamide (1 equiv). The mixture was then purged with N_2 and refluxed for 24 h. The reaction was then cooled to room temperature and 20 mL of H_2O were added and the resulting phases were separated. The resulting aqueous phase was extracted with 3 × 10 mL ethyl acetate. The resulting organic phases were then washed with water (1 × 20 mL) followed by a saturated solution of brine (1 × 20 mL). The resulting organic phase was then dried using Na_2SO_4 and filtered. The solvent was removed under reduced pressure and the crude product was purified using flash chromatography on silica gel (*n*-hexane/EtOAc 5:1 as eluent) to give the desired products which were used in the next step without further purification.

General Procedure for Dehydration of Formamide to Isonitrile. To a solution of N-formyl amide (0.1 mmol, 1 equiv) in anhydrous CH_2Cl_2 was added at 0 °C diisopropylamine (2.5 equiv), then dropwise over a period of 5 min $POCl_3$ (1.5 equiv) was added. The mixture was stirred at 0 °C for 2 h, then a saturated solution of Na_2CO_3 (2 mL) was added slowly. The mixture was transferred into a separatory funnel, diluted with CH_2Cl_2 (20 mL), the organic phase was washed with a saturated solution of Na_2CO_3 (10 mL) and brine (10 mL), then dried over anhydrous Na_2SO_4 and evaporated. The crude product was purified by flash chromatography (hexanes:EtOAc, 10:1) to give the desired *o*-alkenylarylisonitrile.

*Procedure for Preparation of Ethyl-3-(2-isocyanophenyl)acrylate (**1e**).* To a one neck round-bottom flask was added a magnetic stir bar, 2-iodoaniline (9.636 g, 44 mmol), ethyl acrylate (17.6 g, 176 mmol), $Pd(OAc)_2$ (1 g, 4.45 mmol), P(*o*-tolyl)$_3$ (2.7 g, 8.9 mmol), triethylamine (15 mL), and CH_3CN. The mixture was then purged with N_2 and refluxed for 24 h. The mixture was then cooled to room temperature and 20 mL of H_2O were added and the resulting phases were separated. The resulting aqueous phase was extracted with 3 × 10 mL ethyl acetate. The resulting organic phases were then washed with water (1 × 20 mL) followed by a saturated solution of brine (1 × 20 mL). The resulting organic phase was then dried using Na_2SO_4 and filtered. The solvent was removed under reduced pressure and the

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crude product was purified using flash chromatography on silica gel (*n*-hexane/EtOAc, 10:1 as eluent) to give the desired aniline (87%) as a dark yellow oil. Formylation was followed by subsequent dehydration of the aniline according to the general method for dehydration of formamide described above to yield **1f** (200 mg, 63%) as a light brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 16.1 Hz, 1H), 7.77−7.56 (m, 1H), 7.50−7.31 (m, 1H), 6.51 (d, J = 16.0 Hz, 1H), 4.27 (q, J = 7.1 Hz, 1H), 1.41−1.25 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.9, 166.1, 137.7, 130.9, 130.8, 129.7, 127.8, 127.0, 122.6, 77.5, 77.2, 76.9, 61.0, 14.4. HRMS (ESI) m/z: $[M]^+$: Calcd for $C_{12}H_{11}NO_2$ 201.0790, Found: 201.0796. Spectral data match those previously reported.[26]

Procedure for preparation of 3-(2-aminophenyl)prop-2-en-1-ol: To a flame-dried round-bottom flask was added ethyl 3-(2-aminophenyl)-acrylate (3.06 g, 16 mmol), magnetic stir-bar, and dry THF (20 mL). The resulting mixture was placed into an ice bath under an inert atmosphere of N_2. To the resulting solution was added dropwise di-isobutyl aluminum hydride (37 mL, 1 M in THF). The resulting mixture was stirred for 8 h under N_2 and was monitored by TLC. Upon completion of the reaction, MeOH and H_2O were added (10 mL each) and to the mixture was stirred for another 2 h. The resulting mixture was then filtered and the resulting phases were separated. The aqueous phase was extracted with 3 × 10 mL of ethyl acetate. The resulting organic phases were then washed with water (1 × 20 mL) followed by a saturated solution of brine (1 × 20 mL). The resulting organic phase was then dried using Na_2SO_4 and filtered. The solvent was removed under reduced pressure and the crude product was purified using flash chromatography on silica gel (*n*-hexane/EtOAc 6:1 as eluent) to give the desired alcohol (87%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (dd, J = 7.7, 1.1 Hz, 1H), 7.08 (td, J = 7.9, 1.4 Hz, 1H), 6.84−6.72 (m, 1H), 6.70−6.57 (m, 2H), 6.17 (dt, J = 15.7, 5.3 Hz, 1H), 4.23 (d, J = 5.4 Hz, 2H), 3.87 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.6, 130.2, 128.5, 127.2, 125.9, 123.2, 119.1, 116.4, 77.5, 77.2, 76.9, 63.2. HRMS (ESI): Calcd for $[2\ M+Na]^+$: Calcd for $C_{18}H_{22}N_2O_2Na$ 321.1413, Found: 321.1399. Spectral data match those previously reported.[26]

*Procedure for Preparation of 2-(3-Methoxyprop-1-en-1-yl)aniline (**S2a′**).* 3-(2-Aminophenyl)prop-2-en-1-ol (0.110g, 0.737 mmol) was treated with NaH (0.02 g, 0.8 mmol) in dry THF (10 mL). This solution was allowed to stir in an ice bath for 30 min. Then, MeI (0.115 g, 0.81 mmol) was added to the solution. The reaction was stirred for 1 h and was monitored by TLC. Upon completion, 5 mL of water was added. The aqueous phase was separated and washed with ethyl acetate (1 × 20 mL). The organic phases were collected and washed with water (1 × 20 mL) followed by saturated solution of brine (1 × 20 mL). The organic phases were separated and dried using Na_2SO_4 and filtered. The solvent was removed under reduced pressure and the crude product was purified using flash chromatography on silica gel (*n*-hexane/EtOAc, 10:1 as eluent) to give the desired 2-(3-methoxyprop-1-en-1-yl)aniline (60%) as a crème colored oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (dd, J = 7.7, 1.4 Hz, 1H), 7.14−7.03 (m, 1H), 6.76 (ddd, J = 7.6, 1.1, 0.6 Hz, 1H), 6.72−6.54 (m, 1H), 6.17 (dt, J = 15.8, 6.0 Hz, 1H), 4.10 (dd, J = 6.0, 1.5 Hz, 1H), 3.75 (s, 1H), 3.41 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.9, 128.7, 128.1, 127.5, 127.5, 123.0, 118.9, 116.1, 77.5, 77.2, 76.9, 73.3, 58.0. HRMS (ESI) m/z: $[M]^+$: Calcd for $C_{10}H_{13}NO$ 163.0997, found 163.1003. Spectral data match those previously reported.[26]

*Procedure for Preparation of 1-Isocyano-2-(3-methoxyprop-1-en-1-yl)benzene (**1a′**).* Corresponding aniline was transformed into the desired isonitrile via formamidation and dehydration following the general procedures above to give 73% (67 mg) of **1a′** as a light brown oil. R_f = 0.44 (hexanes/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 7.8 Hz, 1H), 7.59 (d, J = 7.8 Hz, 1H), 7.45−7.33 (m, 2H), 6.94 (d, J = 15.9 Hz, 1H), 6.40 (dt, J = 15.9, 5.8 Hz, 1H), 4.25−4.03 (m, 2H), 3.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 133.3, 130.9, 129.5, 128.3, 127.3, 126.2, 77.5, 76.9, 72.9, 58.4, 29.8. HRMS (ESI) m/z: $[M]^+$:Calcd for $C_{11}H_{11}NO$ 173.0841, found 173.0850. Spectral data match those previously reported.[26]

*1-Isocyano-2-(3-phenylprop-1-en-1-yl)benzene Was Prepared Following the General Procedure for Formamidation and Dehydration To Provide **1a**.* 240 mg, 75% (E:Z = 1:3); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.50−7.23 (m, 12H), 6.87 (dd, J = 15.7, 1.8 Hz, 0.3H), 6.76 (d, J = 11.5 Hz, 1H), 6.53 (dt, J = 15.8, 7.1 Hz, 0.3H), 6.17 (dt, J = 11.5, 7.6 Hz, 1H), 3.68 (d, J = 7.1 Hz, 0.6H), 3.64 (d, J = 7.6 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 139.8, 139.3, 134.1, 134.0, 133.9, 129.7, 129.3, 129.0, 128.7, 128.6, 128.5, 128.3, 128.1, 127.9, 127.7, 127.1, 127.0, 126.5, 126.3, 126.3, 126.3, 126.2, 125.8, 125.1, 125.0, 39.6, 34.7. Spectral data match those previously reported.[26]

*2-(3,3-Dimethylbut-1-en-1-yl)-1-isocyano-4-methylbenzene Was Prepared Following the General Procedure for Formamidation, Suzuki Coupling, and Dehydration To Yield **1a″**.* 205 mg, 72%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38−7.32 (m, 1H), 7.20 (s, 1H), 7.06−6.91 (m, 1H), 6.60 (d, J = 16.2 Hz, 1H), 6.36 (d, J = 16.1 Hz, 1H), 2.36 (s, 3H), 1.17 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.9, 146.1, 139.5, 134.3, 133.8, 128.2, 126.9, 126.2, 119.3, 34.0, 29.5, 21.5. HRMS (ESI) m/z: $[M]^+$: Calcd for $C_{14}H_{17}NNa$ 222.1257, found 222.1253.[43]

*3-(2-Isocyanophenyl)-1H-indene Was Prepared Following the General Procedure for Formamidation, Suzuki Coupling, and Dehydration To Yield **1j**.* 103 mg, 50%; ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.59−7.56 (m, 1H), 7.54 (ddd, J = 8.0, 6.7, 1.4 Hz, 2H), 7.49 (tt, J = 7.6, 1.2 Hz, 1H), 7.40 (td, J = 7.7, 1.5 Hz, 1H), 7.34−7.27 (m, 3H), 6.79 (s, 1H), 3.63 (s, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 155.6, 143.7, 140.1, 134.8, 133.4, 130.1, 129.4, 128.5, 128.0, 126.3, 125.3, 124.3, 120.3, 38.9. Spectral data match those previously reported.[26]

*4-(2-Isocyanophenyl)-3,6-dihydro-2H-pyran Was Prepared Following the General Procedure for Formamidation, Suzuki Coupling, and Dehydration To Yield **1i**.* 125 mg, 65%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.22 (d, J = 7.9 Hz, 1H), 7.04 (m, 2H), 5.87 (s, 1H), 4.28 (q, J = 2.8 Hz, 2H), 3.89 (t, J = 5.4 Hz, 2H), 2.52−2.39 (m, 2H), 2.32 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.9, 139.7, 139.0, 132.4, 129.4, 128.5, 127.4, 127.3, 65.3, 64.2, 28.4, 21.2. HRMS (ESI) m/z: $[M]^+$: Calcd for $C_{13}H_{13}NNaO$ 222.0897, found 222.0895.

*1-Isocyano-2-styrylbenzene Was Prepared Following the General Procedure for Formamidation and Dehydration To Provide **1c**.* 98 mg, 76% (E:Z = 0.7:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 7.9 Hz, 1H), 7.58 (d, J = 7.7 Hz, 1H), 7.46−7.13 (m, 15H), 6.83 (d, J = 12.2 Hz, 1H), 6.68 (d, J = 12.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.2, 166.7, 136.4, 136.1, 134.5, 133.7, 133.6, 132.6, 130.0, 129.4, 128.8, 128.8, 128.8, 128.6, 128.3, 128.3, 128.3, 128.0, 128.0, 127.7, 127.2, 127.0, 126.9, 125.4, 124.5, 122.0, 49.0, 49.0, 21.6, 21.5. HRMS (ESI) m/z: $[M]^+$: Calcd for $C_{15}H_{11}N$ 205.0891, Found: 205.0844. Spectral data match those previously reported.[26]

*1-Isocyano-2-(pent-1-en-1-yl)benzene Was Prepared Following the General Procedure for Formamidation and Dehydration To Provide **1d**.* 130 mg, 81% (E:Z = 1:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 8.0 Hz, 1H), 7.33 (dd, J = 6.8, 2.5 Hz, 1H), 7.31−7.26 (m, 1H), 7.26−7.14 (m, 1H), 6.67 (d, J = 15.8 Hz, 1H), 6.50 (dd, J = 11.6, 1.5 Hz, 1H), 6.34 (dt, J = 15.7, 7.0 Hz, 1H), 5.88 (dt, J = 11.6, 7.4 Hz, 1H), 2.21 (dqd, J = 22.2, 7.3, 1.5 Hz, 1H), 1.57−1.39 (m, 1H), 0.92 (dt, J = 24.1, 7.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 166.3, 136.4, 135.7, 134.5, 134.2, 129.8, 129.2, 128.8, 127.4, 127.3, 126.9, 126.7, 125.6, 124.0, 123.8, 35.3, 30.7, 22.7, 22.3, 13.7, 13.7. HRMS (ESI) m/z: $[M]^+$: Calcd for $C_{12}H_{13}N$ 171.1048, Found: 171.1061. Spectral data match those previously reported.[26]

*1-Isocyano-4-methyl-2-(3-phenylprop-1-en-1-yl)benzene Was Prepared Following the General Procedure for Formamidation, Suzuki Coupling, and Dehydration To Yield **1f**.* 120 mg, 59%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35−7.29 (m, 1H), 7.26−7.18 (m, 1H), 7.00 (dd, J = 8.1, 1.0 Hz, 1H), 6.76 (d, J = 15.7 Hz, 1H), 6.44 (dt, J = 15.7, 7.1 Hz, 1H), 3.60 (d, J = 7.1 Hz, 1H), 2.32 (s, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.6, 139.5, 133.6, 133.6, 128.7, 128.7, 128.7, 128.6, 126.9, 126.5, 126.3, 125.2, 39.7, 21.7. HRMS (ESI) m/z: $[M]^+$: Calcd for $C_{17}H_{15}N$ 233.1204, Found: 233.1216. Spectral data match those previously reported.[26]

*4-Fluoro-1-isocyano-2-(3-phenylprop-1-en-1-yl)benzene Was Prepared Following the general Procedure for Formamidation and Dehydration To Provide **1b**.* 313 mg, 56%, (E:Z = 1:3); ^{1}H

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NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 7.4 Hz, 1H), 7.49−7.23 (m, 12H), 6.93−6.82 (m, 1H), 6.76 (d, J = 11.5 Hz, 1H), 6.55 (t, J = 11.4 Hz, 1H), 6.17 (dt, J = 11.5, 7.6 Hz, 1H), 3.68 (d, J = 7.1 Hz, 1H), 3.64 (d, J = 7.6 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 139.8, 139.3, 134.1, 134.0, 129.7, 129.3, 129.0, 128.7, 128.6, 128.5, 128.3, 128.1, 127.9, 127.7, 127.1, 127.0, 126.5, 126.3, 126.2, 125.8, 125.1, 125.0, 77.5, 77.2, 76.9, 34.7. HRMS (ESI) m/z: $[M]^+$: Calcd for $C_{15}H_{12}FN$ 237.0952, Found: 237.0960. Spectral data match those previously reported.[26]

Ethyl (E)-5-chloro-2-isocyano-3-(3-phenylprop-1-en-1-yl)-benzoate Was Prepared Following the General Procedure for Formamidation, Suzuki Coupling, and Dehydration To Yield ***1g.*** 87 mg, 77%; ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.83 (d, J = 2.4 Hz, 1H), 7.50 (dd, J = 2.4, 0.6 Hz, 1H), 7.37 (d, J = 1.0 Hz, 1H), 7.32 (t, J = 7.7 Hz, 2H), 7.25 (d, J = 7.9 Hz, 1H), 6.56 (d, J = 15.8 Hz, 1H), 6.27 (dt, J = 15.8, 7.0 Hz, 1H), 4.46 (q, J = 7.2 Hz, 3H), 3.71 (d, J = 7.0 Hz, 1H), 1.45 (t, J = 7.2 Hz, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 173.7, 163.4, 140.7, 136.7, 135.1, 133.9, 133.3, 129.5, 129.3, 128.9, 128.7, 127.9, 126.5, 124.4, 62.5, 35.9, 14.2. HRMS (ESI) m/z: $[M]^+$: Calcd for $C_{19}H_{16}ClNNaO_2$ 348.0767, found 348.0761.

1-Isocyano-2-(3-phenylprop-1-en-1-yl)naphthalene Was Prepared Following the General Procedure for Formamidation, Suzuki Coupling, and Dehydration To Yield ***1h.*** 110 mg, 79%; ^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.17 (dd, J = 8.5, 1.0 Hz, 1H), 7.88−7.80 (m, 1H), 7.77 (d, J = 8.7 Hz, 1H), 7.69−7.60 (m, 2H), 7.54 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H), 7.38 (dd, J = 8.0, 7.2 Hz, 2H), 7.34−7.27 (m, 3H), 7.08 (d, J = 15.7 Hz, 1H), 6.63 (dt, J = 15.7, 7.1 Hz, 1H), 3.71 (dd, J = 7.1, 1.5 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.3, 139.3, 134.8, 132.4, 131.7, 129.2, 128.8, 128.7, 128.7, 128.3, 128.2, 128.1, 127.0, 126.5, 125.7, 123.3, 122.3, 39.8. HRMS (ESI) m/z: $[M]^+$: Calcd for $C_{20}H_{16}N$ 270.1282, found 270.1297.

General Procedure for the Mn(III) Mediated Radical Cyclization with Boronic Acids and o-Alkenylisonitriles. To an oven-dried 10 mL single neck round-bottom flask, isonitrile (0.2 mmol), boronic acid (0.3 mmol), $Mn(acac)_3$ (0.6 mmol), and dry toluene (4.0 mL) were added sequentially under an atmosphere of nitrogen. The mixture was stirred at 90 °C and monitored by TLC for 4 h or until completion under an atmosphere of nitrogen. The reaction mixture was then allowed to cool to room temperature and directly purified by column chromatography on silica gel to afford the desired products.

*2-Phenylquinoline (**2a**).* 35 mg, 86%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.25−8.15 (m, 4H), 7.88 (d, J = 8.5 Hz, 1H), 7.83 (d, J = 8.1 Hz, 1H), 7.74 (t, J = 7.6 Hz, 1H), 7.59−7.51 (m, 3H), 7.48 (t, J = 7.3 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 157.5, 148.4, 139.8, 136.9, 129.9, 129.8, 129.5, 129.0, 127.7, 127.6, 127.3, 126.4, 119.2. Spectral data match those previously reported.[26]

*6-Phenyl-7H-indeno[2,1-c]quinoline (**2t**).* 42 mg, 72%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.76 (d, J = 8.3 Hz, 1H), 8.49 (d, J = 7.8 Hz, 1H), 8.32 (d, J = 8.3 Hz, 1H), 7.94 (d, J = 7.3 Hz, 1H), 7.78 (t, J = 7.5 Hz, 1H), 7.69 (dd, J = 10.9, 7.6 Hz, 1H), 7.52 (ddd, J = 17.6, 14.4, 7.5 Hz, 3H), 4.18 (s, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.5, 148.5, 145.7, 145.2, 141.0, 140.6, 134.5, 130.9, 129.0, 128.9, 128.9, 128.8, 128.4, 127.5, 126.8, 125.3, 124.5, 124.1, 123.6, 37.9. HRMS (ESI) m/z: $[M]^+$: Calcd for $C_{22}H_{16}N$ 294.1282, Found: 294.1298. Spectral data match those previously reported.[26]

*9-Methyl-5-phenyl-1,4-dihydro-2H-pyrano[3,4-c]quinoline (**2u**).* 31 mg, 57%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.05 (d, J = 8.5 Hz, 1H), 7.68 (d, J = 1.0 Hz, 1H), 7.61−7.40 (m, 6H), 4.75 (s, 2H), 4.15 (t, J = 5.8 Hz, 2H), 3.31−3.17 (m, 2H), 2.58 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.6, 136.7, 131.4, 129.9, 129.0, 128.7, 128.6, 128.6, 128.5, 128.5, 126.4, 126.3, 121.4, 67.2, 64.7, 25.1, 22.1. HRMS (ESI) m/z: $[M]^+$: Calcd for $C_{19}H_{17}NNaO$ 298.1210, found 298.1212

*8-Methyl-2-phenyl-4,5-dihydro-7H-oxepino[5,4,3-de]quinoline (**2u′**).* 2 mg, 9%; ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.62−7.58 (m, 1H), 7.58−7.40 (m, 3H), 5.28 (s, 1H), 3.95 (t, J = 5.4 Hz, 1H), 2.94−2.82 (m, 1H), 2.57 (s, 1H). HRMS (ESI): Calcd for $C_{19}H_{18}NO$ 276.1388, found 276.1392. We were unable to obtain ^{13}CNMR do to the inseparable mixture with 2u and low quantity.

*3-Benzylidene-2-phenylindoline (**2v**).* 38 mg, 68%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (s, 1H), 7.36 (d, J = 7.4 Hz, 3H), 7.28 (d, J = 8.1 Hz, 1H), 7.18 (dd, J = 6.2, 2.5 Hz, 2H), 7.08 (t, J = 6.3 Hz, 6H), 6.96 (t, J = 7.5 Hz, 1H), 6.62 (t, J = 7.6 Hz, 1H), 5.32 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.6, 135.9, 133.4, 129.4, 129.2, 128.5, 128.3, 128.0, 127.8, 125.7, 122.0, 122.0, 121.1, 119.4, 114.9, 110.4, 50.0. HRMS (EI): Calcd for $C_{22}H_{16}N$ 294.1282, Found: 294.1298. Spectral data match those previously reported.[26]

*3-Butyl-2-phenyl-1H-indole (**2w**).* 14 mg, 28%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.64 (d, J = 7.9 Hz, 1H), 7.56 (dd, J = 8.1, 1.0 Hz, 2H), 7.47 (t, J = 7.7 Hz, 3H), 7.39−7.36 (m, 2H), 7.22−7.18 (m, 1H), 7.16−7.12 (m, 1H), 2.94−2.83 (m, 2H), 1.72 (dt, J = 15.4, 7.7 Hz, 2H), 1.48−1.38 (m, 3H), 0.93 (t, J = 7.4 Hz, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.9, 136.1, 134.2, 130.5, 129.5, 129.5, 129.0, 128.1, 127.6, 122.3, 119.6, 119.5, 114.3, 110.9, 33.4, 29.9, 24.5, 23.1. HRMS (ESI) m/z: $[M]^+$: Calcd for $C_{18}H_{18}N$ 248.1439, Found: 248.1452. Spectral data match those previously reported.[26]

*2-(4-Methylphenyl)quinoline (**2b**).* 36 mg, 82%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.36 (s, 3H), 7.25, (d, J = 8.3 Hz, 2H), 7.35−7.45, (m, 1H), 7.60−7.75, (m, 3H), 8.00−8.05 (m, 3H), 8.15 (d, J = 4.4 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 21.1, 118.5, 125.8, 126.8, 127.2, 127.3, 128.0, 129.3, 129.4, 136.4, 136.6, 139.1, 148.0, 156.9. Spectral data match those previously reported.[26]

*2-(4-Fluorophenyl)quinoline (**2c**).* 33 mg, 76%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, J = 8.7 Hz, 1H), 8.20−8.14 (m, 1H), 7.83 (d, J = 8.6 Hz, 1H), 7.74 (ddd, J = 8.4, 6.9, 1.5 Hz, 1H), 7.54 (ddd, J = 8.1, 6.9, 1.1 Hz, 1H), 7.22 (dd, J = 9.7, 7.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 163.8, 156.2, 148.2, 136.8, 135.8, 129.7, 129.4, 129.3, 127.4, 127.1, 126.3, 118.6, 115.7. Spectral data match those previously reported.[26]

*2-(Quinolin-2-yl)benzonitrile (**2d**).* 32 mg, 71%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33−8.24 (m, 2H), 8.21−8.12 (m, 1H), 7.91−7.84 (m, 1H), 7.82−7.73 (m, 3H), 7.70−7.66 (m, 1H), 7.59 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H). ^{13}C NMR ($CDCl_3$, 101 MHz) δ: 112.7, 118.5, 118.8, 127.1, 127.5, 128.0, 132.5, 137.2, 143.6, 148.2, 154.8. Spectral data match those previously reported.[26]

*2-(3,5-Dimethoxyphenyl)quinoline (**2e**).* 43 mg, 82%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.22 (d, J = 8.6 Hz, 1H), 8.18 (d, J = 8.5 Hz, 1H), 7.87−7.81 (m, 2H), 7.76−7.71 (m, 1H), 7.54 (dd, J = 11.0, 3.9 Hz, 1H), 7.33 (d, J = 2.2 Hz, 2H), 6.59 (t, J = 2.2 Hz, 1H), 3.91 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 161.3, 157.2, 148.3, 142.0, 136.9, 129.9, 129.8, 127.6, 127.5, 126.5, 119.3, 105.8, 101.8, 55.7. HRMS (ESI) calculated for $C_{17}H_{15}NO_2Na$ $[M+Na]^+$ m/z 288.0093, found 288.0103. Spectral data match those previously reported.[26]

*2-(2-Thienyl)quinoline (**2f**).* 29 mg, 68%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.11−7.18 (m, 1H), 7.42−7.47 (m, 2H), 7.61−7.74 (m, 4H), 8.05 (d, J = 8.1 Hz, 1H), 8.07 (d, J = 7.5 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 117.1, 125.7, 125.9, 127.0, 127.4, 128.0, 128.5, 129.0, 129.7, 136.5, 145.2, 147.9, 152.2. Spectral data match those previously reported.[26]

*2-Isobutylquinoline (**2g**).* 25 mg, 69%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 8.06 (d, J = 8.4 Hz, 1H), 8.01 (d, J = 8.4 Hz, 1H), 7.74 (dd, J = 8.2, 0.8 Hz, 1H), 7.44−7.40 (m, 1H), 7.67−7.63 (m, 1H), 7.20 (d, J = 8.4 Hz, 1H), 2.81 (d, J = 7.4 Hz, 2H), 2.20 (q, J = 6.8 Hz, 1H), 0.95 (s, 6H). ^{13}C NMR ($CDCl_3$, 101 MHz) δ: 162.2, 148.0, 135.9, 129.2, 128.9, 127.5, 126.7, 125.6, 122.0, 48.3, 29.4, 22.6. Spectral data match those previously reported.[26]

*2-(Naphthalen-1-yl)quinoline (**2h**).* 34 mg, 68%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.47 (t, J = 7.6 Hz, 1H), 7.52 (t, J = 6.9 Hz, 1H), 7.60 (t, J = 7.6 Hz, 2H), 7.72 (t, J = 6.8 Hz, 2H), 7.78 (t, J = 7.1 Hz, 1H), 7.91−7.96 (m, 3H), 8.14 (d, J = 8.4 Hz, 1H), 8.23 (d, J = 8.3 Hz, 1H), 8.30 (d, J = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ: 123.2, 125.3, 125.9, 126.5, 127.0, 127.5, 127.7, 128.4, 129.1, 129.7, 131.3. Spectral data match those previously reported.[26]

*2-(2-Bromophenyl)quinoline (**2i**).* 44 mg, 78%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (dd, J = 16.3, 8.4 Hz, 2H), 7.88 (d, J = 8.1 Hz, 1H), 7.76 (ddd, J = 8.5, 6.9, 1.4 Hz, 1H), 7.71 (dd, J = 8.3, 1.8 Hz, 2H), 7.64 (dd, J = 7.6, 1.7 Hz, 1H), 7.62−7.56 (m, 1H), 7.46 (td, J = 7.4, 1.0 Hz, 1H), 7.31 (td, J = 7.7, 1.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9, 148.1, 141.8, 135.8, 133.4, 131.7, 130.1, 129.9, 129.8, 127.9, 127.7, 127.3, 127.2, 127.0, 122.9, 122.0, 120.0. Spectral data match those previously reported.[26]

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*2-(Pyridin-4-yl)quinoline (**2j**).* 25 mg, 62%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.80 (d, J = 5.7 Hz, 2H), 8.31 (d, J = 8.6 Hz, 1H), 8.21 (d, J = 8.5 Hz, 1H), 8.09 (d, J = 6.0 Hz, 2H), 7.93 (d, J = 8.6 Hz, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.76−7.80 (m, 1H), 7.61 (t, J = 7.5 Hz,1H). ^{13}C NMR ($CDCl_3$, 101 MHz) δ: 118.2, 121.4, 127.0, 127.4, 127.6, 129.8, 129.9, 137.0, 146.3, 148.1, 150.3, 154.1. Spectral data match those previously reported.[26]

*4-(6-Methylquinolin-2-yl)benzaldehyde (**2k**).* 36 mg, 77%; ^{1}H NMR (600 MHz, Chloroform-*d*) δ 10.10 (s, 1H), 8.32 (d, *J* = 8.1 Hz, 2H), 8.17 (d, *J* = 8.5 Hz, 1H), 8.08 (d, *J* = 8.5 Hz, 1H), 8.04−7.98 (m, 2H), 7.87 (d, *J* = 8.5 Hz, 1H), 7.69−7.48 (m, 2H), 2.56 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 192.2, 154.9, 147.1, 145.4, 137.2, 136.6, 136.6, 132.5, 130.3, 129.7, 128.1, 127.7, 126.5, 119.1, 21.8. HRMS (ESI) *m*/*z*: $[M]^+$: Calcd for $C_{17}H_{14}NO$ 248.1077, found 248.1081.

*6-Fluoro-2-phenylquinoline (**2l**).* 38 mg, 86%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.21−8.11 (m, 1H), 7.90 (d, *J* = 8.7 Hz, 1H), 7.50 (dddd, *J* = 21.6, 19.9, 9.1, 5.1 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 161.3, 156.9, 145.5, 139.5, 136.3, 132.4, 132.3, 129.6, 129.1, 127.9, 127.6, 120.1, 119.9, 110.7, 110.6. Spectral data match those previously reported.[26]

*6-Fluoro-2-(4-fluorophenyl)quinoline (**2m**).* 36 mg, 76%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.15 (ddd, *J* = 9.5, 7.6, 5.4 Hz, 3H), 7.85 (d, *J* = 8.6 Hz, 1H), 7.53−7.48 (m, 1H), 7.44 (dd, *J* = 8.7, 2.8 Hz, 1H), 7.25−7.18 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.8, 163.2, 161.4, 159.7, 155.8, 145.5, 136.4, 136.4, 135.7, 132.3, 132.2, 129.5, 129.4, 127.8, 127.7, 120.2, 120.1, 119.5, 116.1, 115.9, 110.7, 110.6. Spectral data match those previously reported.[26]

*6-Fluoro-2-(p-tolyl)quinoline (**2n**).* 39 mg, 82%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.15 (dt, *J* = 4.9, 2.8 Hz, 1H), 8.05 (d, *J* = 8.2 Hz, 1H), 7.88 (d, *J* = 8.7 Hz, 1H), 7.49 (td, *J* = 8.8, 2.8 Hz, 1H), 7.43 (dd, *J* = 8.8, 2.8 Hz, 1H), 7.34 (dd, *J* = 7.9, 0.5 Hz, 1H), 2.44 (s, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 145.5, 139.7, 136.7, 136.2, 132.3, 132.2, 129.8, 129.8, 127.8, 127.5, 120.0, 119.8, 119.7, 110.7, 110.5, 21.5. Spectral data match those previously reported.[26]

*6-Methyl-2-phenylquinoline (**2o**).* 37 mg, 85%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.14 (dd, *J* = 7.9, 4.1 Hz, 1H), 8.06 (d, *J* = 8.6 Hz, 1H), 7.84 (d, *J* = 8.5 Hz, 1H), 7.59 (s, 1H), 7.56 (d, *J* = 8.6 Hz, 1H), 7.52 (t, *J* = 7.7 Hz, 1H), 7.46 (d, *J* = 7.0 Hz, 1H), 7.42 (d, *J* = 3.7 Hz, 1H), 2.55 (s, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 136.3, 132.1, 129.6, 129.3, 129.2, 129.0, 128.0, 128.0, 127.6, 127.4, 126.5, 125.7, 119.2, 21.8. Spectral data match those previously reported.[26]

*6-Methyl-2-(p-tolyl)quinoline (**2p**).* 39 mg, 83%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.6 Hz, 1H), 8.05 (d, *J* = 8.0 Hz, 3H), 7.82 (d, *J* = 8.6 Hz, 1H), 7.57 (s, 1H), 7.55 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 2H), 2.54 (s, 3H), 2.43 (s, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.7, 147.0, 139.3, 137.1, 136.1, 136.1, 132.0, 129.7, 129.5, 127.5, 127.3, 126.5, 119.0, 21.8, 21.7. Spectral data match those previously reported.[26]

*Ethyl 6-Chloro-2-(4-methoxyphenyl)quinoline-8-carboxylate (**2q**).* 46 mg, 67%; ^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.20 (d, *J* = 8.5 Hz, 1H), 8.11 (s, 1H), 7.95 (m, 1H), 7.88 (d, *J* = 2.4 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 1H), 4.57 (q, *J* = 7.1 Hz, 2H), 3.89 (s, 3H), 1.51 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.1, 161.6, 157.3, 143.8, 136.2, 131.3, 130.8, 129.4, 129.2, 129.2, 127.9, 119.5, 114.4, 62.0, 55.6, 14.6. IR cm^{-1}: 3070, 2927, 1721, 1612, 1440, 1322, 1290, 1101, 769, 795. HRMS (ESI) *m*/*z*: $[M]^+$: Cald for $C_{19}H_{17}ClNO_3$ 342.0897, found 342.0890; mp: 179−184°C

*2-(2-Bromophenyl)benzo[h]quinoline (**2s**).* 53 mg, 80%; ^{1}H NMR (600 MHz, Chloroform-*d*) δ 9.41 (d, *J* = 7.3 Hz, 1H), 8.23 (d, *J* = 8.2 Hz, 4H), 7.98−7.91 (m, 4H), 7.89 (d, *J* = 8.2 Hz, 2H), 7.85 (d, *J* = 8.8 Hz, 4H), 7.81 (ddd, *J* = 7.6, 1.8, 0.8 Hz, 4H), 7.79−7.67 (m, 18H), 7.50 (tt, *J* = 7.5, 1.1 Hz, 4H), 7.33 (dddd, *J* = 8.1, 7.3, 1.7, 0.9 Hz, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 157.0, 146.3, 141.9, 135.6, 133.9, 133.7, 132.4, 131.8, 129.9, 128.4, 128.1, 127.9, 127.8, 127.2, 125.3, 125.2, 125.0, 123.2, 122.2. HRMS (ESI) *m*/*z*: $[M]^+$ Calcd for $C_{19}H_{13}BrN$ 334.0231, found 334.0227.

*6-Fluoro-2-(perfluorohexyl)quinoline (**F1**).* 34 mg, 37%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.31 (d, *J* = 8.7 Hz, 1H), 8.27 (dd, *J* = 9.3, 5.3 Hz, 1H), 7.76 (d, *J* = 8.6 Hz, 1H), 7.61 (td, *J* = 8.7, 2.8 Hz, 1H), 7.53 (dd, *J* = 8.5, 2.9 Hz, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 162.5, 160.8, 144.5, 137.0 (d, *J* = 6.4 Hz), 133.0 (d, *J* = 9.6 Hz), 128.8 (d, *J* = 18.5 Hz), 121.3 (d, *J* = 25.9 Hz), 119.0, 110.6 (d, *J* = 21.9 Hz). ^{19}F NMR (376 MHz, Chloroform-*d*) δ −80.8 (t, *J* = 10.1 Hz, 3F), −108.6 − −110.1 (m, 1F), −113.4 (t, *J* = 13.8 Hz, 2F), −121.4 (dt, *J* = 33.3, 14.4 Hz, 3F), −122.3 − −123.3 (m, 3F), −126.1 (t, *J* = 16.0 Hz, 2F). HRMS (ESI) *m*/*z*: $[M]^+$: Calcd for $C_{15}H_5F_{14}N$ 465.0196, found 465.0196.

*6-Methyl-2-(trifluoromethyl)quinoline (**F2**).* 23 mg, 54%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.25 (d, *J* = 8.5 Hz, 1H), 8.12 (d, *J* = 9.3 Hz, 1H), 7.70 (d, *J* = 8.5 Hz, 1H), 7.68−7.62 (m, 2H). HRMS (ESI) *m*/*z*: $[M]^+$: Calcd for $C_{11}H_9F_3$ 212.0689, found: 212.0687. Spectral data matched literature.[44]

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b00262.

Compound characterization data, geometries, and energies of all computed structures (PDF)

X-ray crystallographic data of **2s** (CIF)

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Notes

The authors declare no competing financial interest.

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