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Reaction of α-Oxoketene-*N*,*S*-arylaminoacetals with Vilsmeier Reagents: An Efficient Route to Highly Functionalized Quinolines and Their Benzo/Hetero-Fused Analogues‡

P. K. Mahata, C. Venkatesh, U. K. Syam Kumar, H. Ila,* and H. Junjappa*

Department of Chemistry, Indian Institute of Technology, Kanpur-208016, India

hila@iitk.ac.in

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A simple, highly efficient, and regioselective synthesis of functionalized quinolines through Vilsmeier cyclization of a variety of α-oxoketene-*N*,*S*-anilinoacetals has been reported. The cyclization is found to be facile with *N*,*S*-acetals bearing strongly activating groups on aniline, whereas yields of quinolines are moderate in other cases. The reaction could also be extended for the synthesis of substituted tricyclic benzo[*h*]quinoline, pyrido[2,3-*h*]quinoline, 4,7-diphenylphenanthroline, and tetracyclic quino[8,7-*h*]quinoline by performing a Vilsmeier reaction on *N*,*S*-acetals derived from 1-naphthylamine, *m*-phenylenediamine, *o*-phenylenediamine, and 1,5-diaminonaphthalene, respectively. A few of the newly synthesized quinolines are subjected to further transformation to afford 2-unsubstituted (Raney-Ni/Ethanol), quinoline-5,8-quinone (NBS/H_2SO_4), or 2-alkyl/aryl aminoquinolines through sequential *m*-CPBA oxidation to the corresponding (2-methylsulfonyl)-quinoline followed by replacement with appropriate amines. Similarly, cycloannulation of a few 2-methylthio-3-benzoylquinolines with hydrazine hydrate under microwave irradiation afforded the corresponding substituted and fused pyrazolo[3,4-*b*]quinolines in excellent yields, whereas TBTH/AIBN-mediated cyclization of the corresponding 3-(2-bromobenzoyl)-2-methylthioquinolines yielded the corresponding benzothiopyrano-fused quinolines through radical translocation.

Introduction

Functionalized quinolines and their benzo/hetero-fused analogues represent an important class of organic molecules that have attracted a great deal of attention from synthetic as well as medicinal chemists because of their presence in numerous natural products along with the wide spectrum of physiological activities displayed by these class of compounds.[1] Thus, substituted quinolines have found attractive applications as pharmaceuticals (antimalarials, antibacterials, protein kinase inhibitors), NADH models, and agrochemicals as well as being general synthetic blocks.[1b] Similarly, the benzo- and hetero-fused quinolines are known to bind DNA with high affinity, inhibit DNA topoisomerase I, and display cytotoxic and antitumor activities.[2] On the other hand, 1,10-phenanthrolines[3] have been used as important ligands for vast amount of metal complexes that play an important role in many fields of chemistry.[3] Although numerous elegant syntheses have been developed for quinolines[4−6] and their benzo/hetero-fused derivatives,[7] because of their great importance, it is still challenging to explore new and efficient synthetic routes for this class of compounds, particularly those with wide general applicability to achieve more flexible substitution pattern.

Among the various routes available for the synthesis of functionalized quinolines, the "Vilsmeier approach"[8] involving reaction of enamines,[9a] *N*-arylacetamide,[9b−f] or tautomeric imines[10] with Vilsmeier reagents has only recently been explored. Alternatively, a "reverse Vilsmeier approach"[11] involving ring closure of Vilsmeier reagent derived from *N*-aryl-*N*-methylformamide with

‡ Dedicated to Professor Alan R. Katritzky on the occasion of his 75th birthday.

* To whom correspondence should be addressed. Fax: 91-0512-2597436, 91-0512-2590260.

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electron-rich olefins to give *N*-methylquinolinium salts has also been developed. Recently, Katritzky has reported[10] a highly regioselective one-pot synthesis of 2,3-diakyl/fused quinolines involving cyclocondensation of imines (via the corresponding tautomeric secondary enamines) with a novel Vilsmeier reagent derived from *N*-(trimethylsilyl)benzotriazole, DMF, and $SOCl_2$. All these methods, however, suffer from some limitations such as requiring a large excess of $POCl_3$, nonavailability of highly functionalized imine (or enamine) precursors, or being restricted only for the synthesis of *N*-alkylquinolinium salts. We have been engaged for several years in exploring reactivity and synthetic applications of polarized ketene *N*,*S*- and *N*,*N*-acetals representing a new class of highly versatile functionalized enamines.[12−14] The easy accessibility of these intermediates either via direct nucleophilic displacement on polarized ketene *S*,*S*-acetals by a wide variety of primary and secondary amines[15] or directly from active methylene compounds[12a] makes them attractive candidates for their further synthetic elaboration. Besides, these intermediates are stable at room temperature and can be stored indefinitely without any decomposition. We have demonstrated in our earlier work that a large variety of substituted and fused nitrogen and sulfur heterocycles with diverse structural features and functionalities are accessible from these precursors through tuning of their reactivity pattern by choice of various amines, active methylene compounds, as well as other reactive partners.[12] In continuation of these studies,[13,14] we now report the reaction of α-oxoketene *N*,*S*-acetals with Vilsmeier reagents providing a versatile route to highly functionalized quinolines and their benzo- and hetero-fused analogues.

Results and Discussion

The required α-oxoketene-*N*,*S*-arylaminoacetals **1a**−**l** (Table 1) were prepared by modification of our previously reported procedure by displacement of one of the methylthio groups of the corresponding α-oxoketene dithioacetals by the appropriate aniline in the presence of *n*-BuLi in THF.[15] The Vilsmeier cyclization of *N*,*S*-anilinoacetals **1a**−**d** bearing a strongly activating group (i.e., methoxy group) was first examined. Thus, the *N*,*S*-acetal **1a** derived from *m*-methoxyaniline underwent spontaneous reaction on treatment with DMF/$POCl_3$ at 80 °C to afford only one product (81%), which was characterized as 2-methylthio-3-benzoyl-7-methoxyquinoline (**2a**) on the basis of its spectral and analytical data (Scheme 1, Table 1). The corresponding (2-bromobenzoyl)- (**1b**) and the other *N*,*S*-acetals **1c**−**e** from 3,4-dimethoxy- and 2,5-dimethoxyanilines also reacted smoothly with Vilsmeier reagent under similar conditions to give the respective quinolines **2b**−**e** in high yields (Table 1, entries 2−5). However, the reactions of *N*,*S*-acetals **1f**−**h** without any activating group on aniline were found to be sluggish with Vilsmeier reagent requiring prolonged heating at higher temperature to afford the respective quinolines in poor yields (entries 6−8). Thus, the 3-fluoroanilino-*N*,*S*-acetal **1f** gave a regioisomeric mixture of quinolines **2fa** and **2fb** (entry 6) in low yields, whereas with unsubstituted (**1g**) and 4-chloroanilino (**1h**) *N*,*S*-acetals, the corresponding unsubstituted (**2g**) and 2,6-dichloroquinoline (**2h**) were isolated in 25% and 30% yields, respectively (entries 7 and 8). On the other hand, the *N*,*S*-acetal **1i** derived from α-naphthylamine was efficiently transformed into the condensed 2,3-substituted benzo[*h*]quinoline **2i** in nearly quantitative yield on treatment with Vilsmeier reagent under identical conditions as for **1a**−**e** (Table 1, entry 9). The *N*,*S*-acetals **1a**−**c**,**i** also underwent rapid cyclization with Vilsmeier reagent derived from *N*,*N*-dimethylacetamide to furnish the respective 2-methylthio-3-benzoyl-4-methylquinolines **3a**−**c** and the corresponding benzo[*h*]quinoline derivative **3i** in excellent yields (entries 10−13).

To further study the scope this facile quinoline synthesis, the reaction of α-acetyl-*N*,*S*-anilinoacetal **1j** with

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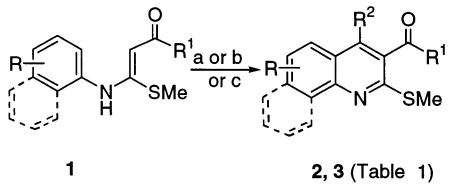
TABLE 1. Synthesis of Quinolines 2 and 3 by Reaction of α-Oxoketene-*N,S*-acetals with Vilsmeier Reagents[a]

Entry	*N,S*-acetals **1**	Method	Quinoline **2, 3**	Yield %
1	**1a**, Ar = C_6H_5	a	**2a**, Ar = C_6H_5	81
2	**1b**, Ar = 2-BrC_6H_4	a	**2b**, Ar = 2-BrC_6H_4	95
3	**1c**, Ar = C_6H_5	a	**2c**, Ar = C_6H_5	98
4	**1d**, Ar = 2-BrC_6H_4	a	**2d**, Ar = 2-BrC_6H_4	95
5	**1e**	a	**2e**	90
6	**1f**	b	**2fa**, X = F; Y = H **2fb**, X = H; Y = F	30 10
7	**1g**	b	**2g**	25
8	**1h**	b	**2h**	30
9	**1i**	a	**2i**	95
10	**1a**, Ar = C_6H_5	c	**3a**, Ar = C_6H_5	80
11	**1b**, Ar = 2-BrC_6H_4	c	**3b**, Ar = 2-BrC_6H_4	95
12	**1c**	c	**3c**	98
13	**1i**	c	**3i**	95
14	**1k**	a	**2k**	51
15	**1l**	a	**2l**	54

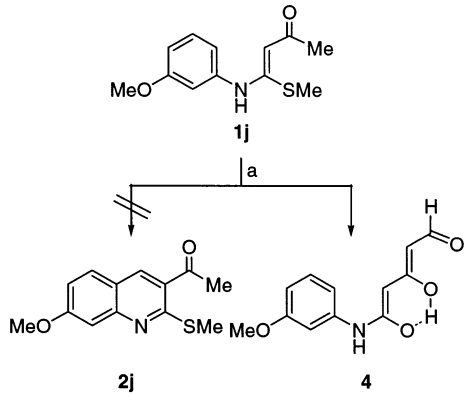
[a] Method: (a) $HCONME_2/POCl_3/\Delta$, 80 °C; (b) $HCONMe_2/POCl_3/Cl_2CHCHCl_2/\Delta$, 80 °C; (c) $MeCONMe_2/POCl_3/\Delta$, 80 °C.

SCHEME 1[a]



[a] Key: (a) $HCONMe_2/POCl_3/\Delta$, 80 °C; (b) $HCONMe_2/POCl_3/Cl_2CHCHCl_2/\Delta$, 80 °C; (c) $MeCONMe_2/POCl_3/\Delta$, 80 °C.

SCHEME 2[a]



[a] Key: (a) $HCONMe_2/POCl_3/\Delta$/80−90 °C.

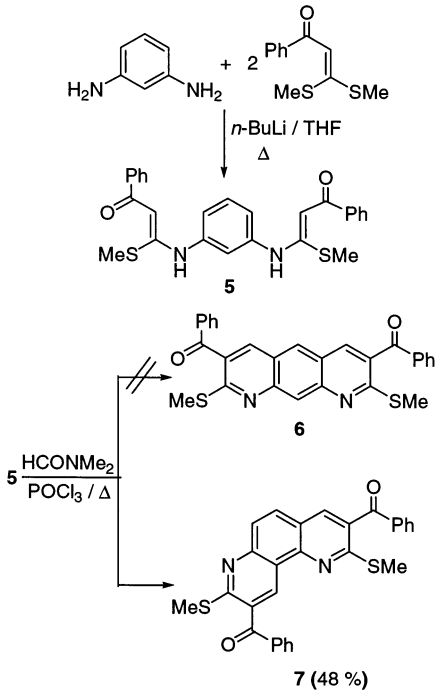
Vilsmeier reagent was examined with a view to synthesize 3-acetylquinoline **2j** (Scheme 2). However, only intractable reaction mixtures were obtained under varying conditions due to the competing side reaction of the acetyl group,[8] and in one of the reactions, the diketone aldehyde enamine **4** was isolated as the only identifiable product in 50% yield (Scheme 2). On the other hand, the corresponding *N,S*-acetals **1k,l** obtained from pyruvaldehyde dimethyl acetal afforded the respective 3-(bismethoxy)acetylquinolines **2k,l** in reasonable yields (51−54%) when subjected to Vilsmeier reaction under described conditions (Table 1, entries 14−15).

The validity of this new quinoline synthesis was further evaluated by performing the Vilsmeier reaction on bisketene-*N,S*-acetals **5**, **8**, and **11** with a view to synthesize planar tricyclic and tetracyclic heterocyclo-fused quinolines as shown in Schemes 3−5.The desired *N,S*-acetals **5**, **8**, and **11** were readily accessible by displacement reaction of *m*-phenylenediamine, *o*-phenylenediamine, and 1,5-diaminonaphthalene, respectively, on 2 equiv of α-benzoylketene dithioacetals in the presence of *n*-BuLi (Schemes 3−5).[15]

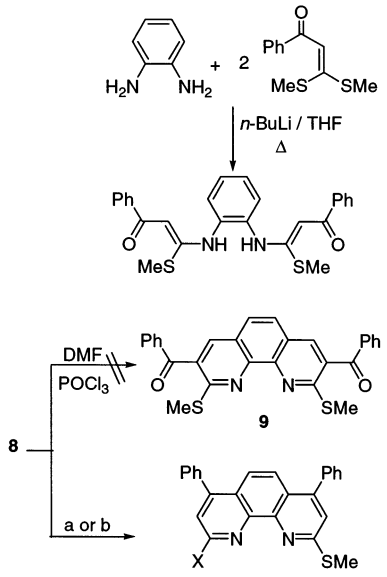
Thus, when the *N,S*-acetal from *m*-phenylenediamine was reacted with 2.5 equiv of Vilsmeier reagent, the product isolated (48%) was characterized as the angularly fused azaphenanthridine **7** and the corresponding linearly fused bisquinoline could not be isolated from the reaction mixture.[16] The bisketene-*N,S*-acetal **8** from *o*-phenylenediamine did not yield any of the expected symmetrical phenanthroline derivative **9** when exposed to varying Vilsmeier reaction conditions ($HCONMe_2/POCl_3$ at rt or at 130 °C) and only intractable reaction

(16) Column chromatography of the reaction mixture gave along with **7** another solid which could not be identified.

SCHEME 3



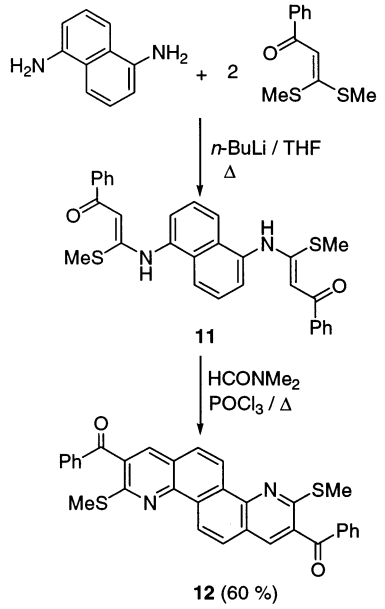
SCHEME 4[a]



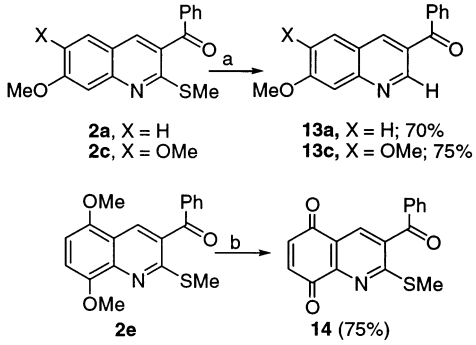
[a] Key: (a) DMA/$POCl_3$/TCE/130 °C; **10A**, X = OH (60%); (b) $POCl_3$/70 °C/3 h; **10B**, X = Cl (54%).

mixtures were formed. However, when **8** was heated with $POCl_3$ in DMA/TCE at 130 °C, the product isolated after workup was characterized as 2-methylthio-9-hydroxy-4,7-diphenylphenanthroline (**10A**) on the basis of its spectral and analytical data. This was further confirmed by subjecting the bisketene-*N*,*S*-acetal **8** to treatment with $POCl_3$ at 70 °C for 3 h, when the product obtained (54%) was characterized as the 2-methylthio-9-chloro-4,7-diphenylphenanthroline **10B** (Scheme 4). Apparently, in the absence of any activation at the site of cyclization with Vilsmeier reagent, intramolecular Combes[4]-type cyclization of the enaminone functionality is the preferred cyclization mode to yield the observed product **10**. The

SCHEME 5



SCHEME 6[a]



[a] Key: (a) Raney Ni/EtOH/Δ; (b) NBS/H_2SO_4/THF/H_2O.

bisketene-*N*,*S*-acetal **11** from 1,5-diaminonaphthalene underwent smooth cyclization with Vilsmeier reagent to afford the 2,8-bis(benzoyl)-3,9-bis(methylthio)quinolino-[8,7-*h*]quinoline **12** in 60% yield (Scheme 5). The structures of the products **7**, **10**, and **12** were confirmed with the help of spectral and analytical data.

With a variety of multifunctional, substituted, and fused quinolines in hand, we further explored the possible transformations of these functionalities to afford new quinolines (Schemes 6 and 7). Thus, the 2-methylthio group in the quinolines **2a** and **2c** could be reductively removed with Raney-Ni to afford 2-unsubstituted quinolines **13a** and **13c** in good yields (Scheme 6).[17] Similarly, the corresponding 2-methylthio-3-benzoyl-5,8-dimethoxyquinoline **1e** was subjected to oxidative demethylation in the presence of aqueous NBS/H_2SO_4[18a] to afford quinoline-5,8-quinone **14** in high yield (Scheme 6).[18]

The 2-methylthio group in one of the quinolines **2a** could be oxidized with *m*-chloroperbenzoic acid to afford the corresponding 2-(methylsulfonyl)quinoline **15a** in

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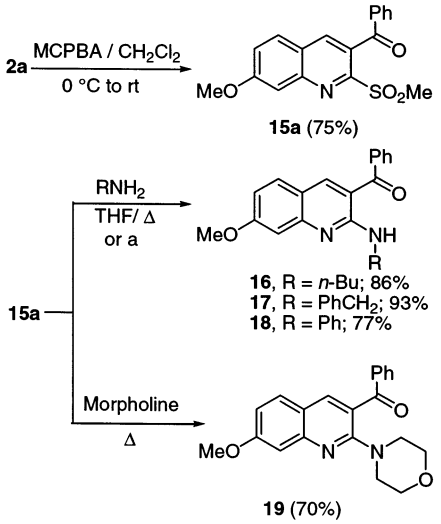
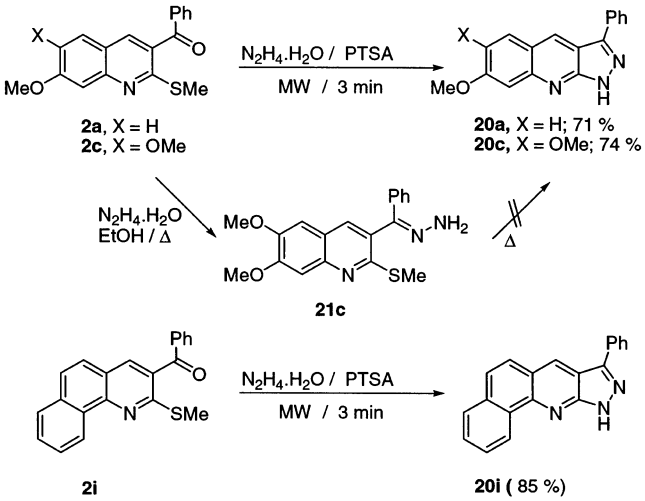
SCHEME 7[a]



[a] Key: (a) $PhNH_2$/MW.

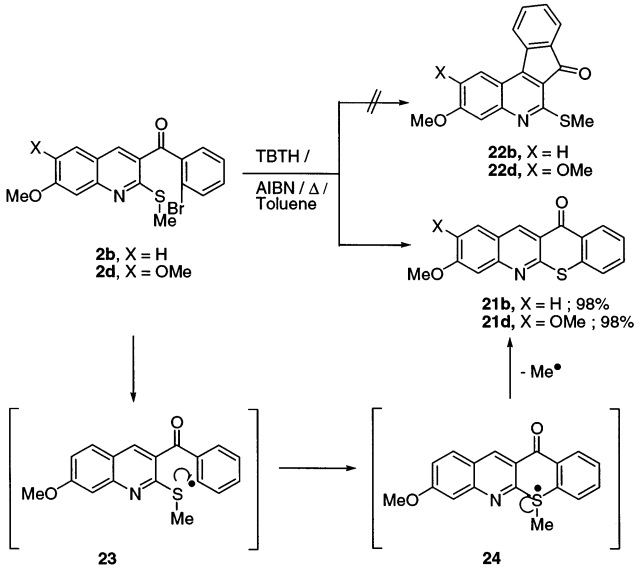
SCHEME 8



75% yield (Scheme 7). The 2-methylsulfonyl group in **15a** could be easily displaced[19] by primary and secondary amines under varying conditions to afford the corresponding 2-alkyl/arylaminoquinolines **16**−**19** in high yields (Scheme 7).

The quinolines **2a**, **2c**, and **2i** were next subjected to annulation reaction with hydrazine hydrate with a view to synthesize pyrazolo[3,4-*b*]quinolines **20a**, **20c**, and **20i** (Scheme 8), which are known to exhibit various biological activities such as antiviral, antimalarial, and lowering of serum choelsterol.[20] Recently, the 3-phenylpyrazolo-

SCHEME 9



[3,4-*b*]quinolin-4-one has been shown to display pH-dependent fluorescent properties for extreme pH measurement.[21] Thus, the reaction of **2c** with hydrazine hydrate afforded the hydrazone **21c** in nearly quantitative yield. The hydrazone **21c** failed to undergo cyclization to pyrazolo[3,4-*b*]quinoline **20c** even after prolonged refluxing which is presumably due to the adoption of the unfavorable *E*-configuration. However the pyrazoloquinolines **20a** and **20c** could be obtained directly from the corresponding quinolines **2a** and **2c** in high yields by reacting them with hydrazine hydrate under microwave irradiation conditions[20] (Scheme 8). Similarly, the synthesis of the corresponding tetracyclic 10*H*-benzo[*h*]-pyrazolo[3,4-*b*]quinoline **20i** could be achieved from benzo[*h*]quinoline precursor **2i** following a similar procedure (Scheme 8). Many of these pyrazolo-fused benzo-[*h*]quinolines are shown to bind with DNA inhibiting topoisomerase I activity.[9d] Finally, further scope of the functional group manipulation in these quinolines was demonstrated by performing radical cyclization on the 3-(*o*-bromobenzoyl)quinolines **2b** by treatment with Bu_3-SnH/AIBN (Scheme 9). The product formed in nearly quantitative yield was found to be not the tetracyclic quinoline **22b**, but was characterized as the novel benzothiopyrano[2,3-*b*]quinoline derivative **21b** on the basis of its spectral and analytical data (Scheme 9). Similarly, the 3-(*o*-bromobenzoyl)-6,7-dimethoxyquinoline **2d** afforded the tetracyclic benzothiopyrano fused quinoline **21d** in 98% yield (Scheme 9). The probable mechanistic pathway for the formation of **21b** and **21d** is shown in Scheme 9. The initially formed *o*-benzoyl radical **23** undergoes radical translocation[22] by attack on the methylthio group to give radical intermediate **24**, which on loss of the methyl radical affords the benzothiopyrano-quinolines **21b** and **21d** in excellent yields (Scheme 9).

Conclusion

In conclusion, we have developed a simple, highly efficient, and regioselective synthesis of functionalized

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quinolines through Vilsmeier cyclization of a variety of α-oxoketene *N,S*-anilinoacetals. Despite the fact that the cyclization is facile with the *N,S*-acetals bearing a strongly activating group (i.e., methoxy group) on aniline and the yields are only moderate in other cases, the reaction provides highly efficient access to multifunctionalized quinolines which are useful intermediates for further chemical manipulation for preparation of either 2-alkyl/arylaminoquinolines or quinoline-fused heterocycles such as pyrazolo[3,4-*b*]quinolines and benzothiopyrano[*b*]quinoline through ring annulation with hydrazine hydrate or via radical cyclization. In addition, the reaction can be extended to include condensed functionalized quinolines such as benzo[*h*]quinoline and pyrido[3,2-*h*]quinoline, phenanthroline, and quino[8,7-*h*]-quinoline with potential biological activities. A number of benzo[*h*]quinolines and azaphenanthridines are known to bind DNA with high affinity inhibiting topisomerase I activity.[9d] We are currently investigating the possibilities of achieving a more flexible substitution pattern on the quinoline ring, especially the synthesis of 3-cyano- or -carbethoxy-2-methylthioquinolines as precursors of quinoline-based models of NADH, which will be published later.

Experimental Section

General Methods. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded in $CDCl_3$ or DMSO-d_6, and TMS was used as an internal reference. Melting points are uncorrected. Chromatographic purification was conducted by column chromatography using 60−120 mesh silica gel obtained from Acme Synthetic Chemicals. DMF was distilled over CaH_2 and stored over molecular sieves. THF was distilled over sodium/benzophenone prior to use. Tetrachloroethane was distilled over P_2O_5. Toluene was distilled and stored over sodium wire. $POCl_3$, AIBN, TBTH, *n*-BuLi (15% in hexane), substituted anilines, and hydrazine hydrate (80% LR) were purchased from standard firms and used directly. The α-oxoketene-*S,N*-acetal **1h** was reported earlier[15] and prepared accordingly.

General Procedure for Preparation of α-Oxoketene-*N,S*-acetals 1a−l and Bisketene-*N,S*-acetals 5, 8, and 11. To a stirred solution of aniline or a substituted aniline (10 mmol) in dry THF (50 mL) was added *n*-BuLi (5.2 mL, 12 mmol) under nitrogen atmosphere over a period of 10 min at −78 °C. The reaction mixture was brought to room temperature and further stirred for 45 min. A solution of an α-oxoketene-*S,S*-acetal (10 mmol) in dry THF (25 mL) was added at 0 °C, and the reaction mixture was further stirred at room temperature for 2 h. It was refluxed for 18−20 h to complete the reaction, cooled, poured into saturated NH_4Cl solution (100 mL), and extracted with $CHCl_3$ (2 × 50 mL). The combined extracts were washed with water (2 × 50 mL) and brine (50 mL), dried (Na_2SO_4), and evaporated to give crude product which was purified by column chromatography over silica gel using hexanes−EtOAc as eluent.

The bisketene-*N,S*-acetals **5**, **8**, and **11** were also prepared following a similar procedure from the corresponding diamines (10 mmol), *n*-BuLi (10.4 mL, 24 mmol), and α-oxoketene-*S,S*-acetal (4.48 g, 20 mmol).

3-(3-Methoxyanilino)-3-methylthio-1-phenylprop-2-en-1-one (1a): yield 82% (2.45 g); light yellow crystals ($CHCl_3$−hexane); mp 75−76 °C; R_f 0.59 (9:1 hexanes−EtOAc); IR (KBr) 3002, 2925, 1564 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 (s, 3H, SCH_3), 3.77 (s, 3H, OCH_3), 5.86 (s, 1H, CH), 6.76 (ddd, J = 8.30, 2.44, 0.76 Hz, 1H, ArH), 6.85 (t, J = 2.2 Hz, 1H, ArH), 6.90 (ddd, J = 7.93, 1.94, 0.76 Hz, 1H, ArH), 7.24 (t, J = 8.04 Hz, 1H, ArH), 7.38−7.46 (m, 3H, ArH), 7.88 (dd, J = 7.8, 1.96 Hz, 2H, ArH), 13.52 (brs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.8, 55.3, 88.8, 110.4, 112.2, 117.2, 127.0, 128.3, 129.7, 130.9, 139.2, 140.1, 160.1, 167.3, 186.1.

3-(1-Aminonaphthyl)-3-methylthio-1-phenylprop-2-en-1-one (1i): yield 90% (2.87 g); light yellow solid ($CHCl_3$−hexane); mp 120−121 °C; R_f 0.55 (9:1 hexanes−EtOAc); IR (KBr) 1522, 1465, 1252 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 (s, 3H, SCH_3), 6.0 (brs, 1H, CH), 7.45−7.50 (m, 4H, ArH), 7.52−7.56 (m, 3H, ArH), 7.81 (d, J = 8.32 Hz, 1H, ArH), 7.88 (dd, J = 8.32, 1.96 Hz, 1H, ArH), 7.98 (dd, J = 7.82, 1.48 Hz, 2H, ArH), 8.14 (d, J = 7.56 Hz, 1H, ArH), 13.82 (brs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.7, 88.6, 122.7, 124.0, 125.0, 126.6, 126.9, 127.1, 127.6, 128.2, 128.3, 129.6, 130.9, 134.2, 134.3, 140.2, 169.3, 186.3.

4-(3-Methoxyanilino)-4-methylthio-3-buten-2-one (1j): yield 75% (1.77 g); red liquid; R_f 0.50 (3:1 hexanes−EtOAc); IR (DCM) 2955, 1591, 1469, 1269 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.14 (s, 3H, CH_3), 2.33 (s, 3H, SCH_3), 3.79 (s, 3H, OCH_3), 5.19 (s, 1H, CH), 6.77 (dd, J = 8.2, 2.8 Hz, 1H, ArH), 6.80 (s, 1H, ArH), 6.85 (d, J = 8.4 Hz, 1H, ArH), 7.22−7.26 (t, J = 8.0 1H, ArH), 12.95 (brs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.6, 29.2, 55.3, 91.6, 110.5, 112.0, 117.3, 129.6, 139.2, 160.0, 165.7, 193.0; MS *m/z* 237 (M^+, 22). Anal. Calcd for $C_{12}H_{15}NO_2S$ (237.33): C, 60.73; H, 6.37; N, 5.90. Found: C, 60.64, H, 6.44; N, 5.80.

1-Bis(methoxy)-4-(3-methoxyanilino)-4-(methylthio)-3-buten-2-one (1k): yield 75% (2.23 g); deep red viscous liquid; R_f 0.45 (8.5:1.5 hexanes−EtOAc); IR (DCM) 2952, 2839, 1554, 1477 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.29 (s, 3H, SCH_3), 3.36 (s, 6H, OCH_3), 3.70 (s, 3H, OCH_3), 4.57 (s, 1H, CH), 5.52 (s, 1H, CH), 6.70 (d, J = 8.00 Hz, 1H, ArH), 6.74 (s, 1H, ArH), 6.79 (d, J = 8.00 Hz, 1H, ArH), 7.17 (t, J = 8.40 Hz, 1H, ArH), 13.04 (brs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.4, 53.8, 55.0, 87.4, 103.5, 110.3, 112.1, 117.0, 129.5, 138.6, 159.8, 168.9, 187.7.

1,3-Bis[(2′-methylthio)-1′-benzoyl-2′-ethenyl]diaminobenzene (5): yield 75% (3.45 g); light yellow solid ($CHCl_3$−hexane); mp 164−165 °C; R_f 0.55 (7:3 hexanes−EtOAc); IR (KBr) 1556, 1470, 1268 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.89 (s, 6H, SCH_3), 5.78 (s, 2H, CH), 7.05 (d, J = 8.08 Hz, 2H, ArH), 7.14−7.32 (m, 8H, ArH), 7.79 (d, J = 7.32 Hz, 4H, ArH), 13.51 (brs, 2H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.6, 89.0, 120.8, 122.2, 126.9, 128.2, 129.5, 130.8, 138.8, 139.8, 166.9, 185.9; MS *m/z* 460 (M^+, 15). Anal. Calcd for $C_{26}H_{24}N_2O_2S_2$ (460.59): C, 67.79; H, 5.25; N, 6.08. Found: C, 67.91, H, 5.17; N, 6.14.

1,2-Bis[(2′-methylthio)-1′-benzoyl-2′-ethenyl]diaminobenzene (8): yield 68% (3.13 g); white solid ($CHCl_3$−hexane); mp 152−153 °C; R_f 0.50 (4:1 hexanes−EtOAc); IR (KBr) 2925, 1552, 1463 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 6H, SCH_3), 5.81 (s, 2H, CH), 7.34 (t, J = 7.04 Hz, 6H, ArH), 7.40 (d, J = 7.36 Hz, 2H, ArH), 7.42−7.46 (m, 2H, ArH), 7.76 (d, J = 7.08 Hz, 4H, ArH), 13.00 (brs, 2H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.7, 89.7, 127.1, 127.8, 128.2, 128.4, 130.7, 135.4, 140.1, 168.5, 186.4; MS *m/z* 460 (M^+, 20). Anal. Calcd for $C_{26}H_{24}N_2O_2S_2$ (460.59): C, 67.79; H, 5.25; N, 6.08. Found: C, 67.72, H, 5.14; N, 6.27.

1,5-Bis[(2′-methylthio)-1′-benzoyl-2′-ethenyl]diaminonaphthalene (11): yield 85% (4.34 g); light yellow solid ($CHCl_3$−hexane); mp 206−207 °C; R_f 0.45 (7:3 hexanes−EtOAc); IR (KBr) 2922, 1552, 1465 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.36 (s, 6H, SCH_3), 5.99 (s, 2H, CH), 7.46 (d, J = 6.6 Hz, 6H, ArH), 7.51−7.59 (m, 4H, ArH), 7.95 (d, J = 6.56 Hz, 4H, ArH), 8.09 (d, J = 8.04 Hz, 2H, ArH), 13.84 (brs, 2H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.8, 88.9, 122.4, 124.8, 126.1, 127.2, 128.4, 130.6, 131.0, 134.8, 140.1, 169.1, 186.5.

General Procedure for Vilsmeier Cyclization of *N,S*-Acetals: Synthesis of Substituted Quinolines 2a−i, 3a−c,i, and 2k,l. A solution of α-oxoketene-*N,S*-acetal (**1a−e**,**i**,**k**,**l**) (5 mmol) in DMF or DMA (5 mL) or in $Cl_2CHCHCl_2$ (5 mL) was added dropwise at 0 °C to a solution of Vilsmeier reagent [prepared from $POCl_3$ (0.7 mL, 7.5 mmol) and DMF or DMA (7.5 mmol) at 0−5 °C] under nitrogen atmosphere. After

further stirring for 5−6 h at room temperature, the reaction mixture was heated to 80−90 °C for 3−4 h (monitored by TLC). It was then cooled, poured into ice cold saturated $NaHCO_3$ solution (100 mL), and extracted with chloroform (4 × 50 mL). The combined organic extracts were washed with water (3 × 50 mL) and brine (1 × 25 mL) and dried (Na_2SO_4), and the solvent was evaporated under reduced pressure to afford crude quinoline which was purified by column chromatography over silica gel using hexanes−EtOAc as eluent. The quinolines **2a**−**d** crystallize out directly after workup without any column chromatographic purification.

3-Benzoyl-7-methoxy-2-methylthioquinoline (2a): yield 81% (1.25 g); light yellow solid ($CHCl_3$−hexane); mp 105−106 °C; R_f 0.60 (9:1 hexanes−EtOAc); IR (KBr) 3904, 3000, 1618, 1500 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.70 (s, 3H, SCH_3), 4.00(s, 3H, OCH_3), 7.12 (d, J = 8.8 Hz, 1H, ArH), 7.41 (s, 1H, ArH), 7.49 (t, J = 8.04 Hz, 2H, ArH), 7.61 (d, J = 8.8 Hz, 2H, ArH), 7.81 (d, J = 7.56 Hz, 2H, ArH), 8.03 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 55.7, 106.4, 118.8, 119.0, 127.8, 128.5, 129.6, 130.1, 133.1, 137.6, 138.4, 150.2, 159.8, 162.8, 195.2; MS m/z 309 (M^+, 18). Anal. Calcd for $C_{18}H_{15}NO_2S$ (309.37): C, 69.88; H, 4.89; N, 4.53. Found: C, 69.85, H, 4.91; N, 4.55.

3-(2-Bromobenzoyl)-7-methoxy-2-methylthioquinoline (2b): yield 95% (1.84 g); light yellow solid ($CHCl_3$−hexane); mp 133−134 °C; R_f 0.45 (8.5:1.5 hexanes−EtOAc); IR (KBr) 2909, 1658, 1614, 1404 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.73 (s, 3H, SCH_3), 3.97 (s, 3H, OCH_3), 7.06 (dd, J = 8.8, 2.44 Hz, 1H, ArH), 7.35−7.45 (m, 4H, ArH), 7.54 (d, J = 8.8 Hz, 1H, ArH), 7.64 (d, J = 7.8 Hz, 1H, ArH), 7.96 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 55.8, 106.1, 118.8, 119.2, 119.9, 125.5, 127.4, 129.4, 130.2, 131.5, 133.3, 140.5, 142.3, 150.5, 161.5, 163.9, 194.5; MS m/z 388 (M^+, 3.47). Anal. Calcd for $C_{18}H_{14}NO_2SBr$ (388.27): C, 55.68; H, 3.63; N, 3.61. Found: C, 55.56, H, 3.72; N, 3.75.

2-Benzoyl-6,7-dimethoxy-2-methylthioquinoline (2c): yield 98% (1.66 g); pale yellow solid ($CHCl_3$−hexane); mp 154−155 °C; R_f 0.60 (8.5:1.5 hexanes−EtOAc); IR (KBr) 2922, 1646, 1500, 1419 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.67 (s, 3H, SCH_3), 3.98 (s, 3H, OCH_3), 4.08 (s, 3H, OCH_3), 6.98 (s, 1H, ArH), 7.39 (s, 1H, ArH), 7.50 (t, J = 7.20 Hz, 2H, ArH), 7.62 (t, J = 7.60 Hz, 1H, ArH), 7.82 (d, J = 7.60 Hz, 2H, ArH), 7.98 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 56.1, 56.3, 105.9, 107.1, 119.0, 128.2, 128.5, 130.1, 133.0, 137.0, 137.7, 146.0, 149.3, 154.2, 156.9, 195.4; MS m/z 339 (M^+, 38). Anal. Calcd for $C_{19}H_{17}NO_3S$ (339.40): C, 67.23; H, 5.05; N, 4.13. Found: C, 67.20, H, 5.07; N, 4.15.

3-(2-Bromobenzoyl)-6,7-dimethoxy-2-methylthioquinoline (2d): yield 95% (1.98 g); yellow solid ($CHCl_3$−hexane); mp 149−150 °C; R_f 0.58 (8.5:1.5 hexanes−EtOAc); IR (KBr) 1661, 1585, 1502, 1427 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.67 (s, 3H, SCH_3), 3.92 (s, 3H, OCH_3), 4.05 (s, 3H, OCH_3), 6.89 (s, 1H, ArH), 7.31 (s, 1H, ArH), 7.34−7.43 (m, 3H, ArH), 7.65 (dd, J = 7.18, 1.24 Hz, 1H, ArH), 7.89 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 56.1, 56.4, 106.1, 107.1, 118.9, 119.9, 125.7, 127.4, 129.3, 131.3, 133.3, 140.7, 140.9, 146.7, 149.3, 155.2, 158.7, 194.7; MS m/z 418 (M^+, 95). Anal. Calcd for $C_{19}H_{16}NO_3SBr$ (418.30): C, 54.55; H, 3.86; N, 3.35. Found: C, 54.62, H, 3.75; N, 3.40.

2-Benzoyl-5,8-dimethoxy-2-methylthioquinoline (2e): yield 90% (1.53 g); yellow solid ($CHCl_3$−hexane); mp 139−140 °C; R_f 0.54 (8.5:1.5 hexanes−EtOAc); IR (KBr) 2923, 1656, 1569, 1470 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.71 (s, 3H, SCH_3), 3.87 (s, 3H, OCH_3), 4.03 (s, 3H, OCH_3), 6.68 (d, J = 8.32 Hz, 1H, ArH), 7.05 (d, J = 8.52 Hz, 1H, ArH), 7.46 (t, J = 7.84 Hz, 2H, ArH), 7.60 (dt, J = 7.08, 0.48 Hz, 1H, ArH), 7.81 (dd, J = 7.90, 1.48 Hz, 2H, ArH), 8.45 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7, 55.7, 57.0, 103.4, 111.6, 117.2, 128.5, 129.9, 130.2, 132.9, 133.3, 137.2, 140.4, 148.4, 149.7, 158.5, 195.3; MS m/z 339 (M^+, 76). Anal. Calcd for $C_{19}H_{17}NO_3S$ (339.40): C, 67.23; H, 5.05; N, 4.13. Found: C, 67.30, H, 5.00; N, 4.09.

3-Benzoyl-7-fluoro-2-methylthioquinoline (2fa): yield 30% (0.45 g); low-melting yellow solid; R_f 0.48 (9.5:0.5 hexanes−EtOAc); IR (DCM) 1661, 1622, 1560, 1492 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.67 (s, 3H, SCH_3), 7.26 (s, 1H, ArH), 7.51 (dt, J = 7.2, 1.68 Hz, 2H, ArH), 7.62−7.68 (m, 2H, ArH), 7.74 (q, J = 8.92, 6.12 Hz, 1H, ArH), 7.83 (dd, J = 7.48, 1.0 Hz, 2H, ArH), 8.05 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 112.1, 116.2, 120.9, 128.6, 130.1, 130.5, 133.5, 137.1, 137.4, 160.4, 165.8, 180.2, 184.5, 195.0; MS m/z 297 (M^+, 28). Anal. Calcd for $C_{17}H_{12}FNOS$ (297.34): C, 68.67; H, 4.07; N, 4.71. Found: C, 68.81, H, 3.89; N, 4.50.

3-Benzoyl-2-methylthio-5-fluoroquinoline (2fb): yield 10% (0.15 g); low-melting yellow solid; R_f 0.40 (9.5:0.5 hexanes−EtOAc); IR (DCM) 1674, 1624, 1562, 1488 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.44 (s, 3H, SCH_3), 7.39 (dt, J = 8.76, 2.44 Hz, 2H, ArH), 7.45−7.49 (m, 2H, ArH), 7.67−7.69 (m, 2H, ArH), 7.81 (dd, J = 10.0, 2.44 Hz, 1H, ArH), 7.91 (q, J = 8.9, 6.12 Hz, 1H, ArH), 8.48 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.7, 113.3 (J_{F-C} = 20.5 Hz), 118 (J_{F-C} = 25.5 Hz), 122.6, 128.3, 129.0, 129.3, 130.4, 131.9, 136.8, 139.1, 149.5, 157.5, 163.1, 194.0; MS m/z 297 (M^+, 8). Anal. Calcd for $C_{17}H_{12}FNOS$ (297.34): C, 68.67; H, 4.07; N, 4.71. Found: C, 68.45, H, 4.13; N, 4.85.

3-Benzoyl-2-methylthioquinoline (2g): yield 25% (0.42 g); low-melting yellow solid; R_f 0.50 (9.5:0.5 hexanes−EtOAc); IR (DCM) 2928, 1660, 1586 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.72 (s, 3H, SCH_3), 7.48−7.53 (m, 3H, ArH), 7.64 (t, J = 7.56 Hz, 1H, ArH), 7.75 (d, J = 7.32 Hz, 2H, ArH), 7.85 (dd, J = 7.82, 1.48 Hz, 2H, ArH), 8.08 (s, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7, 123.1, 124.1, 126.0, 128.0, 128.4, 128.6, 128.8, 130.2, 131.5, 133.5, 137.2, 137.5, 148.5, 176.4; MS m/z 279 (M^+, 30). Anal. Calcd for $C_{17}H_{13}NOS$ (279.34): C, 73.09; H, 4.69; N, 5.01. Found: C, 73.06, H, 4.70; N, 5.04.

3-Benzoyl-2,6-dichloroquinoline (2h): yield 30% (0.45 g); white solid ($CHCl_3$−hexane); mp 168−169 °C; R_f 0.45 (7:3 hexanes−EtOAc); IR (KBr) 1665, 1591, 1539 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.53−7.55 (m, 3H, ArH), 7.60−7.62 (m, 2H, ArH), 7.83 (dd, J = 9.0, 2.44 Hz, 1H, ArH), 8.15 (d, J = 9.0 Hz, 1H, ArH), 8.43 (dd, J = 8.44, 2.2 Hz, 1H, ArH), 10.23 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 124.2, 126.1, 126.6, 128.8, 129.9, 130.0, 131.3, 133.8, 134.8, 137.2, 143.5, 146.8, 159.6, 189.8; MS m/z 301 (M^+, 83), 303 (M^+, 65). Anal. Calcd for $C_{16}H_9NOCl_2$ (301.23): C, 63.79; H, 3.01; N, 4.64. Found: C, 63.45; H, 3.10; N, 4.73.

3-Benzoyl-2-methylthiobenzo[*h*]quinoline (2i): yield 95% (1.56 g); yellow solid ($CHCl_3$−hexane); mp 144−145 °C; R_f 0.54 (9.5:0.5 hexanes−EtOAc); IR (KBr) 1653, 1582, 1498, 1366 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.81 (s, 3H, SCH_3), 7.48 (t, J = 7.68 Hz, 2H, ArH), 7.55 (d, J = 8.76 Hz, 1H, ArH), 7.61 (t, J = 7.44 Hz, 1H, ArH), 7.67−7.73 (m, 3H, ArH), 7.82−7.87 (m, 3H, ArH), 8.09 (s, 1H, ArH), 9.25 (dd, J = 8.30, 2.44 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 121.5, 124.9, 125.0, 126.9, 127.1, 127.8, 128.6, 128.9, 130.0, 130.1, 130.5, 133.2, 134.7, 137.4, 137.9, 146.7, 158.3, 195.4; MS m/z 329 (M^+, 26). Anal. Calcd for $C_{21}H_{15}NOS$ (329.40): C, 76.57; H, 4.59; N, 4.25. Found: C, 76.75, H, 4.47; N, 4.32.

3-[1-Bis(methoxy)acetyl]-7-methoxy-2-methylthioquinoline (2k): yield 51% (0.78 g); yellow solid ($CHCl_3$−hexane); mp 122−123 °C; R_f 0.80 (9.6:0.4 hexanes−EtOAc); IR (KBr) 1612, 1486, 1345, 1217 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.79 (s, 3H, SCH_3), 3.61(s, 6H, OCH_3), 4.97 (s, 3H, OCH_3), 5.69 (s, 1H, CH), 7.12 (dd, J = 8.76, 2.44 Hz, 1H, ArH), 7.34 (s, 1H, ArH), 7.69 (d, J = 9.04 Hz, 1H, ArH), 8.59 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.4, 55.6, 59.0, 91.2, 105.5, 106.8, 119.0, 119.3, 128.2, 129.7, 136.4, 148.3, 157.4, 162.2; MS m/z 307 (M^+, 40). Anal. Calcd for $C_{15}H_{17}NO_4S$ (307.38): C, 58.61; H, 5.57; N, 4.56. Found: C, 58.80, H, 5.45; N, 4.44.

3-[1-(Bismethoxy)acetyl]-6,7-dimethoxy-2-methylthioquinoline (2l): yield 54% (0.91 g); yellow solid ($CHCl_3$−hexane); mp 87−88 °C; R_f 0.60 (9:1 hexanes−EtOAc); IR (KBr) 2924, 1687, 1500 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.56 (s, 3H, SCH_3), 3.45 (s, 6H, OCH_3), 3.95 (s, 3H, OCH_3), 4.01 (s,

3H, OCH_3), 5.04 (s, 1H, CH), 7.03 (s, 1H, ArH), 7.19 (s, 1H, ArH), 8.80 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 55.4, 55.5, 56.1, 56.4, 106.0, 106.4, 106.9, 118.7, 122.6, 139.6, 146.1, 149.2, 155.0, 159.0; MS *m*/*z* 337 (M^+, 14). Anal. Calcd for $C_{16}H_{19}NO_5S$ (337.48): C, 56.94; H, 5.67; N, 4.15. Found: C, 56.75, H, 5.77; N, 4.20.

3-Benzoyl-7-methoxy-4-methyl-2-methylthioquinoline (3a): yield 80% (1.29 g); white solid ($CHCl_3$−hexane); mp 194−195 °C; R_f 0.55 (9.5:0.5 hexanes−EtOAc); IR(KBr) 2925, 1667, 1573, 1498, 1404 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.39 (s, 3H, SCH_3), 2.63 (s, 3H, CH_3), 3.97 (s, 3H, OCH_3), 7.14 (dd, J = 9.0, 2.0 Hz, 1H, ArH), 7.35 (d, J = 2.8 Hz, 1H, ArH), 7.45 (t, J = 7.6 Hz, 2H, ArH), 7.60 (d, J = 7.2 Hz, 1H, ArH), 7.82 (d, J = 9.2 Hz, 1H, ArH), 7.86 (d, J = 7.6 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.3, 15.6, 55.5, 107.2, 118.1, 120.0, 125.1, 128.9, 129.6, 130.0, 134.1, 136.8, 140.2, 149.4, 156.1, 161.1, 197.2; MS *m*/*z* 323 (M^+, 42). Anal. Calcd for $C_{19}H_{17}NO_2S$ (323.40): C, 70.56; H, 5.30; N, 4.33. Found: C, 70.36, H, 5.45; N, 4.50.

3-(2-Bromobenzoyl)-7-methoxy-4-methyl-2-methylthioquinoline (3b): yield 95% (1.90 g); white solid ($CHCl_3$−hexane); mp 165−166 °C; R_f 0.70 (9:1 hexanes−EtOAc); IR (KBr) 2925, 1667, 1573, 1498, 1404 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.47 (s, 3H, SCH_3), 2.67 (s, 3H, CH_3), 3.98 (s, 3H, OCH_3), 7.15 (dd, J = 9.28, 2.68 Hz, 1H, ArH), 7.32−7.39 (m, 2H, ArH), 7.45 (s, 1H, ArH), 7.59 (dd, J = 7.44, 2.2 Hz, 1H, ArH), 7.72 (dd, J = 7.68, 1.48 Hz, 1H, ArH), 7.86 (d, J = 9.28 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 15.7, 55.6, 106.8, 118.5, 120.1, 122.0, 125.5, 127.5, 130.5, 132.6, 133.5, 135.2, 138.1, 142.2, 149.1, 156.6, 161.6, 195.8; MS *m*/*z* 402 (M^+, 3). Anal. Calcd for $C_{19}H_{16}NO_2SBr$ (402.30): C, 56.72; H, 4.01; N, 3.48. Found: C, 56.56, H, 4.14; N, 3.54.

3-Benzoyl-6,7-dimethoxy-4-methyl-2-methylthioquinoline (3c): yield 98% (1.73 g); light brown solid ($CHCl_3$−hexane); mp 200−201 °C; R_f 0.60 (8.5:1.5 hexanes−EtOAc); IR (KBr) 2926, 1666, 1571, 1507, 1428 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.40 (s, 3H, SCH_3), 2.65 (s, 3H, CH_3), 4.02 (s, 3H, OCH_3), 4.08 (s, 3H, OCH_3), 7.14 (s, 1H, ArH), 7.49 (t, J = 7.8 Hz, 3H, ArH), 7.62 (t, J = 7.56 Hz, 1H, ArH), 7.86 (dt, J = 7.68, 1.2 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.5, 15.8, 56.0, 56.1, 102.1, 107.7, 120.2, 128.9, 129.6, 130.4, 134.1, 136.8, 139.0, 144.7, 149.0, 152.6, 153.0, 197.3; MS *m*/*z* 353 (M^+, 55). Anal. Calcd for $C_{20}H_{19}NO_3S$ (353.42): C, 67.96; H, 5.42; N, 3.96. Found: C, 67.74, H, 5.65; N, 3.80.

3-Benzoyl-4-methyl-2-methylthiobenzo[*h*]quinoline (3i): yield 93% (1.59 g); light brown solid ($CHCl_3$−hexane); mp 170−171 °C; R_f 0.60 (9.5:0.5 hexanes−EtOAc); IR (KBr) 2920, 1659, 1572, 1443 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.51 (s, 3H, CH_3), 2.80 (s, 3H, SCH_3), 7.48 (t, J = 7.80 Hz, 2H, ArH), 7.63 (t, J = 7.32 Hz, 1H, ArH), 7.70−7.74 (m, 2H, ArH), 7.82 (d, J = 9.04 Hz, 1H, ArH), 7.87−7.93 (m, 4H, ArH), 9.32 (dd, J = 8.42, 2.2 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.6, 16.0, 121.0, 122.4, 124.8, 126.5, 126.9, 127.6, 128.3, 128.9, 129.6, 131.0, 132.3, 133.8, 134.2, 136.6, 140.5, 145.5, 154.4, 197.2; MS *m*/*z* 343 (M^+, 66.7). Anal. Calcd for $C_{22}H_{17}NOS$ (343.43): C, 76.94; H, 4.99; N, 4.08. Found: C, 76.72, H, 5.12; N, 4.15.

General Procedure for Vilsmeier Cyclization of Bisketene-*N*,*S*-acetals 5, 8, and 11: Synthesis of Condensed Quinolines 7, 10, and 12. The bisquinolines **7** and **12** were prepared following a similar procedure for quinolines **2** by adding 2.5 mmol of *N*,*S*-acetal in DMF (5 mL) to Vilsmeier reagent prepared from DMF (0.48 mL, 6.25 mmol) and $POCl_3$ (0.58 mL, 6.25 mmol).

3,9-Dibenzoyl-2,8-(bismethylthio)pyrido[2,3-*h*]quinoline (7): yield 48% (0.57 g); bright yellow solid ($CHCl_3$−hexane); mp 186−187 °C; R_f 0.77 (4:1 hexanes−EtOAc); IR (KBr) 2918, 1651, 1598, 1446 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.53 (s, 3H, SCH_3), 2.72 (s, 3H, SCH_3), 7.51 (q, J = 14.64, 7.32 Hz, 4H, ArH), 7.62−7.66 (m, 2H, ArH), 7.83 (d, J = 7.32 Hz, 2H, ArH), 7.89−7.94 (m, 4H, ArH), 8.13 (s, 1H, ArH), 9.42 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 13.9, 120.9, 121.1, 127.0, 128.5, 128.6, 130.0, 130.1, 130.2, 130.4, 131.0, 133.2, 133.4, 135.1, 137.0, 137.2, 137.7, 146.1, 150.5, 160.1, 162.1, 194.9, 195.2; MS *m*/*z* 481 (M + 1, 42). Anal. Calcd for $C_{28}H_{20}N_2O_2S_2$ (480.58): C, 69.98; H, 4.19; N, 5.83. Found: C, 69.71, H, 4.32; N, 5.65.

2,8-Bis(benzoyl)-3,9-bis(methylthio)quino[8,7-*h*]quinoline (12): yield 60% (0.79 g); yellow solid ($CHCl_3$−hexane); mp 325−326 °C; R_f 0.65 (9:1 hexanes−EtOAc); IR (KBr) 2924, 1656, 1265 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.81 (s, 6H, SCH_3), 7.48 (t, J = 7.56 Hz, 4H, ArH), 7.61 (t, J = 7.08 Hz, 2H, ArH), 7.84 (d, J = 7.56 Hz, 4H, ArH), 7.88 (d, J = 8.56 Hz, 2H, ArH), 8.20 (s, 2H, ArH), 9.26 (d, J = 8.8 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.0, 122.5, 124.3, 124.8, 124.9, 126.1, 127.2, 128.4, 128.41, 130.5, 131.1, 134.7, 140.0, 186.5; MS *m*/*z* 531 (M^+, 100). Anal. Calcd for $C_{32}H_{22}N_2O_2S_2$ (530.64): C, 72.43; H, 4.18; N, 5.28. Found: C, 72.33, H, 4.09; N, 5.48.

Procedure for Vilsmeier Cyclization of Bisketene-*N*,*S*-acetal 8 to Phenanthroline 10A. The phenanthroline **10A** was obtained by adding a solution of bisketene-*N*,*S*-acetal **8** (1.15 g, 2.5 mmol) in $Cl_2CHCHCl_2$ (5 mL) to Vilsmeier reagent prepared from $POCl_3$ (0.58 mL, 6.25 mmol) and DMA (0.58 mL, 6.25 mmol) and heating the reaction mixture at 120−130 °C for 7−8 h. Workup and column chromatographic purification of the reaction mixture as described earlier yielded the phenanthroline **10A**.

4,7-Diphenyl-9-hydroxy-2-methylthiopyrido[3,2-*h*]quinoline (10A): yield 60% (0.59 g); reddish orange solid ($CHCl_3$−hexane); mp 215−216 °C; R_f 0.45 (9:1 hexanes−EtOAc); IR (KBr) 2921, 1637, 1452 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33 (s, 3H, SCH_3), 6.94 (brs, 1H, OH), 7.14 (dt, J = 7.2, 2.2 Hz, 2H, ArH), 7.23−7.29 (m, 1H, ArH), 7.44−7.49 (m, 5H, ArH), 7.52−7.56 (m, 2H, ArH), 7.65−7.67 (m, 2H, ArH), 7.79−7.82 (m, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.8, 109.2, 117.6, 125.2, 125.9, 126.1, 128.6, 128.9, 129.3, 129.4, 129.9, 130.8, 131.2, 131.8, 132.4, 140.3, 141.7, 157.7, 159.4, 159.9, 160.8; MS *m*/*z* 395 (M + 1, 100). Anal. Calcd for $C_{25}H_{18}N_2OS$ (394): C, 69.98; H, 4.19; N, 5.83. Found: C, 69.71, H, 4.32; N, 5.65.

Procedure for $POCl_3$Cyclization of Bisketene-*N*,*S*-acetal 8 to Phenanthroline 10B. The phenanthroline **10B** was obtained by heating bisketene-*N*,*S*-acetal **8** (0.51 g, 1 mmol) with $POCl_3$ (0.55 mL, 6 mmol) at 70 °C for 3 h. Workup and column chromatographic purification of the reaction mixture as described earlier yielded the phenanthroline **10B**.

4,7-Diphenyl-9-chloro-2-methylthiopyrido[3,2-*h*]quinoline (10B): yield 54% (0.22 g); red crystals ($CHCl_3$−hexane); mp 205−206 °C; R_f 0.75 (1:5 hexanes−EtOAc); IR (KBr) 3057, 1637, 1362, 763 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.32 (s, 3H, SCH_3), 7.09−7.17 (m, 2H, ArH), 7.25 (t, J = 6.8 Hz, 2H, ArH), 7.44−7.48 (m, 5H, ArH), 7.54 (t, J = 7.3 Hz, 1H, ArH), 7.64 (d, J = 7.8 Hz, 2H, ArH), 7.81 (dd, J = 6.8, 2.9 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9, 108.7, 117.2, 125.3, 126.1, 128.7, 128.9, 129.3, 129.5, 129.9, 130.9, 131.0, 132.0, 132.2, 139.6, 141.5, 158.4, 159.4, 159.9, 160.4, 160.9.

General Procedure for Reductive Dethiomethylation of 2a,b Using Raney-Ni. To a solution of **2a** or **2b** (1.3 mmol) in ethanol (25 mL) was added Raney-Ni (W2 or W5, 5 times by weight), and the suspension was refluxed with stirring for 2−3 h (monitored by TLC). The reaction mixture was then cooled and filtered through a sintered funnel, and the residue was washed with ethanol. The filtrate was evaporated under vacuum to give crude products that were purified by column chromatography using hexanes−EtOAc (4:1) as eluent.

3-Benzoyl-7-methoxyquinoline (13a): yield 70% (0.24 g); light brown solid ($CHCl_3$−hexane); mp 79−80 °C; R_f 0.50 (3:2 hexanes−EtOAc); IR (KBr) 3058, 1653, 1614, 1485 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.99 (s, 3H, OCH_3), 7.28 (dd, J = 9.04, 2.44 Hz, 1H, ArH), 7.50−7.55 (m, 3H, ArH), 7.63 (t, J = 8.32 Hz, 1H, ArH), 7.79−7.84 (m, 3H, ArH), 8.54 (s, 1H, ArH), 9.23 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.9, 106.7, 121.4, 122.0, 128.1, 128.6, 129.9, 130.3, 132.9, 133.0, 137.1, 139.2, 150.2, 163.2, 194.5; MS *m*/*z* 263 (M^+, 100). Anal. Calcd

for $C_{17}H_{13}NO_2$ (263.27): C, 77.55; H, 4.98; N, 5.32. Found: C, 77.45, H, 4.72; N, 5.50.

3-Benzoyl-6,7-dimethoxyquinoline (13c): yield 75% (0.28 g); yellow solid ($CHCl_3$−hexane); mp 142−143 °C; R_f 0.45 (4:1 hexanes−EtOAc); IR (KBr) 2935, 1643, 1500, 1254 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.00 (s, 3H, OCH_3),4.07 (s, 3H, OCH_3), 7.12 (s, 1H, ArH), 7.51 (t, J = 7.56 Hz, 2H, ArH), 7.60−7.64 (m, 2H, ArH), 7.80 (m, 2H, ArH), 8.48 (d, J = 1.97 Hz, 1H, ArH), 9.08 (d, J = 1.92 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.2, 56.5, 106.0, 106.9, 122.7, 128.6, 129.9, 132.9, 137.2, 137.6, 145.9, 147.4, 150.9, 155.0, 175.6, 194.5; MS m/z 293 (M^+, 60). Anal. Calcd for $C_{18}H_{15}NO_3$ (293.31): C, 73.70; H, 5.15; N, 4.78. Found: C, 73.57, H, 5.22; N, 4.84.

Procedure for Oxidation of Quinoline 2e to Quinone 14 with NBS/H_2SO_4. A suspension of **2e** (0.34 g, 1.0 mmol), NBS (0.19 g, 1.1 mmol) in THF (10 mL), water (3 mL), and sulfuric acid (0.05 mL) at room temperature was rigorously stirred for 10 min followed by basification with aqueous $NaHCO_3$ solution (10 mL). The reaction mixture was extracted with $CHCl_3$ (3 × 20 mL), washed with water (2 × 25 mL), dried (Na_2SO4), and evaporated under vacuum to give crude product **14**, which was purified by column chromatography over silica gel using hexanes−EtOAc (20:1) as eluent.

3-Benzoyl-2-methylthioquinoline-5,8-quinone (14): yield 70% (0.22 g); yellow solid ($CHCl_3$−hexane); mp 79−80 °C; R_f 0.55 (4:1 hexanes−EtOAc); IR (KBr) 1668, 1577, 1252 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.72 (s, 3H, SCH_3), 7.02 (d, J = 10.48 Hz, 1H, ArH), 7.10 (d, J = 10.52 Hz, 1H, ArH), 7.49 (t, J = 8.08 Hz, 2H, ArH), 7.65 (t, J = 7.56 Hz, 1H, ArH), 7.76 (d, J = 7.68 Hz, 2H, ArH), 8.20 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 124.1, 129.0, 130.0, 134.1, 134.3, 135.1, 135.9, 138.0, 138.6, 146.6, 167.2, 182.5, 184.0, 193.7; MS m/z 309 (M^+, 52.7). Anal. Calcd for $C_{17}H_{11}NO_3S$ (309.33): C, 66.00; H, 3.58; N, 4.53. Found: C, 66.15; H, 3.42; N, 4.64.

Procedure for *m*-CPBA Oxidation of 2-Methylthioquinoline 2a to 2-Methylsulfonylquinoline 15a. To a stirred solution of **2a** (0.92 g, 3 mmol) in dry CH_2Cl_2 (25 mL) was added dropwise a solution of *m*-CPBA (1.14 g, 6.6 mmol) in CH_2Cl_2 (25 mL) over a period of 30 min. The mixture was further stirred at room temperature for 3 h, washed with 10% $NaHCO_3$ solution (2 × 50 mL) and brine (50 mL), dried (Na_2SO_4), and evaporated under vacuum to afford crude product which was purified by column chromatography over silica gel using hexanes−EtOAc as eluent.

3-Benzoyl-7-methoxy-2-methylsulfonylquinoline (15a): yield 75% (0.76 g); colorless solid ($CHCl_3$−hexane); mp 154−155 °C; R_f 0.81 (1:4 hexanes−EtOAc); IR (KBr) 3021, 1665, 1618, 1478, 1307 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.34 (s, 3H, SO_2CH_3), 3.97(s, 3H, OCH_3), 7.37 (dd, J = 9.04, 2.44 Hz, 1H, ArH), 7.44 (t, J = 7.6 Hz, 2H, ArH), 7.57 (dt, J = 7.81, 0.72 Hz, 2H, ArH), 7.76 (d, J = 9.04 Hz, 1H, ArH), 7.83 (d, J = 7.32 Hz, 2H, ArH), 8.16 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 42.4, 55.9, 107.7, 122.9, 124.0, 128.6, 128.9, 129.1, 130.2, 133.9, 136.5, 137.3, 148.7, 155.0, 162.8, 193.7; MS m/z 342 (M + 1, 100). Anal. Calcd for $C_{18}H_{15}NO_4S$ (341.37): C, 63.33; H, 4.43; N, 4.10. Found: C, 63.45, H, 4.36; N, 4.21.

Procedure for Synthesis of 2-Aminoquinolines 16 and 17 from 2-Methylsulfonylquinoline 15a. A solution of 2-methylsulfonylquinoline **15a** (0.34 g, 1 mmol) and *n*-butylamine or benzylamine (5 mmol) was refluxed for 8−11 h (monitored by TLC) in dry THF (25 mL). It was then cooled and evaporated under reduced pressure to afford the product **16** or **17**, which was purified by column chromatography over silica gel using hexanes−EtOAc as eluent.

3-Benzoyl-2-butylamino-7-methoxyquinoline (16): yield 86% (0.28 g); yellow solid ($CHCl_3$−hexane); mp 98−99 °C; R_f 0.95 (3:1 hexanes−EtOAc); IR (KBr) 2926, 1608, 1533, 1397 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.99(t, J = 7.32 Hz, 3H, CH_3), 1.48−1.53 (m, 2H, CH_2), 1.68−1.74 (m, 2H, CH_2), 3.70 (d, J = 5.12 Hz, 2H, N−CH_2), 3.92 (s, 3H, OCH_3), 6.78 (dd, J = 8.8, 2.2 Hz, 1H, ArH), 7.12 (brs, 1H, ArH), 7.36 (d, J = 8.76 Hz, 1H, ArH), 7.48 (t, J = 7.32 Hz, 2H, ArH), 7.57 (t, J = 7.32 Hz, 1H, ArH), 7.63 (d, J = 7.32 Hz, 2H, ArH), 8.09 (s, 1H, ArH), 8.51 (brs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 20.4, 31.4, 41.0, 55.6, 104.5, 113.9, 115.2, 115.7, 128.4, 129.2, 130.6, 131.6, 139.4, 145.6, 148.5, 155.4, 164.2, 198.0; MS m/z 335 (M + 1, 100). Anal. Calcd for $C_{21}H_{22}N_2O_2$ (334.41): C, 75.42; H, 6.63; N, 8.38. Found: C, 75.25, H, 6.74; N, 8.44.

3-Benzoyl-2-benzylamino-7-methoxyquinoline (17): yield 93% (0.34 g); yellow solid ($CHCl_3$−hexane); mp 109−110 °C; R_f 0.85 (8.5:1.5 hexanes−EtOAc); IR (KBr) 1592, 1538, 1401 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.94 (s, 3H, OCH_3), 4.96 (brs, 2H, N−CH_2), 6.83 (d, J = 8.76 Hz, 1H, ArH), 7.27 (d, J = 7.32 Hz, 1H, ArH), 7.34 (t, J = 7.56 Hz, 2H, ArH), 7.40 (d, J = 8.8 Hz, 1H, ArH), 7.45−7.51 (m, 5H, ArH), 7.58 (t, J = 7.32 Hz, 1H, ArH), 7.64 (d, J = 7.32 Hz, 2H, ArH). 8.15 (s, 1H, ArH), 8.86 (brs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.2, 55.6, 104.8, 114.0, 115.5, 116.1, 127.1, 127.9, 127.9, 128.4, 128.5, 128.6, 129.2, 129.6, 130.5, 131.7, 131.9, 139.3, 145.4, 197.9; MS m/z 368 (M^+, 100). Anal. Calcd for $C_{24}H_{20}N_2O_2$ (368.42): C, 78.24; H, 5.47; N, 7.60. Found: C, 78.33, H, 5.51; N, 7.42.

Procedure for Synthesis of 2-Anilinoquinoline 18 from 2-Methylthiosulfonylquinoline 15a. A mixture of **15a** (0.17 g, 0.5 mmol) and aniline (0.22 mL, 2.5 mmol) in 25 mL of conical was irradiated by domestic microwave oven for 5 min. The reaction mixture was cooled and purified by column chromatography over silic agel using hexanes−EtOAc as eluent to afford **18**.

2-Anilino-3-benzoyl-7-methoxyquinoline (18): yield 77% (0.14 g); yellow solid ($CHCl_3$−hexane); mp 168−169 °C; R_f 0.95 (3:1 hexanes−EtOAc); IR (KBr) 1613, 1525, 1210 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.94 (s, 3H, OCH_3), 6.89 (dd, J = 8.76, 2.44 Hz, 1H, ArH), 7.08 (t, J = 7.32 Hz, 1H, ArH), 7.15 (d, J = 2.2 Hz, 1H, ArH), 7.34−7.44 (m, 3H, ArH), 7.51 (t, J = 7.56 Hz, 2H, ArH), 7.60 (t, J = 7.08 Hz, 1H, ArH), 7.69 (d, J = 7.32 Hz, 2H, ArH), 7.95 (d, J = 7.6 Hz, 2H, ArH), 8.21 (s, 1H, ArH), 10.69 (s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.6, 105.3, 114.5, 116.5, 116.7, 118.8, 120.6, 121.5, 122.8, 128.4, 128.8, 129.3, 130.3, 131.9, 139.0, 139.8, 145.5, 153.4, 164.1, 198.1; MS m/z 355 (M + 1, 100). Anal. Calcd for $C_{23}H_{18}N_2O_2$ (354.39): C, 77.95 H, 5.12; N, 7.90. Found: C, 77.74, H, 5.24; N, 8.05.

Procedure for Synthesis of 2-*N*-(Morpholino)-3-benzoylquinoline 19. A mixture of **15a** (0.17 g, 0.5 mmol) and morpholine (0.43 mL, 5 mmol) was heated at 100 °C for 48 h monitored by TLC. The reaction mixture was cooled and purified by column chromatography over silica gel using hexanes−EtOAc as eluent to afford **19**.

3-Benzoyl-7-methoxy-2-morpholinoquinoline (19): yield 70% (0.12 g); light yellow solid ($CHCl_3$−hexane); mp 168−169 °C; R_f 0.75 (3:1 hexanes−EtOAc); IR (KBr) 2847, 1651, 1610, 1494, 1445 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.35 (brs, 4H, CH_2), 3.37 (brs, 4H, CH_2), 3.92 (s, 3H, OCH_3), 6.97 (dd, J = 8.78, 2.44 Hz, 1H, ArH), 7.17 (brs, 1H, ArH), 7.44 (t, J = 7.56 Hz, 2H, ArH), 7.55−7.60 (m, 2H, ArH), 7.79 (d, J = 8.9 Hz, 2H, ArH), 8.06 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 49.5, 55.5, 66.2, 105.7, 116.9, 118.2, 122.2, 128.3, 129.4, 130.0, 133.3, 136.6, 140.6, 150.0, 157.4, 162.5, 196.2; MS m/z 349 (M + 1, 100). Anal. Calcd for $C_{21}H_{20}N_2O_3$ (348.39): C, 72.39; H, 5.79; N, 8.04. Found: C, 72.53, H, 5.85; N, 7.82.

General Procedure for Synthesis of Pyrazolo[2,3-*b*]-quinolines 20a,c,i. A mixture of quinolines (**2a**−**i**) (2 mmol) and excess hydrazine hydrate (0.8 mL, 20 mmol) (80%) and PTSA (100 mg) in a 25 mL beaker was irradiated by a domestic microwave oven for 3 min (monitored by TLC). The reaction mixture was cooled, dissolved in $CHCl_3$ (100 mL), washed with water (2 × 50 mL), dried (Na_2SO_4), and then evaporated under reduced pressure to afford crude product which was purified by column chromatography using hexanes−EtOAc as eluent. In the case of **20i,** pure product was obtained by recrystallization from hexane−$CHCl_3$ (1:9) mixture.

7-Methoxy-3-phenylpyrazolo[3,4-*b*]quinoline (20a): yield 71% (0.39 g); yellow solid ($CHCl_3$−hexane); mp 217−218 °C;

R_f 0.40 (1:1 hexanes−EtOAc); IR (KBr) 2840, 1620, 1498, 1222 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.03 (s, 3H, OCH_3), 7.17 (dd, J = 9.04, 2.44 Hz, 1H, ArH), 7.47−7.51 (m, 2H, ArH), 7.58 (t, J = 7.8 Hz, 2H, ArH), 7.89 (d, J = 9.04 Hz, 1H, ArH), 8.07 (d, J = 7.56 Hz, 2H, ArH), 8.86 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.7, 104.3, 113.3, 118.7, 120.3, 127.2, 128.8, 129.0, 130.5, 131.7, 132.9, 145.3, 149.3, 152.5, 162.5; MS *m/z* 275 (M^+, 74.07). Anal. Calcd for $C_{17}H_{13}N_3O$ (275.29): C, 74.17; H, 4.76; N, 15.26. Found: C, 74.27, H, 4.63; N, 15.34.

6,7-Dimethoxy-3-phenylpyrazolo[3,4-*b*]quinoline (20c): yield 74% (0.45 g); yellow solid ($CHCl_3$−hexane); mp 250−251 °C; R_f 0.45 (2:3 hexanes−EtOAc); IR (KBr) 2927, 1621, 1497, 1245 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.01 (s, 3H, OCH_3), 4.07 (s, 3H, OCH_3) 7.14 (s, 1H, ArH), 7.41−7.45 (m, 2H, ArH), 7.53 (t, J = 7.6 Hz, 2H, ArH), 8.05 (d, J = 7.8 Hz, 2H, ArH), 8.69 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.0, 56.3, 105.4, 105.7, 113.0, 120.4, 127.1, 128.5, 128.9, 128.9, 133.3, 144.3, 145.4, 148.4, 151.9, 154.5; MS *m/z* 305 (M^+, 100). Anal. Calcd for $C_{18}H_{15}N_3O_2$ (305.32): C, 70.80; H, 4.95; N, 13.76. Found: C, 70.65, H, 5.12; N, 13.82.

10*H*-3-Phenylbenzo[*h*]pyrazolo[3,4-*b*]quinoline (20i): yield 85% (0.50 g); light yellow solid ($CHCl_3$−hexane); mp 270−271 °C; R_f 0.60 (9:1 hexanes−EtOAc); IR (KBr) 3174, 1615, 1499, 1377 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.40 (t, J = 7.32 Hz, 1H, ArH), 7.51 (t, J = 7.56 Hz, 2H, ArH), 7.62−7.68 (m, 3H, ArH), 7.77 (d, J = 8.8 Hz, 1H, ArH), 7.83−7.85 (m, 1H, ArH), 8.06 (d, J = 8.08 Hz, 2H, ArH), 8.87 (s, 1H, ArH), 9.29 (d, J = 7.7 Hz, 1H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 112.9, 121.8, 124.2, 124.4, 126.1, 126.4, 126.4, 127.4, 127.8, 128.3, 128.5, 129.7, 130.4, 133.0, 133.7, 142.9, 145.9, 151.8; MS *m/z* 295 (M^+, 100). Anal. Calcd for $C_{20}H_{13}N_3$ (295.32): C, 81.34; H, 4.44; N, 14.23. Found: C, 81.21, H, 4.57; N, 14.31.

Procedure for Preparation of Hydrazone 21c. To a stirred solution of **2c** (0.33 g, 1 mmol) in 95% ethanol was added excess hydrazine hydrate (80%), and the mixture was refluxed for 4 h and monitored by TLC. The reaction mixture was cooled, solvent removed under vacuum, poured into ice-cold water, extracted with $CHCl_3$ (2 × 25 mL), washed with H_2O (2 × 20 mL) and brine (25 mL), dried (Na_2SO_4), and concentrated to give crude product which was recrystallized from hexanes−EtOAc (20:1) mixture.

2-Methylthio-6,7-dimethoxy-quinoyl-3-phenylhydrazone (21c): yield 99% (0.35 g); colorless solid ($CHCl_3$−hexane); mp 199−200 °C; R_f 0.4 (1:4 hexanes−EtOAc); IR (KBr) 3424, 3297, 1586, 1499, 1239 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.58 (s, 3H, SCH_3), 3.91 (s, 3H, OCH_3), 4.01 (s, 3H, OMe), 6.94 (s, 1H, ArH), 7.18 (s, 1H, ArH) 7.21−7.25 (m, 2H, ArH), 7.40−7.42 (m, 3H, ArH), 7.64 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.8, 56.0, 56.1, 105.4, 105.5, 107.0, 107.1, 120.6, 123.4, 125.8, 128.4, 134.9, 137.3, 145.48, 149.1, 153.2, 155.5.

General Procedure for TBTH-Mediated Radical Cyclization of Quinolines 2b and 2d. A solution of quinoline (**2b** or **2d**) (0.72 mmol) in toluene (70 mL) and TBTH (0.50 mL, 1.8 mmol) and AIBN (catalytic) was refluxed for 8−10 h under nitrogen atmosphere (monitored by TLC). The reaction mixture was cooled, evaporated under vacuum, extracted with $CHCl_3$ (3 × 50 mL), washed with water (2 × 50 mL), dried (Na_2SO_4), and evaporated to give pure products which were recrystallized from hexane/$CHCl_3$ mixture.

7-Methoxybenzothiopyrano[2,3-*b*]quinoline (21b): yield 98% (0.21 g); yellow solid ($CHCl_3$-hexane); mp 239−240 °C; R_f 0.40 (9:1 hexanes−EtOAc); IR (KBr) 1629, 1487, 1373 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.00 (s, 3H, OCH_3), 7.23 (dd, J = 9.04, 2.44 Hz, 1H, ArH), 7.36 (d, J = 2.16, 1H, ArH), 7.49 (t, J = 8.04 Hz, 1H, ArH), 7.62−7.68 (m, 2H, ArH), 7.91 (d, J = 9.0 Hz, 1H, ArH), 8.59 (d, J = 8.42 Hz, 1H, ArH), 9.27 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.9, 105.2, 120.9, 121.9, 122.5, 126.3, 126.4, 128.5, 130.0, 131.0, 133.1, 137.2, 139.3, 157.3, 164.1, 181.0, 187.9; MS *m/z* 293 (M^+, 100). Anal. Calcd for $C_{17}H_{11}NO_2S$ (293.33): C, 69.60; H, 3.78; N, 4.78. Found: C, 69.74, H, 3.63; N, 4.85.

6,7-Dimethoxybenzothiopyrano[3,4-*b*]quinoline (21d): yield 98% (0.23 g); yellow solid ($CHCl_3$−hexane); mp 274−275 °C; R_f 0.45 (9:1 hexanes−EtOAc); IR (KBr) 1634, 1507, 1265 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.03 (s, 3H, OCH_3), 4.06 (s, 3H, OCH_3) 7.19 (s, 1H, ArH), 7.36 (s, 1H, ArH), 7.45−7.49 (m, 1H, ArH), 7.60−7.66 (m, 2H, ArH), 8.57 (d, J = 8.43 Hz, 1H, ArH) 9.17 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.2, 56.5, 105.9, 106.0, 122.4, 122.8, 126.3, 126.5, 128.5, 130.1, 132.9, 137.3, 137.4, 147.4, 150.3, 154.5, 156.2, 181.0; MS *m/z* 324 (M + 1, 90). Anal. Calcd for $C_{18}H_{13}NO_3S$ (323.35): C, 66.86; H, 4.05; N, 4.33. Found: C, 66.69, H, 4.16; N, 4.42.

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Supporting Information Available: ^1H and ^{13}C NMR spectral data for compounds **1b**−**g**,**l**. This material is available free of charge via the Internet at http://pubs.acs.org.

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