Pyrylium Salts via Electrophilic Cyclization: Applications for Novel 3-Arylisoquinoline Syntheses

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Pyrylium salts have found uses in many areas of pharmaceutical and materials chemistry as versatile synthetic intermediates for complex heterocyclic skeletons and for their intriguing physical properties.[1] Earlier work in our laboratories explored acid-catalyzed electrophilic cyclizations of aryl acetylenes to provide fully aromatized conjugated materials.[2] Our continued interest in highly unsaturated ladder polymers and related materials has led us to extend this methodology to a new one-component synthesis of pyrylium salts through the use of a carbonyl group in lieu of a proximal arene moiety. According to our proposed mechanism, electrophilic attack at the β carbon of **2** results in a carbocation formation at the α carbon, thereby leading to ring closure of intermediate **A** via lone pair attack (Scheme 1). In this report, we present the scope of a novel acid-induced cyclization of *ortho*-alkynylated aromatic carbonyl functionalities into the isobenzopyrylium salts depicted by **3**. In addition, we describe efficient one- and/or two-pot preparations of the corresponding 3-arylisoquinolines which can serve as key intermediates in the synthesis of many isoquinoline alkaloids but have proven difficult to access through current methodology.[3]

Stetter and Reischl demonstrated that (*Z*)-1,5-diphenyl-2-penten-4-ynone underwent cyclization to the pyrylium perchlorate upon exposure to perchloric acid.[4] However, the inherent difficulty of *Z*-selective substrate preparation diminished the practicality of this finding.[1a] More recently, Neuenschwander and co-workers found that a variety of 5-amino-2-penten-4-ynones cyclized to pyrylium salts in one or two steps upon exposure to HF, HCl, HBr, or HI.[5] In light of this, we endeavored to extend these precedents to aryl systems. Utilization of a synthetically facile modified Sonogashira−Hagihara protocol provided a variety of *ortho*-ynone cyclization precursors as presented in Table 1.[6]

With these precursors, we proceeded to investigate the scope of the proposed cyclization. While trifluoroacetic acid induced a partial degree of apparent cyclization, we found that the reaction proceeded slowly and that the resulting products eluded isolation. As listed in Table 2, use of stronger acids such as HBF_4 and TfOH provided an instant and essentially quantitative cyclization. Compounds **3c**−**e** (R_1 = NMe_2) and compounds **3m**,**n** (R_1 = Ph) initially precipitated out of solution with diethyl ether in 60−80% yields. A second precipitation from MeCN/CH_2Cl_2 provided analytically pure samples. Common to all systems, we found that the reaction required high dilution (0.005 M) and exclusion of water in order to suppress intermolecular chemistry and hydrolysis, respectively. Significantly higher concentrations led to the formation of intractable materials.

In contrast to our earlier findings,[2] the cyclization does not require a strong *para*-electron-donating group on the aryl acetylene to stabilize the positive charge density of the α carbon of **A** as evidenced by the phenyl and tolyl entries for R_2 in Table 2. In fact, in situ NMR observations of acetylenes **2e** and **2m** (with decyloxy donors) showed two distinct products upon intermediate exposure to TfOH and TfOD. Reaction times over 1 day provided one cyclized yet undesired product, apparently the result of decyloxy ether cleavage.[7] NMR showed the presence of only 1 product after 15 min, and keeping reaction times around 30 min provided one isolated product (e.g. in the case of **3e**). Our findings show that the cyclization requires substrates with phenyl-substituted alkynes in order to obtain the desired reactivity: the use of alkyl acetylenes (R_2 = *n*-Bu) led to at least two different and unisolable products while silyl and free acetylenes (R_2 = TMS, H) led to the formation of undesired and apparently noncyclized olefinic products, all as observed by ^{1}H NMR.[8]

Distinct spectroscopic changes accompanied all pyrylium formations. Immediately upon acid addition, an intense red to yellow UV fluorescence developed which persisted in the precipitate. Upon cyclization, the exocyclic amine compounds **3c**−**e** (R_1 = NMe_2) displayed a new UV−vis absorbance between 370 and 400 nm while the 1-phenyl compounds **3m**−**o** (R_1 = Ph) absorbed in the 440−450 nm range. Representative fluorescence data for the isolated salts displayed Stokes shifts of greater than 100 nm, suggesting excited state planarization of the pendant aryl moiety. All isolated salts lacked the alkynyl C−C stretch in the infrared spectra (2200 cm^{-1}) while they exhibited an intense stretching band characteristic of their respective counteranion (1260 cm^{-1} for TfO^-, 1060 cm^{-1} for BF_4^-). High-resolution MS provided evidence for both the intact cation (EI or FAB) as well as the counteranion (negative ion FAB), and all isolated salts gave satisfactory elemental analyses. In the ^{13}C

(1) For some leading reviews, see: (a) Dimroth, K.; Wolf, K. H. In *Newer Methods of Preparative Organic Chemistry*; Foerst, W., Ed. Academic Press: New York, 1964; Vol. 3, pp 357−423. (b) Balaban, A. T.; Schroth, W.; Fischer, G. In *Advances in Heterocyclic Chemistry*; Katritzky, A. R., Boulton, A. J., Eds.; Academic Press: New York, 1969; Vol. 10, pp 241−326. (c) Balaban, A. T.; Dinculescu, A.; Dorofeenko, G. N.; Fischer, G. W.; Koblik, A. V.; Mezheritskii, V. V.; Schroth, W. *Pyrylium Salts: Syntheses, Reactions, and Physical Properties*; Academic Press: New York, 1982.

(2) (a) Goldfinger, M. B.; Swager, T. M. *J. Am. Chem. Soc.* **1994**, *116*, 7895−7896. (b) Goldfinger, M. B.; Crawford, K. B.; Swager, T. M. *J. Am. Chem. Soc.* **1997**, *119*, 4578−4593. (c) Goldfinger, M. B.; Crawford, K. B.; Swager, T. M. *J. Org. Chem.* **1998**, *63*, 1668−1675.

(3) For representative synthetic strategies, see: (a) Bradsher, C. K.; Wallis, T. G. *Tetrahedron Lett.* **1972**, 3149−3150. (b) Garcia, A.; Lete, E.; Villa, M. J.; Dominguez, E.; Badia, M. D. *Tetrahedron* **1988**, *44*, 6681−6686. (c) Fitzgerald, J. J.; Michael, F. E.; Olofson, R. A. *Tetrahedron Lett.* **1994**, *35*, 9191−9194.

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(5) Fischer, F.; Berger, D.; Neuenschwander, M. *Helv. Chim. Acta* **1998**, *81*, 1792−1802.

(6) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467−4470.

(7) Disappearance of the decyloxy group's α-proton triplet (4.18 ppm) led us to this conclusion.

(8) A distinct ^{1}H NMR resonance initially appeared at 5.70 ppm (dd, 2H, J = 13.5, 5.0 Hz) and with further exposure to TfOH shifted to 5.83 ppm (dd, J = 19.5, 4.5 Hz) for both **3a** and **3b**, indicative of olefinic protons and residual F^--promoted TMS cleavage.

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Scheme 1

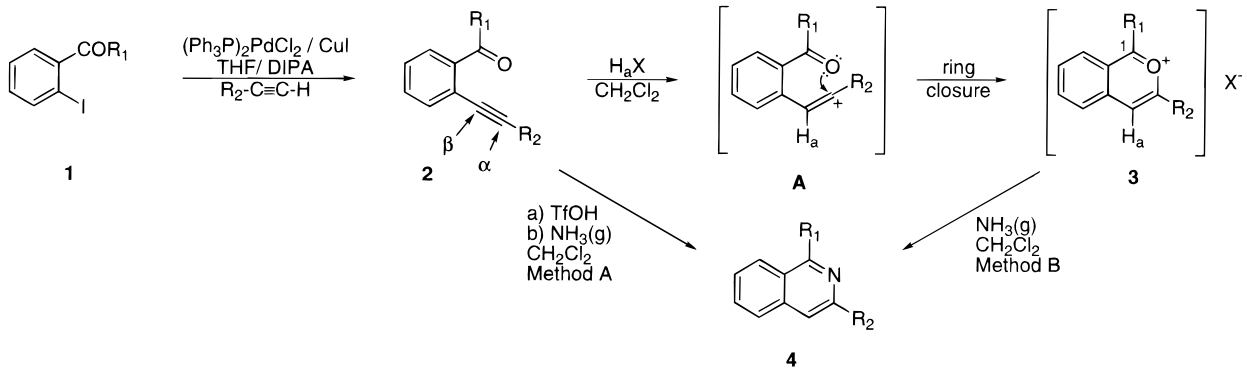


Table 1. Cyclization Precursors 2 via Sonogashira−Hagihara Coupling of *o*-Iodobenzenes 1 and Terminal Acetylenes

entry	R_1	R_2[a]	yield/%
a	NMe_2	TMS	81
b		H	85[b]
c		Ph	87[c]
d		*p*-tol	67[c]
e		*p*-OC_{10}	66
f	OEt	TMS	89
g		Ph	84
h		*p*-tol	90
i		*p*-OC_{10}	55
j	H	TMS	84[d]
k		Ph	36[d]
l		*p*-tol	79[d]
m		*p*-OC_{10}	72[d]
n	Ph	Ph	65
o		*p*-tol	54
p		*n*-Bu	87

[a] *p*-tol = 4-Me−C_6H_4−, *p*-OC_{10} = 4-(*n*-$C_{10}H_{21}$)−C_6H_4−. [b] Prepared by deprotection of **2a** (K_2CO_3/MeOH/THF). [c] Difficulty in removing **1** required a yield determination by ^{1}H NMR integration. [d] Overall yield from *o*-iodobenzyl alcohol coupling (in place of **1**) followed by PCC oxidation.

Table 2. Synthesis of the Isobenzopyrylium Salts 3

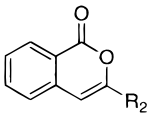
entry	R_1	R_2	X	yield/% [a]
a	NMe_2	TMS	TfO	0[b]
b		H		0[b]
c		Ph		63
d		*p*-tol		64
e		*p*-OC_{10}		50
f	OEt	Ph	BF_4	66[c] (83)[d]
g		*p*-tol		88[c] (95)[d]
h		*p*-OC_{10}		0 (67)[d]
i	H	TMS	TfO	0[b]
j		Ph		>99[b]
k		*p*-tol		>99[b]
l		*p*-OC_{10}		>95[b]
m	Ph	Ph	TfO	74
n		Ph	BF_4	66
o		*p*-tol	TfO	84
p		*n*-Bu	TfO	0

[a] Isolated and analytically pure. [b] In situ ^{1}H NMR observation of the transient intermediate. [c] Isolated alongside hydrolysis product **5a**,**b**, yield determined by ^{1}H NMR integration. [d] Isolated yield of **5a**−**c** after complete hydrolysis.

NMR, the two 85−100 ppm ethynyl carbon resonances disappeared, and a new resonance corresponding to the former carbonyl carbon (C_1 of **3**) appeared at 170−180 ppm. A new aromatic singlet (H_a of **3**) appeared in the ^{1}H spectra upon cyclization but did not appear during TfOD-induced cyclizations.

The triflate salts **3c**−**e** (R_1 = NMe_2) precipitated readily from diethyl ether and maintained stability under ambient conditions. In concurrence with the results for other α-amino pyrylium salts,[9] NMR data indicated that these aminated compounds displayed a significant degree of exocyclic charge localization onto the nitrogen substituent. The *N*-methyl protons appeared as two singlets in the ^{1}H spectrum between 3.7 and 3.9 ppm, and two distinct *N*-methyl carbon resonances appeared around 43−46 ppm in the ^{13}C spectrum. The persistence of imine character in these salts displayed itself in the small upfield shift of the carbonyl carbon observed in the ^{13}C spectrum upon cyclization (C_1 of **3**). When compared to the other pyrylium salts discussed below, the new proton singlet observed at 7.5−7.6 ppm upon cyclization (H_a of **3**) indicated decreased aromatic character, lending credence to the argument that exocyclic charge localization reduces aromaticity. To further verify this claim, the crystal structure determined for **3d** supports a structure with significant exocyclic double bond character as evidenced by the short C_1−N bond of 1.314 Å (typical arylamine value 1.39 Å).[10]

With the absence of a strong nitrogen donor in the ester or aldehyde carbonyl functions, aromaticity should dominate for the ethoxy and *protio* pyrylium systems (R_1 = OEt, H). Indeed, these two systems displayed lower field ^{1}H singlet resonances for H_a at 8.1 and 8.6 ppm, respectively. Unfortunately, the isolation of these salts proved problematic. The tetrafluoroborate salts **3f**,**g** (R_1 = OEt) precipitated out of solution but slowly hydrolyzed at ambient conditions to provide the corresponding isocoumarin compounds **5a**,**b** within hours. This instability



5a (R_2 = Ph)
b (R_2 = *p*-tol)
c (R_2 = *p*-OC_{10})

precluded isolation and characterization in pure form, but full characterization of the hydrolyzed products agreed with data for **5a** and **5b** found in the literature. Similarly, attempts to precipitate compound **3h** resulted in immediate hydrolysis to **5c**. Unlike other functionalities studied, the ethyl esters **2g**−**i** required the use of HBF_4 to induce cyclization: treatment of **2h** with TfOH led to a signifi-

(9) (a) Kleinpeter, E.; Spitzner, R.; Schroth, W. *Magn. Reson. Chem.* **1987**, *25*, 688−695. (b) Kleinpeter, E.; Spitzner, R.; Schroth, W.; Pihlaja, K.; Mattinen, J. *Magn. Reson. Chem.* **1988**, *26*, 707−713.

(10) Please see the Supporting Information for complete experimental and structural data.

Table 3. Isoquinolines 4 from Amination of Pyrylium Salts 3

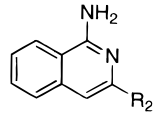
entry	R_1	R_2	X	method	yield/%[a]
a	NMe_2	Ph	TfO	A	22 (32)
b		*p*-tol		B	30 (45)
c		*p*-OC_{10}		A	0 (52)
d	OEt	Ph	BF_4	B	23 (11)[b]
e		*p*-tol		A	21 (66)
f	H	Ph	TfO	A	74
g		*p*-tol		A	67
h		*p*-OC_{10}		A	65
i	Ph	Ph	TfO	B	38
j		*p*-tol		A	67

[a] Values in parentheses refer to **6**. [b] In addition to 30% of hydrolysis product **5a** (GC-MS determination).

cant amount of isocoumarin formation. The triflate salts **3j**−**l** (R_1 = H) did not precipitate from the reaction mixture, so we relied on in situ ^{1}H NMR to characterize these transient intermediates using both TfOH and TfOD prior to further synthetic manipulations. Alkynes **2k** and **2l** cyclized quantitatively while a second undetermined side-product competitively formed during the cyclization of **2m**; again, a possible result of acid-induced aryl ether cleavage.[7]

Due to the charge localization found in the amino compounds and the problematic isolations of the 1-*protio* and ethoxy salts, we set out to study the more traditional pyrylium systems **3m**−**p** (R_1 = Ph). Upon cyclization, the observed downfield proton singlet for H_a at 8.8 ppm indicates the greater expected degree of aromaticity within these systems. Relative to the benzophenone carbonyl ^{13}C NMR resonance, C_1 of **3** shifted upfield by 20 ppm, showing less carbonyl character: carbon NMR data for **3n** correlated well with literature values.[11] While **3n** fluoresced weakly in comparison to the exocyclic amine compounds, it also displayed a significant Stokes shift upon emission.

As a further structural proof and a demonstration of utility, we used anhydrous ammonia to transform the isobenzopyrylium salts **3** into the corresponding isoquinolines **4**.[12] Many syntheses utilize a Bischler−Napieralski cyclization to construct the isoquinoid ring system,[13] but using this procedure for the construction of 3-arylisoquinoline ring systems gives rise to competitive retro-Ritter stilbenic side products.[14] Investigations toward an efficient methodology led to the conclusion that exposure of a triflate salt generated in situ (method A) and an isolation−exposure protocol (method B) provided comparable yields, as outlined in Table 3. Thus, method A serves as an attractive one-pot synthetic strategy for constructing isoquinoline ring systems. The poor yields for compounds **4a**−**e** may result from the exocyclic charge localization (for R_1 = NMe_2) or the hydrolytic instability (for R_1 = OEt) discussed earlier that reduced their full pyrylium character and inhibited their reactivities as pyrylium compounds. We found that these compounds underwent competitive transformation into the corresponding free amino isoquinolines **6**. The precursors to



6a (R_2 = Ph)
b (R_2 = *p*-tol)
c (R_2 = *p*-OC_{10})

4f−**j** (R_1 = H, Ph) have more pyrylium character and therefore readily reacted with ammonia in accordance with literature precedents.[15] We anticipate that this methodology should prove useful for the development of more convergent syntheses of aryl isoquinolines.

In closing, we have shown that the acid-induced electrophilic cyclizations of alkynes with carbonyl oxygens provide a new and efficient route to pyrylium salts and their isoquinoline analogues. Future work shall focus on expanding our methodology to other heteroatomic systems and to polymeric systems in order to open new avenues of postpolymerization modification.

Experimental Section

General. All synthetic manipulations were performed under an argon atmosphere using standard Schlenk techniques unless otherwise noted. All chemicals were of reagent grade; anhydrous methylene chloride was purchased from Aldrich and used without further purification. Column chromatography was performed using Baker 40 μm silica gel. All organic extracts were dried over $MgSO_4$ and filtered prior to removal with a rotary evaporator. NMR chemical shifts are referenced to $CHCl_3$/TMS (7.26 ppm for ^{1}H, 77.23 ppm for ^{13}C) or CD_2HCN (1.94 ppm for ^{1}H, 1.39 ppm for ^{13}C). High-resolution mass spectra were obtained at the MIT Department of Chemistry Instrumentation Facility (DCIF) using a peak matching protocol to determine the mass and error range of the molecular ion; FAB spectra were obtained using a 3-nitrobenzyl alcohol matrix. Fluorescence measurements were recorded on a SPEX Fluorolog-τ2 fluorimeter with a 450 W xenon lamp. Elemental analyses were obtained at Desert Analytics (Tucson, AZ). Melting points are uncorrected.

Isobenzoyrylium Salts 3: Representative Procedure. One equivalent of an alkyne precursor **2** was added to a dry Schlenk flask and placed under argon. A 0.005 M solution of the alkyne in methylene chloride was prepared and stirred vigorously as 20 equiv of the acid (neat trifluoromethanesulfonic acid unless otherwise noted) was added dropwise. The reaction stirred at room temperature for 0.5−1.5 h at which point the salts were precipitated with diethyl ether or used for amination studies as described individually below. For NMR studies, chloroform-*d* (and CF_3SO_3D when specified) was used in lieu of methylene chloride.

1-(*N*,*N*-Dimethylamino)-3-phenylisobenzopyrylium Trifluoromethanesulfonate (3c). Starting from 101 mg of **2c** (0.406 mmol), the reaction stirred for 1 h at which point solvent volume was reduced in vacuo by approximately 50%. **3c** was precipitated with diethyl ether followed by filtration and reprecipitation from $MeCN/CH_2Cl_2$ to provide a greenish-yellow fluffy solid (102 mg, 0.254 mmol, 63%) (mp 204.5−206.0 °C). ^{1}H NMR (500 MHz, CD_3CN) δ: 8.44 (d, 1H, J = 8.5 Hz), 8.03 (t, 1H, J = 8.0 Hz), 7.96 (m, 2H), 7.88 (d, 1H, J = 8.0 Hz), 7.77 (t, 1H, J = 8.5 Hz), 7.63 (s, 1H), 7.61 (m, 3H), 3.87 (s, 3H), 3.69 (s, 3H). ^{13}C NMR (125 MHz, CD_3CN) δ: 165.3, 152.5, 139.2, 138.4, 132.3, 131.3, 130.8, 130.5, 130.4, 129.0, 126.5, 122.2 (q, 319 Hz), 116.3,

(11) Saba, A.; Sib, F. S.; Aycard, J.-P. *Spectrosc. Lett*. **1993**, *26*, 491−496.

(12) During preparation of this manuscript, we found a recently published procedure which effected cyclizations of *o*-ethynylpyridinecarbaldehydes to the corresponding naphthyridines upon exposure to ethanolic ammonia at 80 °C in a sealed tube: Numata, A.; Kondo, Y.; Sakamoto, T. *Synthesis* **1999**, 306−311. Applying this protocol to **2k** gave a 37% crude yield of **4f**.

(13) For a discussion of the Bischler−Napieralski reaction and other related synthetic strategies, see: Kametani, T.; Fukumoto, K. In *Isoquinolines*. Grethe, G., Ed.; John Wiley & Sons: New York, 1981; Part I, pp 139−274.

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(15) (a) Baeyer, A.; Piccard, J. *Ann. Chem*. **1911**, *384*, 208−224. (b) Blount, B. K.; Robinson, R. *J. Chem. Soc*. **1933**, 555−557.

106.6, 46.0, 43.6. FT-IR (KBr): ν/cm^{-1}: 1661, 1610, 1484, 1420, 1266 (vs). UV−vis (CH_3CN) λ_{max}/nm (log ϵ): 271 (4.38), 303 (s, 4.20), 370 (3.94). Emission (CH_3CN) λ_{max}/nm: 474. HR-MS (EI): found m/z = 250.1226 ± 0.0007 (M^+); calcd for $C_{17}H_{16}NO^+$: 250.1232. HR-MS [FAB (−)]: found m/z = 148.9522 ± 0.0005 (M^-); calcd for $CF_3SO_3^-$: 148.9520. Anal. Calcd for $C_{18}H_{16}F_3NO_4S$: C, 54.13; H, 4.04; N, 3.51. Found: C, 53.90; H, 3.91; N, 3.75.

1-(*N*,*N*-Dimethylamino)-3-(4-methylphenyl)isobenzopyrylium Trifluoromethane sulfonate (3d). Starting from 103 mg of **2d** (0.390 mmol), the reaction stirred for 1 h at which point solvent volume was reduced in vacuo by approximately 50%. **3d** was precipitated with diethyl ether followed by filtration and reprecipitation from $MeCN/CH_2Cl_2$ to provide a greenish-yellow fluffy solid (104 mg, 0.251 mmol, 64%) (mp 208−209 °C). ^{1}H NMR (500 MHz, CD_3CN) δ: 8.43 (d, 1H, J = 8.5 Hz), 8.01 (t, 1H, J = 7.5 Hz), 7.85 (m, 2H), 7.75 (t, 1H, J = 8.0 Hz), 7.57 (s, 1H), 7.41 (d, 2H, J = 7.5 Hz), 3.86 (s, 3H), 3.67 (s, 3H), 2.43 (s, 3H). ^{13}C NMR (125 MHz, CD_3CN) δ: 165.2, 152.7, 143.1, 139.3, 138.26, 131.3, 131.0, 130.1, 128.8, 128.0, 126.4, 122.2 (q, J = 328 Hz), 116.1, 105.7, 46.0, 43.6, 21.6. FT-IR (KBr): ν/cm^{-1}: 1658, 1607, 1479, 1420, 1262 (s). UV−vis (CH_3CN) λ_{max}/nm (log ϵ): 306 (s, 4.28), 376 (3.95). Emission (CH_3CN) λ_{max}/nm: 487. HR-MS (EI): found m/z = 264.1385 ± 0.0009 (M^+); calcd for $C_{18}H_{18}NO^+$: 264.1388. HR-MS [FAB (−)]: found m/z = 148.9519 ± 0.0005 (M^-); calcd for $CF_3SO_3^-$: 148.9520. Anal. Calcd for $C_{19}H_{18}F_3NO_4S$: C, 55.20; H, 4.39; N, 3.39. Found: C, 54.95; H, 4.20; N, 3.35.

3-(4-Decyloxyphenyl)-1-(*N*,*N*-dimethylamino)isobenzopyrylium Trifluoromethanesulfonate (3e). Starting from 82 mg of **2e** (0.202 mmol), **3e** was precipitated with diethyl ether followed by filtration and reprecipitation from $MeCN/CH_2Cl_2$ to provide a yellow fluffy solid (54 mg, 0.100 mmol, 50%) (mp 136.5−138 °C). ^{1}H NMR (500 MHz, CD_3CN) δ: 8.41 (d, 1H, J = 8.5 Hz), 7.99 (t, 1H, J = 8.0 Hz), 7.87 (d, 2H, J = 9.0 Hz), 7.82 (d, 1H, J = 7.0 Hz), 7.72 (td, 1H, J = 7.5, 1.0 Hz), 7.48 (s, 1H), 7.09 (d, 2H, J = 9.0 Hz), 4.07 (t, 2H, J = 6.5 Hz), 3.85 (s, 3H), 3.66 (s, 3H), 1.78 (quin, 2H, J = 6.5 Hz), 1.46 (quin, 2H, J = 6.5 Hz), 1.30 (m, 12H), 0.89 (t, 3H, J = 7.0 Hz). ^{13}C NMR (125 MHz, CD_3CN) δ: 165.3, 162.7, 152.9, 139.7, 138.3, 131.2, 129.8, 128.6, 128.3, 122.9, 122.2 (q, J = 319 Hz), 116.3, 115.8, 104.8, 69.4, 46.0, 43.5, 32.7, 30.4, 30.3, 30.1, 29.8, 26.7, 23.5, 14.5. FT-IR (KBr): ν/cm^{-1}: 1656, 1604, 1516, 1481, 1260 (s). UV−vis (CH_3CN) λ_{max}/nm (log ϵ): 239 (4.16), 273 (4.32), 313 (4.39), 387 (4.03). Emission (CH_3CN) λ_{max}/nm: 527. HR-MS (EI): found m/z = 406.2736 ± 0.0012 (M^+); calcd for $C_{27}H_{36}NO_2^+$: 406.2746. HR-MS [FAB (−)]: found m/z = 148.9522 ± 0.0005 (M^-); calcd for $CF_3SO_3^-$: 148.9520. Anal. Calcd for $C_{28}H_{36}F_3NO_5S$: C, 60.52; H, 6.53; N, 2.52. Found: C, 60.18; H, 6.54; N, 2.58.

1-Ethoxy-3-phenylisobenzopyrylium Tetrafluoroborate (3f). Starting from 103 mg of **2g** (0.412 mmol) and 2.5 mL of a 54% solution of HBF_4 in diethyl ether (18 mmol), **3f** was precipitated with diethyl ether along side hydrolysis product **5a** to provide 136 mg of a pale yellow fluffy solid. The instability of this compound prevented isolation in pure form, so peaks attributed to **3f** were assigned by comparison with a pure sample of isocoumarin **5a**. Literature values for 3-phenylisocoumarin were consistent with those obtained for **5a** and can be found in the Supporting Information. Using ^{1}H NMR integration ratios, 0.272 mmol of **3f** was obtained (66%). ^{1}H NMR (500 MHz, CD_3CN) δ: 8.54 (d, 1H, J = 8.5 Hz), 8.29 (td, 1H, J = 8.5, 1.0 Hz), 8.17 (s, 1H), 8.09 (d, 1H, J = 8.0 Hz), 8.04 (m, 2H), 7.96 (td, 1H, J = 7.0, 1.0 Hz), 7.67 (m, 3H), 5.27 (q, 2H, J = 7.0 Hz), 1.74 (t, 3H, J = 7.0 Hz).

1-Ethoxy-3-(4-methylphenyl)isobenzopyrylium Tetrafluoroborate (3g). Starting from 108 mg of **2h** (0.409 mmol) and 1.15 mL of a 54% solution of HBF_4 in diethyl ether (8.35 mmol), **3g** was precipitated with diethyl ether along side hydrolysis product **5b** to provide 138 mg of a pale yellow fluffy solid. The instability of this compound prevented isolation in pure form, so peaks attributed to **3g** were assigned by comparison with a pure sample of isocoumarin **5b**. Literature values for 3-(4-methylphenyl)isocoumarin were consistent with those obtained for **5b** and can be found in the Supporting Information. Using ^{1}H NMR integration ratios, 0.360 mmol of **3g** was obtained (88%). ^{1}H NMR (500 MHz, CD_3CN) δ: 8.51 (d, 1H, J = 8.0 Hz), 8.27 (td, 1H, J = 8.0, 1.0 Hz), 8.10 (s, 1H), 8.06 (d, 1H, J = 8.5 Hz), 7.93 (m, 3H), 7.47 (d, 2H, J = 8.0 Hz), 5.25 (q, 2H, J = 7.0 Hz), 2.46 (s, 3H), 1.73 (t, 3H, J = 7.0 Hz).

3-Phenylisobenzopyrylium Trifluoromethanesulfonate (3j). Generated in situ from **2k** (3.2 mg, 0.0155 mmol) in 2 mL of chloroform-*d* to provide a greenish-yellow fluorescent intermediate which could not be isolated but was observed by ^{1}H NMR approximately 1 h into the reaction. Further structural proof was obtained after exposure to ammonia: characterization data for **4f** was consistent with literature values and can be found in the Supporting Information. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 10.18 (s, 1H), 8.67 (s, 1H), 8.57 (d, 1H, J = 8.5 Hz), 8.54 (t, 1H, J = 8.5 Hz), 8.29 (d, 1H, J 8.5 Hz), 8.16 (m, 3H), 7.78 (t, 1H, J = 7.0 Hz), 7.71 (t, 2H, J = 7.5 Hz). **4-Deuterio-3-phenylisobenzopyrylium Trifluoromethanesulfonate.** Generated as **3j** using TfOH-*d*. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 10.19 (s, 1H), 8.58 (d, 1H, J = 8.5 Hz), 8.54 (td, 1H, J = 8.0, 1.0 Hz), 8.29 (d, 1H, J = 8.5 Hz), 8.16 (m, 3H), 7.78 (t, 1H, J = 7.5 Hz), 7.71 (t, 2H, J = 8.0 Hz).

3-(4-Methylphenyl)isobenzopyrylium Trifluoromethanesulfonate (3k). Generated in situ from **2l** (3.4 mg, 0.0154 mmol) in 2 mL of chloroform-*d* to provide an intensely yellow fluorescent intermediate which could not be isolated but was observed by ^{1}H NMR approximately 1 h into the reaction. Further structural proof was obtained after exposure to ammonia: characterization data for **4g** was consistent with literature values and can be found in the Supporting Information. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 10.11 (s, 1H), 8.60 (s, 1H), 8.52 (d, 1H, J = 8.5 Hz), 8.49 (td, 1H, J = 8.5, 1.0 Hz), 8.24 (d, 1H, J = 8.5 Hz), 8.11 (t, 1H, J = 7.0 Hz), 8.04 (d, 2H, J = 8.5 Hz), 7.51 (d, 2H, J = 8.0 Hz), 2.53 (s, 3H). **4-Deuterio-3-(4-methylphenyl)-isobenzopyrylium Trifluoromethanesulfonate.** Generated as **3k** using TfOH-*d*. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 10.12 (s, 1H), 8.52 (d, 1H, J = 8.0 Hz), 8.49 (t, 1H, J = 7.0 Hz), 8.24 (d, 1H, J = 8.5 Hz), 8.12 (t, 1H, J = 8.0 Hz), 8.04 (d, 2H, J = 8.5 Hz), 7.51 (d, 2H, J = 7.5 Hz), 2.53 (s, 3H).

3-(4-Decyloxyphenyl)isobenzopyrylium Trifluoromethanesulfonate (3l). Generated in situ from **2m** (5.3 mg, 0.0146 mmol) in 2 mL of chloroform-*d* to provide an intense burgandy intermediate which could not be isolated but was observed by ^{1}H NMR after 10 min (NMR data listed below), 60 min (3:1 mixture of products) and 4 d into the reaction (one product, no evidence for alkoxy protons). Further structural proof was obtained after exposure to ammonia: characterization data for **4h** was consistent with the proposed isoquinoline structure. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 10.02 (s, 1H), 8.51 (s, 1H), 8.43 (m, 2H), 8.18 (d, 1H, J = 7.5 Hz), 8.11 (d, 2H, J = 9.0 Hz), 8.05 (t, 1H, J = 8.5 Hz), 7.19 (d, 2H, J = 9.0 Hz), 4.18 (t, 2H, J = 6.5 Hz), 1.86 (quin, 2H, J = 7.5 Hz), 1.48 (quin, 2H, J = 7.5 Hz), 1.29 (bm, 12H), 0.88 (t, 3H, J = 7.0 Hz).

1,3-Diphenylisobenzopyrylium Trifluoromethanesulfonate (3m). Starting from 101 mg of **2n** (0.358 mmol) and following addition of diethyl ether, the solution was stored overnight at 0 °C. The resulting solids were filtered and washed with ether to give **3m** as an orange powder (114 mg, 0.264 mmol, 74%) (mp 189.5−190.0 °C). ^{1}H NMR (500 MHz, CD_3CN) δ: 8.80 (s, 1H), 8.68 (d, 1H, J = 8.5 Hz), 8.46 (t, 1H, J = 7.0 Hz), 8.34 (d, 1H, J = 8.0 Hz), 8.23 (m, 4H), 8.09 (t, 1H, J = 7.5 Hz), 7.99 (t, 1H, J = 7.5 Hz), 7.87 (t, 2H, J = 8.5 Hz), 7.73 (m, 3H). ^{13}C NMR (125 MHz, CD_3CN) δ: 182.2, 161.8, 145.1, 144.1, 136.6, 134.2, 134.1, 134.0, 133.7, 131.0 (2 Cs), 130.5, 130.3, 129.4, 127.9, 124.3, 122.2 (q, J = 319 Hz), 116.5. FT-IR (KBr): ν/cm^{-1}: 1621, 1541, 1499, 1417, 1272 (vs). UV−vis (CH_3CN) λ_{max}/nm (log ϵ): 228 (4.22), 267 (4.44), 303 (s, 4.36), 441 (3.99). HR-MS (EI): found m/z = 283.1126 ± 0.0008 (M^+); calcd for $C_{21}H_{15}O^+$: 283.1123. HR-MS [FAB (−)]: found m/z = 148.9522 ± 0.0005 (M^-); calcd for $CF_3SO_3^-$: 148.9520. Anal. Calcd for $C_{22}H_{15}F_3O_4S$: C, 61.11; H, 3.50. Found: C, 60.98; H, 3.45.

1,3-Diphenylisobenzopyrylium Tetrafluoroborate (3n).[11] Starting from 101 mg of **2n** (0.358 mmol), **3n** was precipitated with diethyl ether followed by filtration to provide an orange solid (88 mg, 0.237 mmol, 66%) [mp 241−242.5 °C (dec)]. ^{1}H NMR (500 MHz, CD_3CN) δ: 8.80 (s, 1H), 8.68 (d, 1H, J = 8.5 Hz), 8.46 (t, 1H, J = 7.0 Hz), 8.34 (d, 1H, J = 8.5 Hz), 8.23 (m, 4H), 8.09 (t, 1H, J = 7.0 Hz), 7.99 (t, 1H, J = 7.5 Hz), 7.87 (t, 2H, J = 8.0 Hz), 7.73 (m, 3H). ^{13}C NMR (125 MHz, CD_3CN) δ: 182.2, 161.8, 145.1, 144.1, 136.6, 134.2, 134.1, 134.0, 133.7, 131.0 (2C), 130.5, 130.3, 129.4, 127.9, 124.3, 116.5. FT-IR (KBr):

ν/cm^{-1}: 1619, 1540, 1502, 1417, 1056 (vs). UV−vis (CH_3CN) λ_{max}/nm (log ϵ): 302 (4.36), 440 (4.01). Emission (CH_3CN) λ_{max}/nm: 538 (very weak). HR-MS (EI): found m/z = 283.1117 ± 0.0008 (M^+); calcd for $C_{21}H_{15}O^+$: 283.1123. HR-MS [FAB (−)]: found m/z = 87.0028 ± 0.0003 (M^-); calcd for BF_4^-: 87.0029.

3-(4-Methylphenyl)-1-phenylisobenzopyrylium Trifluoromethanesulfonate (3o). Starting from 100 mg of **2o** (0.338 mmol) and following addition of diethyl ether, the solution was stored at 0 °C overnight. The precipitated solids were filtered off and washed with ether to provide **3o** as an orange solid (126 mg, 0.283 mmol, 84%) [mp 220.5−221.5 °C (sub)]. ^{1}H NMR (500 MHz, CD_3CN) δ: 8.76 (s, 1H), 8.66 (d, 1H, J = 9.0 Hz), 8.45 (t, 1H, J = 7.5 Hz), 8.32 (d, 1H, J = 8.5 Hz), 8.23 (d, 2H, J = 7.0 Hz), 8.14 (d, 2H, J = 8.0 Hz), 8.08 (t, 1H, J = 7.5 Hz), 8.00 (t, 1H, J = 7.5 Hz), 7.88 (t, 2H, J = 8.0 Hz), 7.55 (d, 2H, J = 8.0 Hz), 2.51 (s, 3H). ^{13}C NMR (125 MHz, CD_3CN) δ: 181.6, 162.1, 145.6, 145.3, 143.9, 136.4, 133.8, 133.8, 133.6, 131.7, 131.0, 130.5, 129.3, 127.9, 127.5, 124.1, 122.2 (q, J = 318 Hz), 115.9, 21.8. FT-IR (KBr): ν/cm^{-1}: 1621, 1540, 1499, 1418, 1265 (vs). UV−vis (CH_3CN) λ_{max}/nm (log ϵ): 233 (4.23), 271 (4.41), 304 (4.35), 329 (s), 452 (3.98). HR-MS (FAB): found m/z = 297.1276 ± 0.0009 (M^+); calcd for $C_{22}H_{17}O$: 297.1279. HR-MS [FAB (−)]: found m/z = 148.9523 ± 0.0005 (M^-); calcd for $CF_3SO_3^-$: 148.9520. Anal. Calcd for $C_{23}H_{17}F_3O_4S$: C, 61.88; H, 3.84. Found: C, 61.93; H, 3.73.

Isoquinolines 4. Representative Procedures. Method A: The pyrylium salts **3** were prepared as described above at which point anhydrous ammonia was bubbled through the reaction mixture for 30−45 min, placed under a positive pressure of ammonia and stirred for a total of 20 h. The reaction mixture was washed with $NaHCO_3$ (aq) and NaCl (aq). The organic layer was separated, dried, and removed in vacuo to provide a crude material which was purified on silica gel to yield the isoquinolines listed below.

Method B: The isolated salt **3** was placed under argon in a dry Schlenk flask and brought to a concentration of 0.005 M in methylene chloride. The suspension was stirred vigorously to effect some dissolution, and anhydrous ammonia was bubbled through the flask for 30−45 min. The system was placed under a positive ammonia pressure and stirred for a total of 20 h. Washing the organic phase as described for method A followed by column chromatography provided the desired isoquinolines.

For further purification, the isoquinolines were taken up in ether and precipitated as the hydrochloride salts upon addition of 12 M HCl. Rinsing the solids twice with ether and a basic workup [2 M KOH, $NaHCO_3$, and NaCl (aq)] again provided the isoquinolines which were pure by ^{1}H NMR and GC-MS (96%+). Reported yields are for products obtained after chromatography.

1-(*N*,*N*-Dimethylamino)-3-phenylisoquinoline (4a). Using 106 mg of **2c** (0.425 mmol) in method A followed by column chromatography (3:1 hexane/ ethyl acetate) provided **4a** as a yellow oil (24 mg, 0.095 mmol, 22%). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.19 (d, 2H, J = 7.5 Hz), 8.14 (d, 1H, J = 8.5 Hz), 7.79 (d, 1H, J = 8.5 Hz), 7.65 (s, 1H), 7.58 (td, 1H, J = 8.0, 1.0 Hz), 7.47 (m, 3H), 7.38 (t, 1H, J = 7.5 Hz), 3.20 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 161.4, 148.1, 140.0, 139.4, 129.6, 128.7, 128.3, 127.7, 126.8, 126.2, 125.4, 120.5, 110.3, 43.3. FT-IR (KBr) ν/cm^{-1}: 1618, 1561, 1501, 1385, 1344. HR-MS (EI): found m/z = 248.1309 ± 0.0007 (M^+); calcd for $C_{17}H_{16}N_2$: 248.1313. Further elution with 2:1 hexane/ ethyl acetate provided **1-amino-3-phenylisoquinoline (6a)** as a pale yellow solid (34 mg, 0.135 mmol, 32%) (mp 95.5−96.5 °C, lit.[16] 97.5−99 °C).

1-(*N*,*N*-Dimethylamino)-3-(4-methylphenyl)isoquinoline (4b). Using 50 mg of **3d** (0.120 mmol) in method B followed by column chromatography (2:1 hexane/methylene chloride) provided **4b** as a yellow oil (9 mg, 0.036 mmol, 30%). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.12 (d, 1H, J = 8.0 Hz), 8.08 (d, 2H, J = 8.0 Hz), 7.76 (d, 1H, J = 8.0 Hz), 7.61 (s, 1H), 7.56 (td, 1H, J = 7.0, 1.0 Hz), 7.43 (td, 1H, J = 7.0, 1.0 Hz), 7.28 (d, 2H, J = 8.0 Hz), 3.19 (s, 6H), 2.41 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 161.4, 148.3, 139.6, 138.2, 137.3, 129.6, 129.5, 127.6, 126.7, 126.3, 125.3, 120.4, 109.9, 43.2, 21.5. FT-IR (KBr): ν/cm^{-1}: 1616, 1561, 1515, 1497, 1385. HR-MS (EI): found m/z = 262.1464 ± 0.0008 (M^+); calcd for $C_{18}H_{18}N_2$: 262.1470. Further elution with 3:1 hexane/ ethyl acetate afforded **1-amino-3-(4-methylphenyl)-isoquinoline (6b)** as a pale yellow oil which solidified upon standing (13 mg, 0.054 mmol, 45%) (mp 105.5−106.5 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.96 (d, 2H, J = 8.5 Hz), 7.71 (m, 2H), 7.56 (t, 1H, J = 7.5 Hz), 7.44 (s, 1H), 7.38 (t, 1H, J = 7.0 Hz), 7.26 (d, 2H, J = 8.0 Hz), 5.29 (bs, 2H), 2.39 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 156.1, 149.8, 138.4, 138.2, 137.3, 130.3, 129.5, 127.6, 126.9, 125.8, 122.8, 117.0, 108.5, 21.5. FT-IR (KBr) ν/cm^{-1}: 3487, 3453, 3290, 1620, 1561, 1495, 1432. HR-MS (EI): found m/z = 234.1155 ± 0.0007 (M^+); calcd for $C_{16}H_{14}N_2$: 234.1157.

1-Ethoxy-3-phenylisoquinoline (4d).[17] The salt **3f** was prepared from 106 mg of **2g** (0.4235 mmol) by method A using ethereal HBF_4. The precipitate was filtered, washed with ether, and immediately placed under argon. Using method B followed by column chromatography (3:1 hexane/ methylene chloride) provided **4d** as a white oily solid (24.5 mg, 0.0298 mmol, 23%). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.27 (d, 1H, J = 8.0 Hz), 8.16 (d, 2H, J = 7.5 Hz), 7.78 (d, 1H, J = 8.0 Hz), 7.68 (s, 1H), 7.64 (t, 1H, J = 7.0 Hz), 7.49 (m, 3H), 7.39 (t, 1H, J = 7.5 Hz), 4.72 (q, 2H, J = 7.0 Hz), 1.56 (t, 3H, J = 7.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 160.2, 147.9, 139.7, 138.9, 130.6, 128.7, 128.4, 126.8, 126.7 (2C), 126.4, 124.4, 119.1, 110.3, 62.2, 15.0. FT-IR (KBr) ν/cm^{-1}: 1626, 1574, 1500, 1378. HR-MS (EI): found m/z = 249.1157 ± 0.0007 (M^+); calcd for $C_{17}H_{15}NO$: 249.1154. Gradually increasing the elution solvent polarity led to the isolation of 43.6 mg of a solid containing primarily the isocoumarin **5a** (65% by GC-MS, 30% estimated overall yield). Further elution provided 11 mg of **6a** (0.047 mmol, 11%) as a yellowish solid.

1-Ethoxy-3-(4-methylphenyl)isoquinoline (4e). Using 101.6 mg of **2h** (0.3844 mmol) in method A with ethereal HBF_4 in lieu of TfOH followed by chromatography (2:1 hexane/methylene chloride) provided **4e** as a oily white solid (20.9 mg, 0.0794 mmol, 21%). Further elution with 4:1 hexane/ethyl acetate also provided **6b** (59 mg, 0.252 mmol, 66%). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.25 (d, 1H, J = 8.0 Hz), 8.05 (d, 2H, J = 8.0 Hz), 7.76 (d, 1H, J = 8.0 Hz), 7.63 (m, 2H), 7.48 (t, 1H, J = 8.0 Hz), 7.28 (d, 2H, J = 8.0 Hz), 4.71 (q, 2H, J = 7.0 Hz), 2.42 (s, 3H), 1.55 (t, 3H, J = 6.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 160.2, 148.1, 139.1, 138.4, 137.0, 130.6, 129.5, 126.7 (2C), 126.2, 124.4, 119.1, 109.8, 62.1, 21.5, 14.9. FT-IR (KBr): ν/cm^{-1}: 1626, 1576, 1411, 1377. HR-MS (EI): found m/z = 263.1304 ± 0.0007 (M^+); calcd for $C_{18}H_{17}NO$: 263.1310.

3-Phenylisoquinoline (4f). Using 106 mg of **2k** (0.515 mmol) in method A followed by column chromatography (7.5:1 hexane/ ethyl acetate) provided **4f** as yellow flakes (78 mg, 0.382 mmol, 74%). (mp 101−101.5 °C, lit.[18] 102.5−103.5 °C).

3-(4-Methylphenyl)isoquinoline (4g). Using 101 mg of **2l** (0.458 mmol) in method A followed by purification on silica gel (5:1 hexane/ethyl acetate) provided **4g** as a light brown solid (67 mg, 0.306 mmol, 67%). (mp 74−75 °C, lit.[18] 76−76.5 °C).

3-(4-Decyloxyphenyl)isoquinoline (4h). Using 50 mg of **2m** (0.138 mmol) in method A followed by column chromatography (9:1 hexane/ethyl acetate) provided **4h** as a light brown solid (32 mg, 0.0891 mmol, 65%). Further purification as described above gave 16 mg of **4h** as a white solid (0.043 mmol, 31%) (mp 78.5−79 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.30 (s, 1H), 8.07, d, 2H, J = 8.5 Hz), 7.99 (s, 1H), 7.97 (d, 1H, J = 8.5 Hz), 7.84 (d, 1H, J = 8.0 Hz), 7.67 (t, 1H, J = 7.0 Hz), 7.55 (t, 1H, J = 7.5 Hz), 7.03 (d, 2H, J = 8.5 Hz), 4.03 (t, 2H, J = 7.0 Hz), 1.82 (quin, 2H, J = 6.5 Hz), 1.48 (quin, 2H, J = 6.5 Hz), 1.28 (bm, 12H), 0.89 (t, 3H, J = 6.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 160.0, 152.5, 151.4, 137.0, 132.2, 130.6, 128.4, 127.8, 127.6, 127.0, 126.8, 115.5, 115.0, 68.3, 32.1, 29.82, 29.79, 29.66, 29.56, 29.52, 26.3, 22.9, 14.4. FT-IR (KBr): ν/cm^{-1}: 1625, 1605, 1512, 1446, 1251. HR-MS (EI): found m/z = 361.2402 ± 0.0010 (M^+); calcd for $C_{25}H_{31}NO$: 361.2406.

1,3-Diphenylisoquinoline (4i). Using 80 mg of **3m** (0.186 mmol) in method B followed by column chromatography (1:1

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hexane/methylene chloride) provided **4i** as an oily opaque solid (19.8 mg, 0.0704 mmol, 38%) (mp 73−74.5 °C, lit.[19] 71−73 °C).

3-(4-Methylphenyl)-1-phenylisoquinoline (4j). Using 100 mg of **2o** (0.337 mmol) in method A followed by column chromatography (2:2 hexane/methylene chloride) provided **4j** as a pale orange solid (67 mg, 0.226 mmol, 67%) (mp 116−117 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.12 (d, 3H, J = 8.0 Hz), 8.04 (s, 1H), 7.92 (d, 1H, J = 8.5 Hz), 7.81 (d, 2H, J = 7.5 Hz), 7.67 (t, 1H, J = 7.0 Hz), 7.52 (m, 4H), 7.30 (d, 2H, J = 7.5 Hz), 2.42 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 160.4, 150.4, 140.1, 138.5, 138.0, 137.0, 130.4, 130.1, 129.6, 128.7, 128.5, 127.71, 127.57, 127.1, 126.9, 125.8, 115.4, 21.5. FT-IR (KBr): ν/cm^{-1}: 1621, 1562, 1516, 1445, 1386. HR-MS (EI): found m/z = 295.1356 ± 0.0009 (M^+); calcd for $C_{22}H_{17}N$: 295.1361.

1-Amino-3-(4-decyloxyphenyl)isoquinoline (6c). Using **2e** (49 mg, 0.121 mmol) in method A followed by column chromatography (4:1 hexane/ethyl acetate) provided **6c** as a clear oil (25 mg, 0.0675 mmol, 52%). Purification as described above provided 13 mg of **6c** as a white solid (0.033 mmol, 27%) (mp 66−67.5 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.99 (d, 2H, J = 8.5 Hz), 7.79 (d, 1H, J = 8.0 Hz), 7.73 (d, 1H, J = 8.0 Hz), 7.60 (t, 1H, J = 7.5 Hz), 7.43 (t, 1H, J = 7.5 Hz), 7.41 (s, 1H), 6.98 (d, 2H, J = 8.5 Hz), 5.26 (s, 2H), 4.01 (t, 2H, J = 6.5 Hz), 1.81 (quin, 2H, J = 7.5 Hz), 1.47 (quin, 2H, J = 7.5 Hz), 1.28 (bm, 12H), 0.89 (t, 3H, J = 6.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 159.7, 156.0, 149.4, 138.6, 132.3, 130.5, 128.2, 127.6, 125.8, 122.8, 116.8, 114.8, 108.0, 68.3, 32.1, 29.81, 29.79, 29.66, 29.56, 29.51, 26.3, 22.9, 14.36. FT-IR (KBr) ν/cm^{-1}: 3466, 3393, 3347, 1605, 1563, 1513, 1420. HR-MS (EI): found m/z = 376.2518 ± 0.0011 (M^+); calcd for $C_{25}H_{32}N_2O$: 376.2515.

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Supporting Information Available: Full experimental details and characterization data for **2a**−**p** and **5a**−**c**; additional characterization data for literature compounds **4f**, **4g**, **4i**, and **6a**; copies of ^{1}H and ^{13}C spectra of all new compounds; ORTEP diagram and X-ray crystallographic data for **3d**. This material is available free of charge via the Internet at http://pubs.acs.org.

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