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First construction of 12*H*-thiochromeno[2,3-*b*]quinolines and 5*H*-benzo[7,8]thiocino-[2,3-*b*]quinolines via intramolecular Friedel–Crafts reaction of Morita–Baylis–Hillman adducts

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ABSTRACT

An acid-promoted intramolecular Friedel–Crafts reaction of the Morita–Baylis–Hillman adducts **3** derived from 2-arylthioquinolin-3-carbaldehydes **2** was investigated. Interestingly, promoted by sulfuric acid, the substrates with electron-donating groups on the aromatic ring gave six-membered fused-ring 12*H*-thiochromeno[2,3-*b*]quinolines **4** with good yields, while those with electron-withdrawing groups afforded eight-membered fused-ring 5*H*-benzo[7,8]thiocino[2,3-*b*]quinolines **5** in moderate yields. Using triflic acid instead of sulfuric acid, only products **4** could be obtained under the similar condition.

1. Introduction

Quinolines and their analogues, play important roles in the heterocycles chemistry due to their various biological acitivities, such as antimalarials,[1] bactericidal,[2] antitumor,[3] anti-inflammatory,[4] antiproliferative,[5] antiviral,[6] and etc. Quinoline containing fused-rings, such as 3,4-dihydro-2*H*-thiopyrano[2,3-*b*]quinoline **I** showed metabotropic glutamate receptor antagonistic activity, in particular mGlu 1 receptor activity,[7] and 2*H*-thiopyrano[2,3-*b*]quinoline-2-carboxylic acid **II** could be used as a strong antioxidant to protect oxidative DNA damage from harmful free radicals (Fig. 1).[8] Although numerous elegant synthetic methods have been developed, it still need to explore new and efficient synthetic routes for the synthesis of this class of compounds, particularly those with general applicability in achieving more flexible substitution pattern.[9]

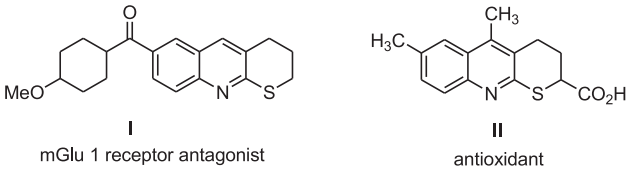

Fig. 1. Representative biologically active molecules containing 2*H*-thiopyrano[2,3-*b*]quinoline ring systems.

The Morita–Baylis–Hillman (MBH) reaction is a useful carbon–carbon bond formation reaction from aldehydes and activated alkenes, which is a one-pot, atom economical reaction and provides multi-functionalized adducts catalyzed by a tertiary amine.[10] These MBH adducts and their derivatives were widely employed for the synthesis of a variety of useful heterocyclic compounds by us[11] and other groups.[12]

Recently, Junjappa et al. reported the synthesis of benzothiopyrano[2,3-*b*]quinoline derivatives by treatment of 3-(*o*-bromobenzoyl)quinoline with Bu_3SnH/AIBN.[13] Ramesh demonstrated thiopyanoquinoline derivatives could be prepared through imino Diels–Alder reaction using silica gel impregnated with indium trichloride as a catalyst.[14] To the best of our knowledge, the preparation of 2*H*-thiochromeno[2,3-*b*]quinoline derivatives from MBH adducts has not been reported. With our ongoing interest in the synthesis of heterocycles from MBH adducts, we herein report the first construction of 12*H*-thiochromeno[2,3-*b*]quinolines and 5*H*-benzo[7,8]thiocino[2,3-*b*]quinolines via intramolecular Friedel–Crafts reaction of MBH adducts (Fig. 2).

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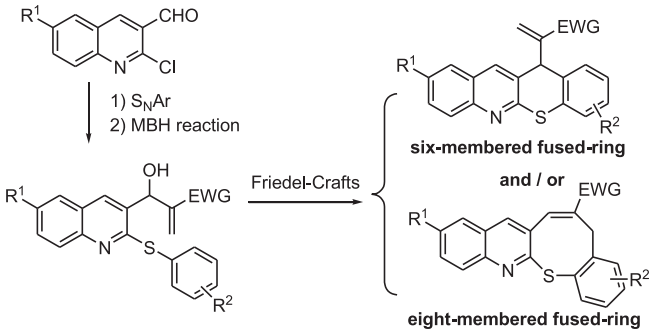
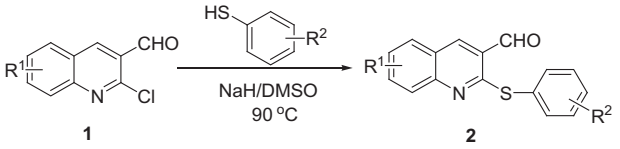


Fig. 2. Synthetic schedule of 12*H*-thiochromeno[2,3-*b*]quinolines and 5*H*-benzo[7,8]thiocino[2,3-*b*]quinolines from 2-chloro-3-formylquinolines.

2. Results and discussion

The starting 2-chloro-3-formylquinolines **1** were prepared from the corresponding acetanilides by treatment with the Vilsmerier reagent generated in situ from $POCl_3$/DMF system.[15] When we mixed 2-chloro-3-formylquinolines **1a**, 4-isopropylbenzenethiol, and NaH in DMSO at 90 °C for 2 h, the desired 2-(4-isopropylphenylthio)quinoline-3-carbaldehyde **2a** was isolated in 82% yield (Table 1, entry 1). Similarly, the corresponding compounds **2b**–**o** were prepared from 2-chloro-3-formylquinolines **1** with moderate to high yields under the same conditions (Table 1). With 2-arylthioquinoline-3-carbaldehydes **2** in hand, we intended to test the MBH reaction between **2** and activated alkenes in the presence of DABCO at room temperature (Table 2). The desired compounds **3a**–**f** and **3h** were obtained in 84–98% isolated yields (Table 2, entries 1–8). Unfortunately, the substrates with electron-withdrawing groups (**2g** and **2h**) gave MBH adducts **3i** and **3j** in lower yields with prolonged reaction times, respectively (Table 2, entries 9 and 10). Then we tried to use DMAP[16] to promote this MBH reaction, and it is gratifying to find that **3g** and **3i**–**l** were successfully isolated in moderate yields with CH_2Cl_2 as a solvent at room temperature for 9 days. Similarly, the desired products **3m** and **3n** derived from 8-position substituted quinolines **2k** and **2l** were obtained in good yields (Table 2, entries 13 and 14). However the 5- or 7-position substituted quinolines gave the desired compounds **3o**–**q** in relatively low yields (Table 2, entries 15–17). It seems that the substituent group plays an important role in governing the reactivity of the substrates.

Table 1
Synthesis of 2-arylthioquinoline-3-carbaldehydes **2** from 2-chloro-3-formylquinolines **1**[a]

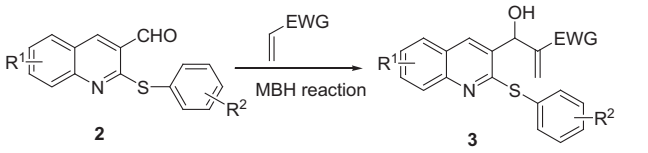


1 2

Entry	R^1	R^2	Time (h)	Products	Yield[b] (%)
1	H	4-*i*-Pr	2	**2a**	82
2	H	2-Me	3	**2b**	86
3	H	H	3	**2c**	77
4	Me	4-*i*-Pr	2	**2d**	69
5	Cl	4-*i*-Pr	2	**2e**	61
6	H	3-Me	2	**2f**	83
7	H	4-Cl	3	**2g**	86
8	H	2-Cl	3	**2h**	89
9	H	4-Br	3	**2i**	85
10	H	2,4-Cl_2	4	**2j**	88
11	8-Me	2,4-Cl_2	3	**2k**	88
12	8-Me	4-Me	2	**2l**	81
13	7-Me	4-Me	2	**2m**	70
14	5,7-Me_2	2,4-Cl_2	3	**2n**	87
15	5,7-Me_2	4-Me	2	**2o**	67

[a] Conditions: **1** (10 mmol), thiophenol (11 mmol), NaH (20 mmol), DMSO (20 mL).
[b] Isolated yields based on quinoline-3-aldehydes **1**.

Table 2
Synthesis of MBH adducts **3** from 2-arylthioquinoline-3-carbaldehydes **2**[a]

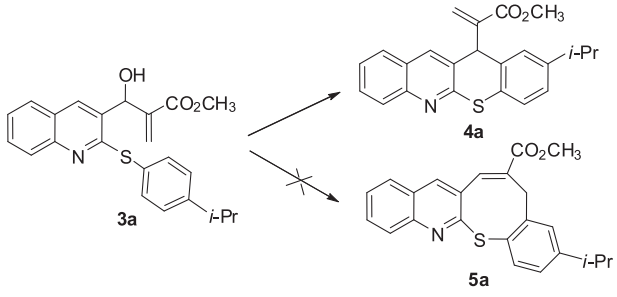


2 3

Entry	R^1	R^2	EWG	Time (d)	Products	Yield[b] (%)
1	H	4-*i*-Pr	CO_2Me	3	**3a**	97
2	H	4-*i*-Pr	CO_2Et	3	**3b**	98
3	H	4-*i*-Pr	CO_2Bu-*n*	5	**3c**	95
4	H	2-Me	CO_2Me	3	**3d**	98
5	H	H	CO_2Me	28	**3e**	84
6	Me	4-*i*-Pr	CO_2Me	5	**3f**	90
7	Cl	4-*i*-Pr	CO_2Me	9	**3g**	46[c]
8	H	3-Me	CO_2Me	3	**3h**	98
9	H	4-Cl	CO_2Me	15	**3i**	5 (47)[c]
10	H	2-Cl	CO_2Me	15	**3j**	10 (67)[c]
11	H	4-Br	CO_2Me	9	**3k**	43[c]
12	H	2,4-Cl_2	CO_2Me	9	**3l**	69[c]
13	8-Me	2,4-Cl_2	CO_2Me	19	**3m**	63c
14	8-Me	4-Me	CO_2Me	3	**3n**	98
15	7-Me	4-Me	CO_2Me	4(7)	**3o**	Trace (10)[c]
16	5,7-Me_2	2,4-Cl_2	CO_2Me	20	**3p**	6[c]
17	5,7-Me_2	4-Me	CO_2Me	4	**3q**	Trace

[a] Conditions: **2** (2 mmol), alkene (10 mmol), DABCO (0.6 mmol), rt.
[b] Isolated yields based on **2**.
[c] Conditions: **2** (2 mmol), alkene (10 mmol), DMAP (1 mmol), CH_2Cl_2, rt, 9 days.

Encouraged by these results, we turned our attention to the intramolecular Friedel–Crafts reaction of MBH adducts **3** (Scheme 1). Preliminary experiments indicated that, the desired product **4a** and/or the expected eight-membered fused-ring **5a** was not detected by treatment of compound **3a** in CH_3NO_2 or CH_2Cl_2 with various Lewis acids, such as $AlCl_3$, $Zn(OTf)_2$, $Yb(OTf)_3$ or BF_3–OEt_2 (Table 3, entries 1–5).[17] Then CF_3SO_3H was employed and **4a** was isolated in only 48% yield (Table 3, entry 6).[18] In order to optimize the reaction conditions, various factors including the identity and amount of promoters, solvents, reaction temperature were screened and the results were summarized in Table 3. The Optimal conditions were obtained by the treatment of **3a** with 95% concentrated H_2SO_4 (preferly 8.0 equiv) in CH_2Cl_2 at room temperature, providing **4a** in 79% within 1.5 h (Table 3, entry 11).[19]



Scheme 1. The intramolecular Friedel–Crafts reaction of **3a**.

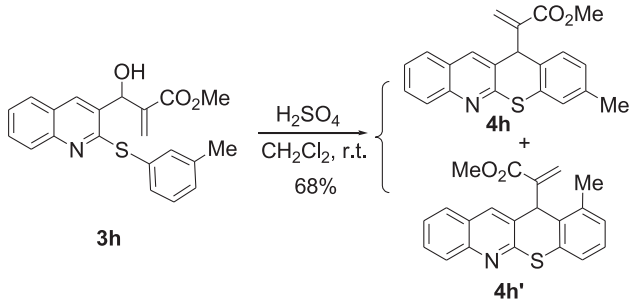
Under the above optimized conditions, **4b**–**g** were obtained in 62–90% yields (Table 4, entries 2–7). Interestingly, treatment of **3h** with 95% concentrated H_2SO_4 gave a mixture of isomers **4h** and **4h′** in 68% yield with a ratio of 1:1 (determined by ^1H NMR spectra)

Table 3
Synthesis of **4a** under various conditions[a]

Entry	Reagents	Amount (equiv)	Solvent	Temp (°C)	Time (h)	Yield[b] (%)
1	$AlCl_3$	1.1	CH_3NO_2	60	5	0
2	$AlCl_3$	3.0	CH_3NO_2	60	5	0
3	$Zn(OTf)_2$	0.5	CH_3NO_2	100	10	0
4	$Yb(OTf)_3$	0.3	CH_2Cl_2	Reflux	15	0
5	BF_3–OEt_2	1.0	CH_2Cl_2	Reflux	10	0
6	CF_3SO_3H	3.0	$(ClCH_2)_2$	Reflux	4	48
7	95%H_2SO_4	1.2	DMF	rt	10	Trace
8	95%H_2SO_4	2.0	CH_2Cl_2	Reflux	7	Trace
9	95%H_2SO_4	4.0	CH_2Cl_2	rt	6	24
10	95%H_2SO_4	6.0	CH_2Cl_2	rt	2	33
11	95%H_2SO_4	8.0	CH_2Cl_2	rt	1.5	79

[a] Reaction conditions: **3a** (1 mmol), solvent (10 mL).
[b] Isolated yield based on **3a**.

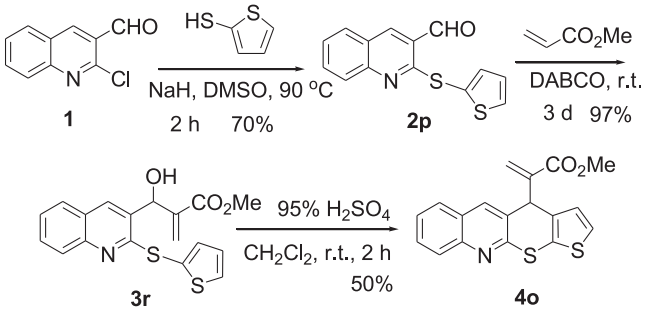
(Scheme 2). To our delight, 95% concentrated H_2SO_4 mediated the intramolecular Friedel–Crafts reaction of substrate **3i** could give the desired product **4i** in 8% yield and the novel eight-membered fused-ring **5i** (sulfate!) was isolated with 63% yield (Table 4, entry 9). Similarly, the corresponding products (**5j**–**m**) were isolated in 66–82% yield when other substrates bearing electron-withdrawing groups was used (Table 4, entries 10–13). While promoted by CF_3SO_3H, the intramolecular Friedel–Crafts reaction of



Scheme 2. The intramolecular Friedel–Crafts reaction of **3h**.

MBH adducts could be performed and provided only the six-membered fused-rings **4i**, **4j**, and **4l** in 27–49% yields (Table 4, entries 9, 10, and 12). The MBH adduct **3n** derived from 8-position substituted quinoline gave the eight-membered fused-ring **5n** in 57% yield and **4n** in 21% yield (Table 4, entry 14). The MBH adducts with electron-withdrawing groups required longer reaction time and gave lower yields than those with electron-donating groups (Table 4).

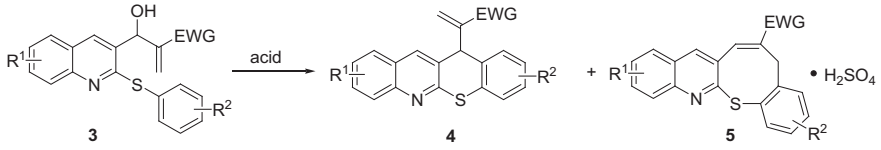
In order to extend the scope, the preparation of compound **4o** from 2-chloro-3-formyl quinoline **1** was also investigated (Scheme 3). Treatment of **1** with thiophene-2-thiol in the presence of NaH gave 2-(thiophen-2-ylthio)quinoline-3-carbaldehyde **2p** in 70% yield, which was then converted into MBH adduct **3r** by treatment with methyl acrylate in the presence of DABCO. Finally, the intramolecular Friedel–Crafts reaction of **3r** mediated by 95% concentrated H_2SO_4 could produce a six-membered fused-ring **4o** in 50% yield.



Scheme 3. Synthesis of **4o** from 2-chloro-3-formyl quinoline **1**.

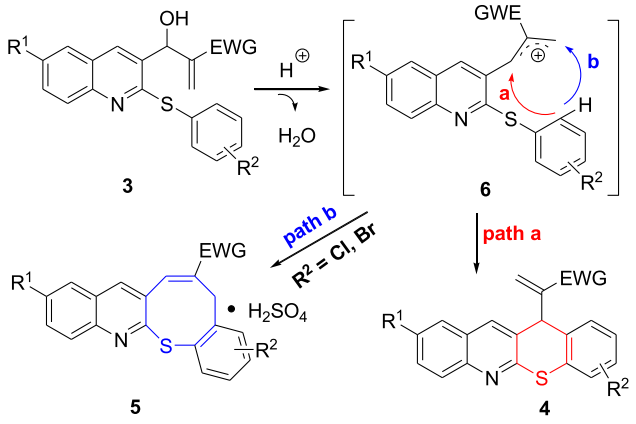
According to the above results, a plausible mechanism for the formation of compounds **4** and **5** from MBH adducts **3** was shown in Scheme 4.[20] When the substrates **3** were treated with sulfuric or triflic acid, the allyl cation intermediates **6** could be formed, which were readily transformed into six-(path a) or eight-(path b) membered fused-rings via intramolecular Friedel–Crafts reaction.

Table 4
Synthesis of 12*H*-thiochromeno[2,3-*b*]quinolines **4** and 5*H*-benzo[7,8]thiocino[2,3-*b*]quinolines **5** from MBH adducts **3**[a]



Entry	R^1	R^2	EWG	Time (h)	Isolated yields (%)[b]	
					Products (**4**)	Products (**5**)
1	H	4-*i*-Pr	CO_2Me	1.5	**4a** (79)	n.d.[c]
2	H	4-*i*-Pr	CO_2Et	1.5	**4b** (83)	n.d.[c]
3	H	4-*i*-Pr	CO_2Bu-*n*	2.5	**4c** (67)	n.d.[c]
4	H	2-Me	CO_2Me	1.5	**4d** (90)	n.d.[c]
5	H	H	CO_2Me	2.5	**4e** (62)	n.d.[c]
6	4-Me	4-*i*-Pr	CO_2Me	2.5	**4f** (83)	n.d.[c]
7	Cl	4-*i*-Pr	CO_2Me	1	**4g** (68)	n.d.[c]
8	H	3-Me	CO_2Me	2	**4h**+**4h′** (68)	n.d.[c]
9	H	4-Cl	CO_2Me	0.5 (6)	**4i** (8/27)[d]	**5i** (63)
10	H	2-Cl	CO_2Me	0.5 (6)	**4j** (7/49)[d]	**5j** (66)
11	H	4-Br	CO_2Me	0.5	**4k** (n.d.)[c]	**5k** (82)
12	H	2,4-Cl_2	CO_2Me	0.5	**4l** (3/40)[d]	**5l** (66)
13	8-Me	2,4-Cl_2	CO_2Me	1	**4m** (n.d.)[c]	**5m** (73)
14	8-Me	4-Me	CO_2Me	1.5	**4n** (21)	**5n** (57)

[a] Conditions: **3** (1 mmol), 95%H_2SO_4 (8.0 mmol), CH_2Cl_2, rt.
[b] Isolated yields based on **3**.
[c] n.d.=not detected.
[d] Conditions: **3** (1 mmol), CF_3SO_3H (3.0 mmol), $ClCH_2CH_2Cl$, reflux.



Scheme 4. A plausible mechanism for the formation of **4** and **5**.

3. Conclusion

In conclusion, we developed a new protocol for the synthesis of 12*H*-thiochromeno[2,3-*b*]quinolines **4** via sulfuric acid or triflic acid-promoted intramolecular Friedel–Crafts reaction of MBH adducts. Very interestingly, those MBH adducts with electron-withdrawing groups could give 5*H*-benzo[7,8]thiocino[2,3-*b*]quinolines **5** in moderate yields in the presence of sulfuric acid. This strategy is attractive as it employs commonly available cheap reagents and does not require any elaborate reaction conditions.

4. Experimental

4.1. General

Melting points were determined using a Büchi B-540 capillary melting point apparatus and were uncorrected. IR spectra were recorded on a Nicolet Avatar-370 instrument. ^{1}H and ^{13}C NMR spectra were recorded on Varian (400 MHz) instruments using TMS as an internal standard. Mass spectra were measured with a Finnigan Trace DSQ instrument or GCT Premier mass spectrometer. High-resolution mass spectral (HRMS) analyses were measured on an APEX (Bruker) mass III spectrometer or GCT Premier mass spectrometer using ESI (electrospray ionization) or EI (electron impact) techniques. Silica gel for column chromatography was purchased from Qingdao Haiyang Chemical Co., Ltd. (200–300 mesh). All yields described herein are the isolated yields after column chromatography.

4.2. General procedure for the preparation of 2-arylthioquinoline-3-carbaldehyde 2

To a mixture of thiophenol (11 mmol), NaH (20 mmol), and DMSO (20 mL) was added 2-chloro-3-formylquinolines **1** (10 mmol) and the mixture was heated at 90 °C for the given time. Then the reaction was quenched with water (60 mL) and extracted with CH_2Cl_2 (3×50 mL). The combined organic layer was washed with brine solution, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The desired products **2** were obtained by flash column chromatography on silica (*n*-hexane/EtOAc, 10:1→6:1, v/v).

4.2.1. 2-(4-Isopropylphenylthio)quinoline-3-carbaldehyde (***2a***). Yellow solid; mp 83.4–84.3 °C (*n*-hexane/EtOAc); R_f=0.45 (*n*-hexane/EtOAc, 4:1); IR (KBr): 1693 (CHO) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=10.42 (1H, s, CHO), 8.54 (1H, s, ArH), 7.86 (1H, d, *J*=8.0 Hz, ArH), 7.75 (1H, d, *J*=8.0 Hz, ArH), 7.69–7.73 (1H, m, ArH), 7.53 (2H, d, *J*=8.0 Hz, ArH), 7.47–7.51 (1H, m, ArH), 7.30 (2H, d, *J*=8.0 Hz, ArH), 2.92–3.02 (m, 1H, C*H*(CH$_3$)$_2$), 1.30 (6H, d, *J*=7.2 Hz, CH(C*H*$_3$)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ=190.0, 159.1, 149.7, 149.5, 142.1, 135.0 (2C), 132.7, 129.0, 128.6, 127.2, 127.1 (3C), 126.5, 125.1, 33.9, 23.8 (2C); MS (EI) *m*/*z*=307 (M$^+$, 16), 279 (52), 278 (100); HRMS (EI) calcd for $C_{19}H_{17}NOS$ (M$^+$): 307.1043; found: 307.1046.

4.2.2. 2-(o-Tolylthio)quinoline-3-carbaldehyde (***2b***). Yellow solid; mp 91.8–92.5 °C (*n*-hexane/EtOAc); R_f=0.46 (*n*-hexane/EtOAc, 4:1); IR (KBr): 1694 (CHO) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=10.38 (1H, s, CHO), 8.51 (1H, s, ArH), 7.83 (1H, d, *J*=8.0 Hz, ArH), 7.62–7.68 (2H, m, ArH), 7.55 (1H, d, *J*=8.0 Hz, ArH), 7.45 (1H, t, *J*=7.6 Hz, ArH), 7.33–7.38 (2H, m, ArH), 7.20–7.24 (1H, m, ArH), 2.37 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=189.8, 158.3, 149.4, 143.0, 142.3, 136.0, 132.6, 130.3, 129.4, 129.0, 128.9, 128.5, 127.0, 126.3 (2C), 124.8, 21.0; MS (EI) *m*/*z*=279 (M$^+$, 13), 250 (39), 236 (40), 218 (100); HRMS (EI) calcd for $C_{17}H_{13}NOS$ (M$^+$): 279.0728; found: 279.0722.

4.2.3. 2-(Phenylthio)quinoline-3-carbaldehyde (***2c***). Yellow solid; mp 136.1–136.9 °C (*n*-hexane/EtOAc); R_f=0.48 (*n*-hexane/EtOAc, 4:1); IR (KBr): 1686 (CHO) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=10.37 (1H, s, CHO), 8.52 (1H, s, ArH), 7.84 (1H, d, *J*=8.4 Hz, ArH), 7.68–7.70 (2H, m, ArH), 7.58–7.60 (2H, m, ArH), 7.45–7.49 (1H, m, ArH), 7.40–7.42 (3H, m, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ=190.1, 158.8, 149.6, 142.5, 135.2 (2C), 133.0, 130.1, 129.2, 129.1 (2C), 129.0, 128.81, 127.4, 126.8, 125.3; MS (EI) *m*/*z*=265 (M$^+$, 15), 237 (39), 236 (100); HRMS (EI) calcd for $C_{16}H_{11}NOS$ (M$^+$): 265.0617; found: 265.0623.

4.2.4. 2-(4-Isopropylphenylthio)-6-methylquinoline-3-carbaldehyde (***2d***). Yellow solid; mp 90.2–91.1 °C (*n*-hexane/EtOAc); R_f=0.46 (*n*-hexane/EtOAc, 4:1); IR (KBr): 1682 (CHO) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=10.37 (1H, s, CHO), 8.42 (1H, s, ArH), 7.64 (1H, d, *J*=8.8 Hz, ArH), 7.58 (1H, s, ArH), 7.48–7.52 (3H, m, ArH), 7.26 (2H, d, *J*=8.0 Hz, ArH), 2.90–3.00 (1H, m, C*H*(CH$_3$)$_2$), 2.49 (3H, s, CH_3), 1.29 (6H, d, *J*=6.8 Hz, CH(C*H*$_3$)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ=190.3, 158.0, 149.7, 148.4, 141.5, 136.8, 135.2, 134.9 (2C), 128.5, 128.0, 127.5, 127.3 (2C), 127.2, 125.4, 34.3, 24.3 (2C), 21.9; MS (EI) *m*/*z*=321 (M$^+$, 9), 293 (47), 292 (100); HRMS (EI) calcd for $C_{20}H_{19}NOS$ (M$^+$): 321.1252; found: 321.1242.

4.2.5. 6-Chloro-2-(4-isopropylphenylthio)quinoline-3-carbaldehyde (***2e***). Yellow solid; mp 100.1–101.0 °C (*n*-hexane/EtOAc); R_f=0.44 (*n*-hexane/EtOAc, 4:1); IR (KBr): 1686 (CHO) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=10.37 (1H, s, CHO), 8.40 (1H, s, ArH), 7.79 (1H, d, *J*=2.4 Hz, ArH), 7.63 (1H, d, *J*=8.8 Hz, ArH), 7.58 (1H, dd, *J*=8.8, 2.4 Hz, ArH), 7.50 (2H, d, *J*=8.0 Hz, ArH), 7.28 (2H, d, *J*=8.0 Hz, ArH), 2.92–3.02 (1H, m, C*H*(CH$_3$)$_2$), 1.30 (6H, d, *J*=7.2 Hz, CH(C*H*$_3$)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ=189.4, 159.5, 149.8147.6, 140.7, 135.0 (2C), 133.2, 131.9, 130.0, 127.5, 127.3, 127.1 (2C), 125.9, 125.5, 34.0, 24.0 (2C); MS (EI) *m*/*z*=341 (M$^+$, 19), 314 (45), 312 (100); HRMS (EI) calcd for $C_{19}H_{16}ClNOS$ (M$^+$): 341.0611; found: 341.0619.

4.2.6. 2-(m-Tolylthio)quinoline-3-carbaldehyde (***2f***). Yellow solid; mp 97.8–98.5 °C (*n*-hexane/EtOAc); R_f=0.44 (*n*-hexane/EtOAc, 4:1); IR (KBr): 1692 (CHO) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=10.37 (1H, s, CHO), 8.51 (1H, s, ArH), 7.84 (1H, d, *J*=8.0 Hz, ArH), 7.73 (1H, d, *J*=8.0 Hz, ArH), 7.66–7.71 (1H, m, ArH), 7.45–7.49 (1H, m, ArH), 7.41 (1H, s, ArH), 7.38 (1H, d, *J*=7.6 Hz, ArH), 7.30 (1H, t, *J*=7.6 Hz, ArH), 7.20 (1H, d, *J*=7.6 Hz, ArH), 2.38 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=189.8, 158.7, 149.3, 141.9, 138.6, 135.1, 132.7, 131.8, 129.6, 129.5, 128.9, 128.6, 128.5, 127.2, 126.5, 125.1, 21.5; MS (EI) *m*/*z*=279 (M$^+$, 13), 251 (47), 250 (100); HRMS (EI) calcd for $C_{17}H_{13}NOS$ (M$^+$): 279.0733; found: 279.0745.

4.2.7. 2-(4-Chlorophenylthio)quinoline-3-carbaldehyde (***2g***). Yellow solid; mp 143.0–143.6 °C (*n*-hexane/EtOAc); R_f=0.41 (*n*-hexane/EtOAc, 4:1); IR (KBr): 1690 (CHO) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$)

δ=10.33 (1H, s, CHO), 8.52 (1H, s, ArH), 7.85 (1H, d, *J*=8.0 Hz, ArH), 7.68–7.73 (2H, m, ArH), 7.53 (2H, d, *J*=8.4 Hz, ArH), 7.47–7.51 (1H, m, ArH), 7.39 (2H, d, *J*=8.4 Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ=189.7, 157.9, 149.2, 143.0, 136.5 (2C), 135.0, 132.9, 129.0 (2C), 128.8, 128.4, 128.1, 126.8, 126.6, 124.9; MS (EI) *m*/*z*=299 (M^+, 13), 272 (44), 270 (100); HRMS (EI) calcd for $C_{16}H_{10}ClNOS$ (M^+): 300.0239; found 300.0241.

*4.2.8. 2-(2-Chlorophenylthio)quinoline-3-carbaldehyde (**2h**).* Yellow solid; mp 110.2–111.3 °C (*n*-hexane/EtOAc); R_f=0.43 (*n*-hexane/EtOAc, 4:1); IR (KBr): 1685 (CHO) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=10.34 (1H, s, CHO), 8.53 (1H, s, ArH), 7.85 (1H, d, *J*=8.0 Hz, ArH), 7.63–7.70 (3H, m, ArH), 7.53 (1H, d, *J*=8.0 Hz, ArH), 7.47 (1H, t, *J*=7.6 Hz, ArH), 7.36–7.40 (1H, m, ArH), 7.3 (1H, t, *J*=7.6 Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ=189.9, 157.0, 1128.5, 49.3, 142.9, 139.4, 137.1, 132.8, 130.4, 129.8, 129.4, 128.8, 127.03, 126.95, 126.5, 124.9; MS (ESI) *m*/*z*=300.2 (M^++1, 100); HRMS (ESI) calcd for $C_{16}H_{10}ClNOS$ (M^+): 299.0250; found: 299.0249.

*4.2.9. 2-(4-Bromophenylthio)quinoline-3-carbaldehyde (**2i**).* Yellow solid; mp 150.2–150.9 °C (*n*-hexane/EtOAc); R_f=0.43 (*n*-hexane/EtOAc, 4:1); IR (KBr): 1689 (CHO) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=10.33 (1H, s, CHO), 8.52 (1H, s, ArH), 7.86 (1H, d, *J*=8.0 Hz, ArH), 7.70 (2H, s, ArH), 7.45–7.56 (5H, m, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ=189.7, 157.8, 149.2, 143.0, 136.7 (2C), 132.9, 131.9 (2C), 128.9, 128.7, 128.4, 126.8, 126.6, 124.9, 123.3; MS (EI) *m*/*z*=343 (M^+, 13), 317 (35), 316 (100), 315 (35), 314 (92), 238 (40); HRMS (EI) calcd for $C_{16}H_{10}BrNOS$ (M^+): 342.9763; found: 342.9781.

*4.2.10. 2-(2,4-Dichlorophenylthio)quinoline-3-carbaldehyde (**2j**).* Yellow solid; mp 138.2–139.1 °C (*n*-hexane/EtOAc); R_f=0.42 (*n*-hexane/EtOAc, 4:1); IR (KBr): 1691 (CHO) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=10.31 (1H, s, CHO), 8.53 (1H, s, ArH), 7.86 (1H, d, *J*=8.0 Hz, ArH), 7.65–7.73 (2H, m, ArH), 7.60 (1H, d, *J*=8.4 Hz, ArH), 7.56 (1H, d, *J*=2.0 Hz, ArH), 7.47–7.51 (1H, m, ArH), 7.30 (1H, dd, *J*=8.4, 2.0 Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ=189.9, 156.6, 149.2, 143.5, 140.6, 138.1, 135.9, 133.0, 129.8, 128.9, 128.6, 128.0, 127.4, 126.8, 126.7, 124.9; MS (EI) *m*/*z*=333 (M^+, 1), 300 (36), 298 (100), 270 (39); HRMS (EI) calcd for $C_{16}H_9Cl_2NOS$ (M^+): 332.9826; found: 332.9835.

*4.2.11. 2-(2,4-Dichlorophenylthio)-8-methylquinoline-3-carbaldehyde (**2k**).* Yellow solid; mp 152.3–153.1 °C (*n*-hexane/EtOAc); R_f=0.45 (*n*-hexane/EtOAc, 4:1); IR (KBr): 1687 (CHO) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=11.28 (1H, s, CHO), 8.48 (1H, s, ArH), 7.69 (1H, d, *J*=7.6 Hz, ArH), 7.62 (1H, d, *J*=8.4 Hz, ArH), 7.58(1H, d, *J*=2.4 Hz, ArH), 7.54(1H, d, *J*=2.4 Hz, ArH), 7.37 (1H, t, *J*=7.6 Hz, ArH), 7.31(1H, dd, *J*=8.4, 2.4 Hz, ArH), 2.21(3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=190.3, 155.6, 148.2, 144.4, 141.5, 138.7, 136.9, 136.2, 133.4, 129.9, 128.6, 127.7, 126.9, 126.7 (2C), 125.0, 17.3; MS (EI) *m*/*z*=347.0 (M^+, 4), 314.0 (43), 312.0 (100), 284.0 (33); HRMS (EI) calcd for $C_{17}H_{11}Cl_2NOS$ (M^+): 346.9938; found: 346.9965.

*4.2.12. 8-Methyl-2-(p-tolylthio)quinoline-3-carbaldehyde (**2l**).* Yellow solid; mp 101.6–102.4 °C (*n*-hexane/EtOAc); R_f=0.44 (*n*-hexane/EtOAc, 4:1); IR (KBr): 1693 (CHO) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=10.33 (1H, s, CHO), 8.43 (1H, s, ArH), 7.64(1H, d, *J*=8.0 Hz, ArH), 7.51(3H, d, *J*=8.0 Hz, ArH), 7.32(1H, *J*=8.0 Hz, ArH), 7.24(2H, d, *J*=8.0 Hz, ArH), 2.42(3H, s, CH_3), 2.24(3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=190.2, 158.3, 148.4, 143.0, 139.1, 136.9, 135.9 (2C), 133.1, 129.8 (2C), 126.9, 126.8, 126.4, 126.3, 125.0, 21.8, 17.4; MS (EI) *m*/*z*=293.1 (M^+, 43), 264.1 (100); HRMS (EI) calcd for $C_{18}H_{15}NOS$ (M^+): 293.0874; found: 293.0887.

*4.2.13. 7-Methyl-2-(p-tolylthio)quinoline-3-carbaldehyde (**2m**).* Yellow solid; mp 155.2–156.3 °C (*n*-hexane/EtOAc); R_f=0.44 (*n*-hexane/EtOAc, 4:1); IR (KBr): 1689 (CHO) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=10.34 (1H, s, CHO), 8.44 (1H, s, ArH), 7.71 (1H, d, *J*=8.0 Hz, ArH), 7.47 (3H, d, *J*=8.0 Hz, ArH), 7.28 (1H, dd, *J*=8.0, 1.6 Hz, ArH), 7.23 (2H, d, *J*=8.0 Hz, ArH), 2.47 (3H, s, CH_3), 2.42 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=189.8, 158.9, 149.5, 143.8, 141.8, 138.7, 134.9 (2C), 129.6 (2C), 128.6, 128.5, 127.6, 126.4, 126.2, 123.0, 22.2, 21.5; MS (EI) *m*/*z*=293.1 (M^+, 24), 265.1 (44), 264.1 (100); HRMS (EI) calcd for $C_{18}H_{15}NOS$ (M^+): 293.0874; found: 293.0897.

*4.2.14. 2-(2,4-Dichlorophenylthio)-5,7-dimethylquinoline-3-carbaldehyde (**2n**).* Yellow solid; mp 198.7–199.1 °C (*n*-hexane/EtOAc); R_f=0.45 (*n*-hexane/EtOAc, 4:1); IR (KBr): 1689 (CHO) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=10.33 (1H, s, CHO), 8.65 (1H, s, ArH), 7.61 (1H, d, *J*=7.6 Hz, ArH), 7.58 (1H, d, *J*=2.4 Hz, ArH), 7.32 (2H, dd, *J*=8.0, 2.4 Hz, ArH), 7.18 (1H, s, ArH), 2.70 (3H, s, CH_3), 2.47(3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=189.9, 156.2, 150.0, 143.9, 140.5, 139.6, 138.0, 135.9, 135.7, 129.7, 129.5, 128.3, 127.3, 125.9, 125.7, 122.6, 22.1, 18.6; MS (EI) *m*/*z*=361.0 (M^+, 1), 328.0 (44), 326.0 (100), 298.0 (48); HRMS (EI) calcd for $C_{18}H_{13}Cl_2NOS$ (M^+): 361.0095; found: 361.0125.

*4.2.15. 5,7-Dimethyl-2-(p-tolylthio)quinoline-3-carbaldehyde (**2o**).* Yellow solid; mp 184.0–184.7 °C (*n*-hexane/EtOAc); R_f=0.47 (*n*-hexane/EtOAc, 4:1); IR (KBr): 1697 (CHO) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=10.37 (1H, s, CHO), 8.60 (1H, s, ArH), 7.46 (2H, d, *J*=8.0 Hz, ArH), 7.34 (1H, s, ArH), 7.22 (2H, d, *J*=8.0 Hz, ArH), 7.12 (1H, s, ArH), 2.65 (3H, s, CH_3), 2.42 (6H, d, *J*=4.4 Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=189.9, 158.5, 150.2, 143.5, 138.6, 138.1, 136.0, 134.8 (2C), 129.8, 129.6 (2C), 129.3, 126.5, 125.9, 122.7, 22.1, 21.5, 18.6; MS (EI) *m*/*z*=307.1 (M^+, 16), 279.1 (46), 278.1 (100); HRMS (EI) calcd for $C_{19}H_{17}NOS$ (M^+): 307.1031; found: 307.1056.

*4.2.16. 2-(Thiophen-2-ylthio)quinoline-3-carbaldehyde (**2p**).* Yellow solid; mp 118.8–119.7 °C (*n*-hexane/EtOAc); R_f=0.45 (*n*-hexane/EtOAc, 4:1); IR (KBr): 1698 (CHO) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=10.29 (1H, d, *J*=4.4 Hz, CHO), 8.50 (1H, d, *J*=4.8 Hz, ArH), 7.85 (1H, dd, *J*=8.0, 2.4 Hz, ArH), 7.78 (1H, dd, *J*=8.0 Hz, 2.4 Hz, ArH), 7.72 (1H, t, *J*=7.2 Hz, ArH), 7.49 (1H, t, *J*=7.2 Hz, ArH), 7.60 (1H, d, *J*=5.2 Hz, ArH), 7.34 (1H, d, *J*=3.6 Hz, ArH), 7.13 (1H, t, *J*=4.0 Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ=189.7, 158.2, 149.2, 143.4, 135.4, 133.0, 131.6, 128.8, 128.5, 127.2, 127.1, 126.6 (2C), 124.9; MS (EI) *m*/*z*=271 (M^+, 41), 243 (62), 242 (100), 128 (53); HRMS (EI) calcd for $C_{14}H_9NOS_2$ (M^+): 271.0189; found: 271.0196.

4.3. General procedure for the preparation of MBH adducts 3

A mixture of compounds **2** (2 mmol), activated olefins (10 mmol), and DABCO (0.6 mmol) or (DMAP (1 mmol) in CH_2Cl_2 (10 mL)) was kept at room temperature for the given time. Then the mixture was extracted with CH_2Cl_2 (3×15 mL) and water (20 mL). The combined organic layer was washed with brine solution (3×15 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuo. The desired product **3** was obtained by flash column chromatography on silica (*n*-hexane/EtOAc, 6:1, v/v).

*4.3.1. Methyl 2-(hydroxy(2-(4-isopropylphenylthio)quinolin-3-yl)methyl)acrylate (**3a**).* White solid; mp 123.6–124.7 °C (*n*-hexane/EtOAc); R_f=0.55 (*n*-hexane/EtOAc, 2:1); IR (KBr): 3422 (OH), 1726 (CO_2CH_3) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=8.19 (1H, s, ArH), 7.79 (1H, d, *J*=8.0 Hz), 7.75 (1H, d, *J*=8.0 Hz), 7.56–7.60 (1H, m), 7.49 (2H, d, *J*=8.0 Hz, ArH), 7.41–7.45 (1H, m, ArH), 7.24 (2H, d, *J*=8.0 Hz, ArH), 6.42 (1H, s, =C*H*H), 6.15 (1H, s, =CH*H*), 5.70 (1H, s, C*H*OH), 3.80 (3H, s, OCH_3), 3.45 (1H, s, OH), 2.89–2.99 (1H, m, C*H*(CH_3)$_2$), 1.28 (6H, d, *J*=6.8 Hz, CH(C*H*$_3$)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ=167.2, 157.6, 149.6, 147.8, 140.7, 134.6 (2C), 134.4, 133.3, 129.9, 128.6, 128.04, 127.99, 127.9, 127.4 (2C), 126.7, 126.3, 69.0,

52.6, 34.2, 24.2 (2C); MS (ESI) m/z=394.2 (M^++1, 100); HRMS (ESI) calcd for $C_{23}H_{23}NO_3S$ (M^+): 393.1472; found: 393.1458.

*4.3.2. Ethyl 2-(hydroxy(2-(4-isopropylphenylthio)quinolin-3-yl)methyl) acrylate (**3b**).* White solid; mp 103.9–105.0 °C (*n*-hexane/EtOAc); R_f=0.56 (*n*-hexane/EtOAc, 2:1); IR (KBr): 3423 (OH), 1720 (CO_2Et) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=8.17 (1H, s, ArH), 7.76 (1H, d, J=8.0 Hz, ArH), 7.73 (1H, d, J=8.0 Hz, ArH), 7.54–7.58 (1H, m, ArH), 7.47 (2H, d, J=8.0 Hz, ArH), 7.39–7.43 (1H, m, ArH), 7.23 (2H, d, J=8.0 Hz, ArH), 6.40 (1H, s, =C*H*H), 6.13 (1H, s, =CH*H*), 5.68 (1H, s, C*H*OH), 4.24 (2H, q, J=7.2 Hz, OCH_2CH_3), 3.48 (1H, s, OH), 2.93 (1H, m, C*H*(CH_3)$_2$), 1.27–1.31 (9H, m, CH(CH_3)$_2$, and OCH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=166.6, 157.5, 149.4, 147.6, 140.8, 134.5 (2C), 134.2, 133.2, 129.7, 128.5, 127.9, 127.8, 127.6, 127.3 (2C), 126.6, 126.1, 69.1, 61.6, 34.3, 24.3 (2C), 14.6; MS (ESI) m/z=408.3 (M^++1, 100); HRMS (ESI) calcd for $C_{24}H_{25}NO_3S$ (M^+): 407.1636; found: 407.1629.

*4.3.3. Butyl 2-(hydroxy(2-(4-isopropylphenylthio)quinolin-3-yl)methyl) acrylate (**3c**).* Yellow oil; R_f=0.55 (*n*-hexane/EtOAc, 2:1); IR (neat): 3431 (OH), 1716 (CO_2Bu-*n*) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=8.16 (1H, s, ArH), 7.76 (1H, d, J=8.0 Hz, ArH), 7.32 (1H, d, J=8.0 Hz, ArH), 7.56 (1H, t, J=8.0 Hz, ArH), 7.47 (2H, d, J=8.0 Hz, ArH), 7.41 (1H, t, J=8.0 Hz, ArH), 7.23 (2H, d, J=8.0 H, ArH), 6.41 (1H, s, =C*H*H), 6.13 (1H, s, =CH*H*), 5.70 (1H, s, C*H*OH), 4.13–4.22 (2H, m, O$CH_2CH_2CH_2CH_3$), 3.46 (1H, s, OH), 2.88–2.99 (1H, m, C*H*(CH_3)$_2$), 1.59–1.66 (2H, m, O$CH_2CH_2CH_2CH_3$), 1.29–1.38 (2H, m, O$CH_2CH_2CH_2CH_3$), 1.28 (6H, d, J=6.8 Hz, CH(CH_3)$_2$), 0.88 (3H, t, J=7.2 Hz, O$CH_2CH_2CH_2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ=166.3, 157.2, 149.1, 147.3, 140.5, 134.2 (2C), 133.9, 132.9, 129.4, 128.2, 127.5, 127.4, 127.3, 127.0 (2C), 126.2, 125.8, 68.7, 65.1, 34.0, 30.6, 24.0 (2C), 19.2, 13.8; MS (EI) m/z=435 (M^+, 4), 334 (100); HRMS (EI) calcd for $C_{26}H_{29}NO_3S$ (M^+): 435.1966; found: 435.1961.

*4.3.4. Methyl 2-(hydroxy(2-(o-tolylthio)quinolin-3-yl)methyl) acrylate (**3d**).* White solid; mp 82.7–83.5 °C (*n*-hexane/EtOAc); R_f=0.57 (*n*-hexane/EtOAc, 2:1); IR (KBr): 3287 (OH), 1725 (CO_2CH_3) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=8.17 (1H, s, ArH), 7.72 (1H, d, J=8.0 Hz, ArH), 7.66 (1H, d, J=8.0 Hz, ArH), 7.49–7.54 (2H, m, ArH), 7.39 (1H, t, J=7.2 Hz, ArH), 7.28–7.31 (2H, m, ArH), 7.17–7.21 (1H, m, ArH), 6.42 (1H, s, =C*H*H), 6.13 (1H, s, =CH*H*), 5.70 (1H, s, C*H*OH), 3.79 (3H, s, OCH_3), 3.49 (1H, s, OH), 2.30 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=166.7, 156.7, 147.4, 142.3, 140.3, 135.6, 133.7, 132.5, 130.3, 129.7, 129.4, 129.0, 128.1, 127.5 (2C), 126.2, 126.0, 125.7, 68.7, 52.3, 21.0; MS (ESI) m/z=366.2 (M^++1, 100); HRMS (ESI) calcd for $C_{21}H_{19}NO_3S$ (M^+): 365.1164; found: 365.1168.

*4.3.5. Methyl 2-(hydroxy(2-(phenylthio)quinolin-3-yl)methyl) acrylate (**3e**).* White solid; mp 111.3–112.2 °C (*n*-hexane/EtOAc); R_f=0.56 (*n*-hexane/EtOAc, 2:1); IR (KBr): 3304 (OH), 1725 (CO_2CH_3) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=8.18 (1H, s, ArH), 7.72–7.53 (2H, m, ArH), 7.52–7.58 (3H, m, ArH), 7.41 (1H, t, J=8.0 Hz, ArH), 7.34–7.39 (3H, m, ArH), 6.41 (1H, s, =C*H*H), 6.13 (1H, s, =CH*H*), 5.69 (1H, s, C*H*OH), 3.78 (3H, s, OCH_3), 3.48 (1H, s, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ=166.6, 156.7, 147.3, 140.3, 134.0 (3C), 132.9, 130.9, 129.5, 128.7 (2C), 128.1 (2C), 127.64, 127.55, 126.3, 126.0, 68.7, 52.3; MS (EI) m/z=351 (M^+, 5), 293 (23), 292 (100); HRMS (EI) calcd for $C_{20}H_{17}NO_3S$ (M^+): 351.0953; found: 351.0938.

*4.3.6. Methyl 2-(hydroxy(2-(4-isopropylphenylthio)-6-methylquinolin-3-yl)methyl)acrylate (**3f**).* Yellow oil; R_f=0.52 (*n*-hexane/EtOAc, 2:1); IR (neat): 3406 (OH), 1724 (CO_2CH_3) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=8.08 (1H, s, ArH), 7.68 (1H, d, J=8.4 Hz, ArH), 7.49 (1H, s, ArH), 7.44 (2H, d, J=8.0 Hz, ArH), 7.39 (1H, dd, J=8.4, 1.6 Hz, ArH), 7.20 (2H, d, J=8.0 Hz, ArH), 6.38 (1H, s, =C*H*H), 6.12 (1H, s, =CH*H*), 5.66 (1H, s, C*H*OH), 3.77 (3H, s, OCH_3), 3.46 (1H, s, OH), 2.87–2.97 (1H, m, C*H*(CH_3)$_2$), 2.47 (3H, s, CH_3), 1.26 (6H, d, J=6.8 Hz, CH(CH_3)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ=166.7155.8, 148.9, 146.0, 140.4, 135.8, 133.7 (2C), 133.4, 133.1, 131.7, 128.0, 127.9, 127.5, 126.9 (2C), 126.4, 126.3, 68.7, 52.3, 33.9, 24.0 (2C), 21.6; MS (EI) m/z=407 (M^+, 6), 349 (28), 348 (100); HRMS (EI) calcd for $C_{24}H_{25}NO_3S$ (M^+): 407. 1686; found: 407.1694.

*4.3.7. Methyl 2-((6-chloro-2-(4-isopropylphenylthio)quinolin-3-yl) (hydroxy)methyl)acrylate (**3g**).* Yellow oil; R_f=0.53 (*n*-hexane/EtOAc, 2:1); IR (neat): 3433 (OH), 1724 (CO_2CH_3) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=8.07 (1H, s, ArH), 7.69 (1H, d, J=2.0 Hz, ArH), 7.65 (1H, d, J=8.8 Hz, ArH), 7.44–7.48 (3H, m, ArH), 7.23 (2H, d, J=8.0 Hz, ArH), 6.41 (1H, s, =C*H*H), 6.09 (1H, s, =CH*H*), 5.67 (1H, s, C*H*OH), 3.79 (3H, s, OCH_3), 3.59 (1H, s, OH), 2.89–2.99 (1H, m, C*H*(CH_3)$_2$), 1.28 (6H, d, J=7.2 Hz, CH(CH_3)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ=166.6, 157.8, 149.4, 145.6, 140.0, 134.5 (2C), 133.6, 132.8, 131.2, 130.2, 129.7, 127.8, 127.0 (3C), 126.7, 126.2, 68.5, 52.4, 34.0, 24.0 (2C); MS (ESI) m/z=428.3 (M^++1, 100); HRMS (ESI) calcd for $C_{23}H_{22}ClNO_3S$ (M^+): 427.1054; found: 427.1051.

*4.3.8. Methyl 2-(hydroxy(2-(m-tolylthio)quinolin-3-yl)methyl)acrylate (**3h**).* Colorless oil; R_f=0.53 (*n*-hexane/EtOAc, 2:1); IR (neat): 3408 (OH), 1722 (CO_2CH_3) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=8.18 (1H, s, ArH), 7.76 (1H, d, J=8.0 Hz, ArH), 7.73 (1H, d, J=8.0 Hz, ArH), 7.56 (1H, t, J=8.4 Hz, ArH), 7.41 (1H, t, J=8.0 Hz, ArH), 7.35 (1H, s, ArH), 7.32 (1H, d, J=8.0 Hz, ArH), 7.23 (1H, t, J=7.6 Hz, ArH), 7.14 (1H, d, J=7.6 Hz, ArH), 6.40 (1H, s, =C*H*H), 6.13 (1H, s, =CH*H*), 5.69 (1H, s, C*H*OH), 3.78 (3H, s, OCH_3), 3.50 (1H, s, OH), 2.34 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=167.0, 157.1, 147.6, 140.6, 138.8, 134.7, 134.3, 133.3, 131.3, 130.9, 129.8, 129.3, 128.9, 128.5, 127.94, 127.87, 126.6, 126.3, 69.0, 52.6, 21.8; MS (EI) m/z=365 (M^+, 5), 307 (27), 306 (100); HRMS (EI) calcd for $C_{21}H_{19}NO_3S$ (M^+): 365.1179; found: 365.1194.

*4.3.9. Methyl 2-((2-(4-chlorophenylthio)quinolin-3-yl)(hydroxy)methyl) acrylate (**3i**).* White solid; mp 121.3–121.9 °C (*n*-hexane/EtOAc); R_f=0.51 (*n*-hexane/EtOAc, 2:1); IR (KBr): 3276 (OH), 1723 (CO_2CH_3) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=8.18 (1H, s, ArH), 7.74 (2H, d, J=8.0 Hz, ArH), 7.55–7.60 (1H, m, ArH), 7.47 (2H, d, J=8.4 Hz, ArH), 7.41–7.45 (1H, m, ArH), 7.34 (2H, d, J=8.4 Hz, ArH), 6.42 (1H, s, =C*H*H), 6.09 (1H, s, =CH*H*), 5.69 (1H, s, C*H*OH), 3.80 (3H, s, OCH_3), 3.46 (1H, s, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ=166.6, 156.2, 147.3, 140.2, 135.6 (2C), 134.4, 134.1, 132.6, 129.7, 129.1, 128.9 (2C), 128.1, 127.7, 127.6, 126.2, 126.1, 68.6, 52.4; MS (ESI) m/z=386.2 (M^++1, 100); HRMS (ESI) calcd for $C_{20}H_{16}ClNO_3S$ (M^+): 385.0576; found: 385.0573.

*4.3.10. Methyl 2-((2-(2-chlorophenylthio)quinolin-3-yl)(hydroxy) methyl)acrylate (**3j**).* Colorless oil; R_f=0.52 (*n*-hexane/EtOAc, 2:1); IR (neat): 3435 (OH), 1723 (CO_2CH_3) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=8.22 (1H, s, ArH), 7.76 (1H, d, J=8.0 Hz, ArH), 7.72 (1H, d, J=8.0 Hz, ArH), 7.55–7.59 (2H, m, ArH), 7.42–7.48 (2H, m, ArH), 7.31 (1H, ddd, J=24.8, 7.6, 1.6 Hz, ArH), 7.26 (1H, dd, J=7.6, 1.6 Hz, ArH), 6.43 (1H, s, =C*H*H), 6.14 (1H, s, =C*H*H), 5.73 (1H, s, C*H*OH), 3.80 (3H, s, OCH_3), 3.48 (1H, s, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ=166.6, 155.5, 147.4, 140.2, 137.9, 136.0, 134.1, 133.1, 130.6, 129.8, 129.63, 129.56, 128. 3, 127.8, 127.6, 126.9, 126.3, 126.1, 68.9, 52.3; MS (ESI) m/z=386.2 (M^++1, 100); HRMS (ESI) calcd for $C_{20}H_{16}ClNO_3S$ (M^+): 385.0576; found: 385.0575.

*4.3.11. Methyl 2-((2-(4-bromophenylthio)quinolin-3-yl)(hydroxy) methyl)acrylate (**3k**).* Yellow solid; mp 98.7–99.6 °C (*n*-hexane/EtOAc); R_f=0.55 (*n*-hexane/EtOAc, 2:1); IR (KBr): 3435 (OH), 1723 (CO_2CH_3) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=8.19 (1H, s, ArH), 7.74 (2H, d, J=8.4 Hz, ArH), 7.58 (1H, t, J=8.0 Hz, ArH), 7.49 (2H, d, J=8.4 Hz, ArH), 7.39–7.45 (3H, m, ArH), 6.42 (1H, s, =C*H*H), 6.09 (1H, s, =CH*H*), 5.69 (1H, s, C*H*OH), 3.80 (3H, s, OCH_3), 3.50 (1H, s, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ=166.6, 156.1, 147.3, 140.2, 135.7 (2C), 134.1, 132.6, 131.8 (2C), 129.8, 129.7, 128.1, 127.7, 127.6, 126.3,

126.1, 122.6, 68.6, 52.4; MS (ESI) m/z=430.1 (M^++1, 100); HRMS (ESI) calcd for $C_{20}H_{16}BrNO_3S$ (M^+): 429.0084; found: 429.0071.

*4.3.12. Methyl 2-((2-(2,4-dichlorophenylthio)quinolin-3-yl)(hydroxy) methyl)acrylate (**3l**).* White solid; mp 108.3–109.5 °C (*n*-hexane/EtOAc); R_f=0.56 (*n*-hexane/EtOAc, 2:1); IR (KBr): 3435 (OH), 1723 (CO_2CH_3) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=8.21 (1H, s, ArH), 7.76 (1H, d, J=8.0 Hz, ArH), 7.72 (1H, d, J=8.0 Hz, ArH), 7.56–7.60 (1H, m, ArH), 7.53 (1H, d, J=8.4 Hz, ArH), 7.49 (1H, d, J=2.0 Hz, ArH), 7.42–7.46 (1H, m, ArH), 7.25 (1H, dd, J=8.4, 2.4 Hz, ArH), 6.44 (1H, s, =C*H*H), 6.11 (1H, s, =CH*H*), 5.73 (1H, s, C*H*OH), 3.80 (3H, s, OCH_3), 3.52 (1H, s, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ=166.9, 155.5, 147.6, 140.4, 139.3, 137.4, 135.5, 134.6, 133.1, 130.0 (2C), 129.3, 128.4, 128.1, 127.9, 127.6, 126.6, 126.5, 69.2, 52.7; MS (ESI) m/z=420.1 (M^++1, 100); HRMS (ESI) calcd for $C_{20}H_{15}Cl_2NO_3S$ (M^+): 419.0143; found: 419.0129.

*4.3.13. Methyl 2-((2-(2,4-dichlorophenylthio)-8-methylquinolin-3-yl)(hydroxy)methyl)acrylate (**3m**).* Yellow oil; R_f=0.53 (*n*-hexane/EtOAc, 2:1); IR (neat): 3393 (OH), 1707 (CO_2CH_3) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=8.14 (1H, s, ArH), 7.63 (1H, d, J=8.0 Hz, ArH), 7.58 (1H, d, J=8.0 Hz, ArH), 7.55 (1H, d, J=2.0 Hz, ArH), 7.40 (1H, d, J=6.8 Hz, ArH), 7.31 (2H, t, J=7.2 Hz, ArH), 6.46 (1H, s, =C*H*H), 6.07 (1H, s, =CH*H*), 5.75 (1H, s, C*H*OH), 3.81 (3H, s, OCH_3), 3.47 (1H, d, J=4.4 Hz, OH), 2.27 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=166.7, 154.1, 146.1, 140.4, 140.0, 138.3, 136.1, 135.6, 134.2, 131.6, 129.7, 129.6, 128.7, 127.8, 127.2, 126.0, 125.8, 125.5, 68.9, 52.4, 17.1; MS (ESI) m/z=434.2 (M^++1, 100); HRMS (ESI) calcd for $C_{21}H_{17}Cl_2NO_3S$ (M^+): 433.0384; found: 433.0385.

*4.3.14. Methyl 2-(hydroxy(8-methyl-2-(p-tolylthio)quinolin-3-yl)methyl)acrylate (**3n**).* Colorless oil; R_f=0.56 (*n*-hexane/EtOAc, 2:1); IR (neat): 3435 (OH), 1723 (CO_2CH_3) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=8.10 (1H, s, ArH), 7.55 (1H, d, J=8.0 Hz, ArH), 7.50 (2H, d, J=8.4 Hz, ArH), 7.38 (1H, d, J=7.2 Hz, ArH), 7.27 (1H, t, J=7.2 Hz, ArH), 7.20 (2H, d, J=8.0 Hz, ArH), 6.43 (1H, s, =C*H*H), 6.09 (1H, s, =CH*H*), 5.73 (1H, s, C*H*OH), 3.80 (3H, s, OCH_3), 3.42 (1H, d, J=4.4 Hz, OH), 2.40 (3H, s, CH_3), 2.32 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=166.7, 156.3, 146.1, 140.1, 138.6, 136.0, 135.4 (2C), 133.8, 131.7, 129.5, 129.4 (2C), 127.7, 126.5, 125.9, 125.42, 125.39, 68.7, 52.3, 21.5, 17.3; MS (ESI) m/z=380.2 (M^++1, 100); HRMS (ESI) calcd for $C_{22}H_{21}NO_3S$ (M^+): 379.1320; found: 379.1326.

*4.3.15. Methyl 2-(hydroxy(7-methyl-2-(p-tolylthio)quinolin-3-yl) methyl)acrylate (**3o**).* Colorless oil; R_f=0.52 (*n*-hexane/EtOAc, 2:1); IR (neat): 3435 (OH), 1721 (CO_2CH_3) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=8.11 (1H, s, ArH), 7.62 (1H, d, J=8.4 Hz, ArH), 7.53 (1H, s, ArH), 7.43 (2H, d, J=8.4 Hz, ArH), 7.24 (1H, dd, J=8.0, 1.6 Hz, ArH), 7.18 (2H, d, J=8.0 Hz, ArH), 6.41 (1H, s, =C*H*H), 6.11 (1H, s, =CH*H*), 5.70 (1H,s, C*H*OH), 3.78 (3H, s, OCH_3), 3.41 (1H, s, OH), 2.45 (3H, s, CH_3), 2.39 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=166.7, 157.0, 147.6, 140.4, 139.8, 138.2, 134.3 (2C), 133.5, 131.8, 129.5 (2C), 128.9, 127.5, 127.3, 127.24, 127.17, 124.2, 68.7, 52.3, 21.8, 21.4; MS (ESI) m/z=380.2 (M^++1, 100); HRMS (ESI) calcd for $C_{22}H_{21}NO_3S$ (M^+): 379.1320; found: 379.1327.

*4.3.16. Methyl 2-((2-(2,4-dichlorophenylthio)-5,7-dimethylquinolin-3-yl)(hydroxy)methyl)acrylate (**3p**).* Yellow oil; R_f=0.53 (*n*-hexane/EtOAc, 2:1); IR (neat): 3434 (OH), 1723 (CO_2CH_3) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=8.31 (1H, s, ArH), 7.47 (2H, dd, J=5.2, 2.8 Hz, ArH), 7.35 (1H, s, ArH), 7.23 (1H, d, J=9.2 Hz, ArH), 7.11 (1H, s, ArH), 6.40 (1H, s, =C*H*H), 6.11 (1H, s, =CH*H*), 5.67 (1H, s, C*H*OH), 3.79 (3H, s, OCH_3), 3.61 (1H, s, OH), 2.60 (3H, s, CH_3), 2.42 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=166.7, 154.3, 148.0, 140.4, 139.8, 138.7, 136.7, 134.8, 134.3, 131.4, 130.7, 129.6, 129.5, 129.1, 127.6, 127.2, 125.5, 123.8, 69.0, 52.3, 21.8, 18.7; MS (ESI) m/z=448.2 (M^++1, 100); HRMS (ESI) calcd for $C_{22}H_{19}Cl_2NO_3S$ (M^+): 447.0541; found: 447.0558.

*4.3.17. Methyl 2-(hydroxy(2-(thiophen-2-ylthio)quinolin-3-yl)methyl) acrylate (**3r**).* White solid; mp 87.2–87.9 °C (*n*-hexane/EtOAc); R_f=0.58 (*n*-hexane/EtOAc, 2:1); IR (KBr): 3286 (OH), 1723 (CO_2CH_3) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=8.15 (1H, s, ArH), 7.79 (1H, d, J=8.0 Hz, ArH), 7.73 (1H, d, J=8.0 Hz, ArH), 7.57 (1H, t, J=7.2 Hz, ArH), 7.54 (1H, dd, J=5.2, 0.8 Hz, ArH), 7.41 (1H, t, J=7.2 Hz, ArH), 7.31 (1H, dd, J=3.2, 1.2 Hz, ArH), 7.08 (1H, dd, J=5.2, 3.6 Hz, ArH), 6.42 (1H, s, =C*H*H), 6.09 (1H, s, =CH*H*), 5.70 (1H, s, C*H*OH), 3.79 (3H, s, OCH_3), 3.50 (1H, s, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ=166.6, 156.6, 147.3, 140.1, 135.3, 133.9, 131.9, 131.3, 129.6, 128.1, 127.8, 127.6 (2C), 127.0, 126.2, 126.0, 68.5, 52.4; MS (EI) m/z=357 (M^+, 7), 299 (23), 298 (100); HRMS (EI) calcd for $C_{18}H_{15}NO_3S_2$ (M^+): 357.0528; found: 357.0533.

4.4. General procedure for the preparation of 4 and 5

Method A: A stirred solution of **3** (1 mmol), CH_2Cl_2 (10 mL), and 95% concentrated H_2SO_4 (8 mmol) was kept at room temperature for the given time. The mixture was concentrated in vacuo and extracted with EtOAc (3×15 mL). The combined organic layer was washed in turns with 15% sodium carbonate solution (20 mL) and brine solution (3×15 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuo. The desired products **4a**–**h′**, **4n**, and **4o** were obtained by flash column chromatography on silica (*n*-hexane/EtOAc, 16:1, v/v).

Method B: A stirred solution of **3** (1 mmol), $ClCH_2CH_2Cl$ (10 mL), and CF_3SO_3H (3 mmol) was heated at reflux for the given time. The mixture was extracted with CH_2Cl_2 (3×15 mL) and the combined organic layer was washed in turns with 15% sodium carbonate solution (20 mL) and brine solution (3×15 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuo. The desired products **4i**–**j** and **4l** were obtained by flash column chromatography on silica (*n*-hexane/EtOAc, 16:1, v/v).

Method C: A stirred solution of **3** (1 mmol), CH_2Cl_2 (10 mL), and 95% concentrated H_2SO_4 (8 mmol) was kept at room temperature for the given time. Then the mixture was concentrated in vacuo and followed by addition of EtOAc (20 mL). When the pH value of this system was adjusted to over 12 with 15% sodium hydroxide solution (20 mL), a deposit was formed and filtered. The crude products were re-crystallized from ethanol to give the desired products **5i**–**n**.

*4.4.1. Methyl 2-(2-isopropyl-12H-thiochromeno[2,3-b]quinolin-12-yl) acrylate (**4a**).* White solid; mp 114.5–115.3 °C (*n*-hexane/EtOAc); R_f=0.68 (*n*-hexane/EtOAc, 16:1); IR (KBr): 1707 (CO_2CH_3) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=8.20 (1H, s, ArH), 7.97 (1H, d, J=8.0 Hz, ArH), 7.77 (1H, d, J=8.0 Hz, ArH), 7.63–7.67 (1H, m, ArH), 7.44 (1H, t, J=7.6 Hz, ArH), 7.34 (1H, d, J=8.0 Hz, ArH), 7.24 (1H, s, ArH), 7.11 (1H, dd, J=8.0, 1.6 Hz, ArH), 6.17 (1H, s, =CH*H*), 5.54 (1H, s, =C*H*H), 5.31 (1H, s, CH), 3.70 (3H, s, OCH_3), 2.85–2.95 (1H, m, C*H*$(CH_3)_2$), 1.25 (6H, d, J=6.8 Hz, CH(C*H*$_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ=166.5, 157.1, 148.4, 146.6, 137.6, 136.4, 132.4, 131.0, 129.7, 129.5, 128.3, 127.7, 127.5, 126.9, 126.5, 125.8, 125.4, 125.2, 52.1, 47.9, 33.8, 24.0, 23.9; MS (ESI) m/z=376.3 (M^++1, 100); HRMS (ESI) calcd for $C_{23}H_{21}NO_2S$ (M^+): 375.1304; found: 375.1311.

*4.4.2. Ethyl 2-(2-isopropyl-12H-thiochromeno[2,3-b]quinolin-12-yl) acrylate (**4b**).* White solid; mp 122.0–122.9 °C (*n*-hexane/EtOAc); R_f=0.68 (*n*-hexane/EtOAc, 16:1); IR (KBr): 1708 (CO_2Et) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=8.21 (1H, s, ArH), 7.97 (1H, d, J=8.0 Hz, ArH), 7.76 (1H, d, J=8.0 Hz, ArH), 7.65 (1H, t, J=8.0 Hz, ArH), 7.44 (1H, t, J=8.0 Hz, ArH), 7.34 (1H, d, J=8.0 Hz, ArH), 7.30 (1H, d, J=1.6 Hz, ArH), 7.11 (1H, dd, J=8.0, 1.6 Hz, ArH), 6.17 (1H, s, =CH*H*), 5.54 (1H, s, =C*H*H), 5.29 (1H, s, CH), 4.08–4.22 (2H, m, O*CH*$_2CH_3$), 2.85–2.95 (1H, m, C*H*$(CH_3)_2$), 1.22–1.26 (9H, m, OCH_2CH_3, and CH $(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ=166.4, 157.5, 148.7, 146.9,

138.2, 136.7, 132.7, 131.4, 130.1, 129.8, 128.7, 128.0, 127.8, 127.2, 126.5, 126.1, 125.7, 125.5, 61.4, 48.2, 34.2, 24.30, 24.26, 14.6; MS (ESI) *m*/*z*=390.4 (M^++1, 100); HRMS (ESI) calcd for $C_{24}H_{23}NO_2S$ (M^+): 389.1528; found: 389.1541.

*4.4.3. Butyl 2-(2-isopropyl-12H-thiochromeno[2,3-b]quinolin-12-yl) acrylate (**4c**).* Yellow oil; R_f=0.64 (*n*-hexane/EtOAc, 16:1); IR (neat): 1712 (CO_2Bu-*n*) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=8.20 (1H, s, ArH), 7.97 (1H, d, *J*=8.0 Hz, ArH), 7.76 (1H, d, *J*=8.0 Hz, ArH), 7.65 (1H, t, *J*=8.0 Hz, ArH), 7.44 (1H, t, *J*=8.0 Hz, ArH), 7.33 (1H, d, *J*=8.0 Hz, ArH), 7.30 (1H, d, *J*=2.0 Hz, ArH), 7.11 (1H, dd, *J*=8.0, 1.6 Hz, ArH), 6.15 (1H, s, =CH*H*), 5.54 (1H, s, =C*H*H), 5.30 (1H, s, CH), 4.04–4.15 (2H, m, OCH_2CH$_2$CH$_2$CH$_3$), 2.85–2.95 (1H, m, C*H*(CH_3)$_2$), 1.54–1.61 (2H, m, OCH$_2$CH_2CH$_2$CH$_3$), 1.24–1.33 (8H, m, OCH$_2$CH$_2$CH_2CH$_3$, and CH(CH_3)$_2$), 0.86 (3H, t, *J*=7.2 Hz, OCH$_2$CH$_2$CH$_2$CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=166.2, 157.1, 148.4, 146.5, 138.0, 136.4, 132.3, 131.1, 129.7, 129.5, 128.4, 127.7, 127.5, 126.9, 126.1, 125.8, 125.3, 125.1, 64.9, 47.9, 33.8, 30.6, 24.0, 23.9, 19.2, 13.8; MS (ESI) *m*/*z*=418.3 (M^++1, 100); HRMS (ESI) calcd for $C_{26}H_{27}NO_2S$ (M^+): 417.1826; 417.1819.

*4.4.4. Methyl 2-(4-methyl-12H-thiochromeno[2,3-b]quinolin-12-yl) acrylate (**4d**).* White solid; mp 140.4–141.3 °C (*n*-hexane/EtOAc); R_f=0.66 (*n*-hexane/EtOAc, 16:1); IR (KBr): 1712 (CO_2CH_3) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=8.34 (1H, s, ArH), 7.94 (1H, d, *J*=8.0 Hz, ArH), 7.78 (1H, d, *J*=8.0 Hz, ArH), 7.61–7.66 (1H, m, ArH), 7.41–7.45 (1H, m, ArH), 7.32 (1H, d, *J*=8.0 Hz, ArH), 7.17 (1H, t, *J*=8.0 Hz, ArH), 7.11 (1H, d, *J*=8.0 Hz, ArH), 6.14 (1H, s, =CH*H*), 5.80 (1H, s, =C*H*H), 5.40 (1H, s, CH), 3.70 (3H, s, OCH_3), 2.40 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=166.5, 156.7, 146.6, 136.9, 136.7, 136.2, 133.1, 133.0, 129.7, 128.9, 127.6 (2C), 127.5, 127.3, 126.9, 126.5, 125.6, 125.1, 52.1, 44.1, 20.0; MS (ESI) *m*/*z*=348.2 (M^++1, 100); HRMS (ESI) calcd for $C_{21}H_{17}NO_2S$ (M^+): 347.1042; found: 347.1053.

*4.4.5. Methyl 2-(12H-thiochromeno[2,3-b]quinolin-12-yl)acrylate (**4e**).* White solid; mp 153.1–153.7 °C (*n*-hexane/EtOAc); R_f=0.63 (*n*-hexane/EtOAc, 16:1); IR (KBr): 1712 (CO_2CH_3) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=8.22 (1H, s, ArH), 7.96 (1H, d, *J*=8.0 Hz, ArH), 7.77 (1H, d, *J*=8.0 Hz, ArH), 7.63–7.67 (1H, m, ArH), 7.40–7.46 (3H, m, ArH), 7.23–7.28 (2H, m, ArH), 6.17 (1H, s, =CH*H*), 5.57 (1H, s, =C*H*H), 5.29 (1H, s, CH), 3.69 (3H, s, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=166.4, 158.8, 146.7, 137.4, 136.5, 133.7, 132.8, 129.8, 129.6, 128.0, 127.8, 127.5 (2C), 127.2, 127.0, 126.9, 126.5, 125.8, 52.1, 48.3; MS (ESI) *m*/*z*=334.3 (M^++1, 100); HRMS (ESI) calcd for $C_{20}H_{15}NO_2S$ (M^+): 333.0813; found: 333.0809.

*4.4.6. Methyl 2-(2-isopropyl-9-methyl-12H-thiochromeno[2,3-b]quinolin-12-yl)acrylate (**4f**).* Yellow oil; R_f=0.68 (*n*-hexane/EtOAc, 16:1); IR (neat): 1718 (CO_2CH_3) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=8.11 (1H, s, ArH), 7.86 (1H, d, *J*=8.4 Hz, ArH), 7.53 (1H, s, ArH), 7.48 (1H, dd, *J*=8.4, 2.0 Hz, ArH), 7.33 (1H, d, *J*=8.0 Hz, ArH), 7.29 (1H, d, *J*=2.0 Hz, ArH), 7.10 (1H, dd, *J*=8.0, 2.0 Hz, ArH), 6.15 (1H, s, =CH*H*), 5.52 (1H, s, =C*H*H), 5.30 (1H, s, CH), 3.69 (3H, s, OCH_3), 2.84–2.90 (1H, m, C*H*(CH_3)$_2$), 2.50 (3H, s, CH_3), 1.24 (6H, d, *J*=6.8 Hz, CH(CH_3)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ=166.5, 156.0, 148.3, 145.3, 137.7, 135.8, 135.6, 132.6, 132.0, 131.1, 129.5, 128.3, 127.4, 127.0, 126.4, 126.3, 125.3, 125.2, 52.1, 48.0, 33.8, 24.0, 23.9, 21.7; MS (ESI) *m*/*z*=390.4 (M^++1, 100); HRMS (ESI) calcd for $C_{24}H_{23}NO_2S$ (M^+): 389.1422; found: 389.1421.

*4.4.7. Methyl 2-(9-chloro-2-isopropyl-12H-thiochromeno[2,3-b]quinolin-12-yl)acrylate (**4g**).* Yellow solid; mp 58.4–59.7 °C (*n*-hexane/EtOAc); R_f=0.65 (*n*-hexane/EtOAc, 16:1); IR (KBr): 1717 (CO_2CH_3) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=8.14 (1H, s, ArH), 7.89 (1H, d, *J*=8.8 Hz, ArH), 7.50 (1H, d, *J*=2.4 Hz, ArH), 7.57 (1H, dd, *J*=8.8, 2.4 Hz, ArH), 7.32 (1H, d, *J*=8.0 Hz, ArH), 7.30 (1H, d, *J*=1.6 Hz, ArH), 7.12 (1H, dd, *J*=8.0, 1.6 Hz, ArH), 6.18 (1H, s, =CH*H*), 5.53 (1H, s, =C*H*H), 5.31 (1H, s, CH), 3.70 (3H, s, OCH_3), 2.90 (1H, m, C*H*(CH_3)$_2$), 1.25 (6H, d, *J*=6.8 Hz, CH(CH_3)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ=166.1, 157.2, 148.2, 144.6, 137.0, 135.1, 131.8, 131.0, 130.5, 130.3, 129.2, 129.0, 127.1, 126.5, 125.8, 125.2, 125.0, 124.9, 51.8, 47.5, 33.5, 23.6 (2C); MS (EI) *m*/*z*=409 (M^+, 68), 366 (42), 349 (47), 326 (38), 324 (100), 308 (55); HRMS (EI) calcd for $C_{23}H_{20}ClNO_2S$ (M^+): 409.0932; found: 409.0926.

*4.4.8. Methyl 2-(3-methyl-12H-thiochromeno[2,3-b]quinolin-12-yl) acrylate (**4h**) and methyl 2-(1-methyl-12H-thiochromeno[2,3-b]quinolin-12-yl)acrylate (**4h′**).* Yellow oil; R_f=0.68 (*n*-hexane/EtOAc, 16:1); IR (neat): 1716 (CO_2CH_3) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=8.21–8.34 (1H, m, ArH), 7.96–8.00 (1H, m, ArH), 7.76–7.79 (1H, m, ArH), 7.63–7.65 (1H, m, ArH), 7.42–7.46 (1H, m, ArH), 7.04–7.35 (3H, m, ArH), 6.16–6.17 (1H, m, =CH*H*), 5.53–5.80 (1H, m, =C*H*H), 5.29–5.40 (1H, m, CH), 3.69 (3H, s, OCH_3), 2.48 (1.0H, s, CH_3, 4h′), 2.40 (0.4H, s, CH_3, 4h′), 2.34 (1.5H, s, CH_3, 4 h); ^{13}C NMR (100 MHz, $CDCl_3$) δ=166.5, 157.1, 156.8, 146.7, 146.5, 137.4, 136.9, 136.5, 136.4, 135.4, 133.7, 133.4, 130.2, 129.8, 129.4, 129.2, 128.9, 128.8, 128.4, 128.10, 128.06, 127.9, 127.7, 127.6, 127.5 (2C), 127.3, 127.2, 127.1, 127.0, 126.9, 126.6, 126.5, 126.4, 125.83, 125.76, 125.7, 125.1, 52.1, 48.6, 48.2, 47.8, 44.1, 20.1, 20.4, 20.0; MS (ESI) *m*/*z*=348.3 (M^++1, 100); HRMS (ESI) calcd for $C_{21}H_{17}NO_2S$ (M^+): 347.1062; found: 347.1051.

*4.4.9. Methyl 2-(2-chloro-12H-thiochromeno[2,3-b]quinolin-12-yl) acrylate (**4i**).* Yellow oil; R_f=0.61 (*n*-hexane/EtOAc, 16:1); IR (neat): 1718 (CO_2CH_3) m^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=8.21 (1H, s, ArH), 7.98 (1H, d, *J*=8.0 Hz, ArH), 7.78 (1H, d, *J*=8.0 Hz, ArH), 7.65–7.70 (1H, m, ArH), 7.45–7.49 (1H, m, ArH), 7.43 (1H, dd, *J*=8.0, 2.0 Hz, ArH), 7.37 (1H, d, *J*=8.0 Hz, ArH), 7.22 (1H, dd, *J*=8.0, 2.4 Hz, ArH), 6.18 (1H, s, =CH*H*), 5.55 (1H, s, =C*H*H), 5.29 (1H, s, CH), 3.70 (3H, s, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=166.2, 155.9, 146.6, 137.4, 136.5, 134.6, 133.2, 132.0, 130.7, 130.0, 127.7, 127.6, 127.4, 127.0, 126.9, 126.7, 126.5, 126.0, 52.1, 47.6; MS (ESI) *m*/*z* (%)=368.3 (M^++1, 100); HRMS (ESI) calcd for $C_{20}H_{14}ClNO_2S$ (M^+): 367.0512; 367.0517.

*4.4.10. Methyl 2-(4-chloro-12H-thiochromeno[2,3-b]quinolin-12-yl) acrylate (**4j**).* White solid; mp 162.4–163.3 °C (*n*-hexane/EtOAc); R_f=0.62 (*n*-hexane/EtOAc, 16:1); IR (KBr): 1710 (CO_2CH_3) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=8.42 (1H, s, ArH), 7.95 (1H, d, *J*=8.0 Hz, ArH), 7.81 (1H, d, *J*=8.0 Hz, ArH), 7.64–7.68 (1H, m, ArH), 7.44–7.48 (1H, m, ArH), 7.38 (1H, dd, *J*=8.0, 1.2 Hz, ArH), 7.33 (1H, dd, *J*=8.0, 1.2 Hz, ArH), 7.22 (1H, t, *J*=8.0 Hz, ArH), 6.18 (1H, s, =CH*H*), 6.15 (1H, s, =C*H*H), 5.39 (1H, s, CH), 3.72 (3H, s, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=166.1, 155.8, 146.6, 137.4, 136.0, 135.4, 134.3, 132.3, 130.0, 128.4, 127.8, 127.7, 127.6, 127.0, 126.8, 126.4, 125.9, 125.7, 52.2, 44.7; MS (ESI) *m*/*z*=368.3 (M^++1, 100); HRMS (ESI) calcd for $C_{20}H_{14}ClNO_2S$ (M^+): 367.0512; found: 367.0519.

*4.4.11. Methyl 2-(2,4-dichloro-12H-thiochromeno[2,3-b]quinolin-12-yl)acrylate (**4l**).* White solid; mp 207.3–208.5 °C (*n*-hexane/EtOAc); R_f=0.61 (*n*-hexane/EtOAc, 16:1); IR (KBr): 1713 (CO_2CH_3) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=8.41 (1H, s, ArH), 7.95 (1H, d, *J*=8.0 Hz, ArH), 7.81 (1H, d, *J*=8.0 Hz, ArH), 7.65–7.69 (1H, m, ArH), 7.47 (1H, t, *J*=7.2 Hz, ArH), 7.39 (1H, d, *J*=2.0 Hz, ArH), 7.34 (1H, d, *J*=2.0 Hz, ArH), 6.19 (1H, s, =CH*H*), 6.09 (1H, s, =C*H*H), 5.39 (1H, s, CH), 3.72 (3H, s, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=165.9, 154.9, 146.6, 137.6, 137.0, 136.0, 134.8, 133.6, 130.9, 130.2, 127.7, 127.6 (2C), 127.0, 126.5, 126.3, 126.2, 125.4, 52.2, 44.4; MS (ESI) *m*/*z*=402.2 (M^++1, 100); HRMS (ESI) calcd for $C_{20}H_{13}Cl_2NO_2S$ (M^+): 401.0024; found: 367.0041.

*4.4.12. Methyl 2-(2,7-dimethyl-12H-thiochromeno[2,3-b]quinolin-12-yl)acrylate (**4n**).* Yellow oil; R_f=0.62 (*n*-hexane/EtOAc, 16:1); IR (neat): 1718 (CO_2CH_3) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=8.15

(1H, s, ArH), 7.60 (1H, d, *J*=8.0 Hz, ArH), 7.48 (1H, d, *J*=6.8 Hz, ArH), 7.34 (1H, d, *J*=8.0 Hz, ArH), 7.30 (1H, d, *J*=8.0 Hz, ArH), 7.25 (1H, s, ArH), 7.04 (1H, d, *J*=8.0 Hz, ArH), 6.14 (1H, s, =C*H*H), 5.52 (1H, s, =CH*H*), 5.29 (1H, s, CH), 3.68 (3H, s, OCH_3), 2.76 (3H, s, CH_3), 2.34 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ=166.5, 155.8, 145.8, 137.8, 137.3, 136.6, 135.8, 132.8, 130.8, 129.8, 129.4, 127.8 (2C), 127.5, 126.9, 126.2, 125.6, 125.4, 52.1, 47.8, 21.1, 18.0; MS (ESI) *m*/*z*=362.2 (M^++1, 100); HRMS (ESI) calcd for $C_{22}H_{19}NO_2S$ (M^+): 361.1215; found: 361.1226.

*4.4.13. Methyl 2-(4H-thieno[3′,2′:5,6]thiopyrano[2,3-b]quinolin-4-yl)acrylate (**4o**).* White solid; mp 130.2–131.0 °C (*n*-hexane/EtOAc); R_f=0.66 (*n*-hexane/EtOAc, 16:1); IR (KBr): 1717 (CO_2CH_3) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=8.15 (1H, s, ArH), 7.96 (1H, d, *J*=8.0 Hz, ArH), 7.75 (1H, d, *J*=8.0 Hz, ArH), 7.64–7.68 (1H, m, ArH), 7.43–7.47 (1H, m, ArH), 7.30 (1H, d, *J*=5.2 Hz, ArH), 6.97 (1H, d, *J*=5.2 Hz, ArH), 6.24 (1H, s, =CH*H*), 5.74 (1H, s, =C*H*H), 5.42 (1H, s, CH), 3.74 (3H, s, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 156.1, 146.5, 139.1, 136.8, 130.1, 128.9, 127.6, 127.5, 126.8 (2C), 126.7, 126.6, 126.0, 125.5, 125.2, 52.3, 42.7; MS (ESI) *m*/*z*=340.2 (M^++1, 100); HRMS (ESI) calcd for $C_{18}H_{13}NO_2S_2$ (M^+): 339.0474; found: 339.0481.

*4.4.14. (E)-Methyl 3-chloro-5H-benzo[7,8]thiocino[2,3-b]quinoline-6-carboxylate sulfate (**5i**).* White solid; mp 242 °C(decomposed) (EtOH); R_f=0.56 (DCM/EtOH, 9:1); IR (KBr): 3464 (OH), 1712 (CO_2CH_3) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ=8.65 (1H, s, ArH), 7.94 (1H, s, ArH), 7.89 (1H, d, *J*=7.2 Hz, ArH), 7.68–7.72 (1H, m, ArH), 7.63 (1H, d, *J*=8.0 Hz, ArH), 7.57–7.61 (2H, m, ArH), 7.50–7.54 (2H, m, ArH), 4.56 (2H, s, CH_2), 3.82 (3H, s, OCH_3), 3.35 (2H, s, OH×2); ^{13}C NMR (100 MHz, DMSO-d_6) δ=166.1, 156.5, 146.6, 137.8, 137.1, 135.8 (2C), 133.6, 130.8, 130.7, 128.9 (2C), 128.6, 128.4, 127.1, 126.2, 125.8, 125.6, 60.3, 52.2; MS (ESI) *m*/*z*=464.2 (M^+–1, 100); HRMS (ESI) calcd for $C_{20}H_{16}ClNO_6S_2$ (M^+): 465.0118; found: 465.0129.

*4.4.15. (E)-Methyl 1-chloro-5H-benzo[7,8]thiocino[2,3-b]quinoline-6-carboxylate sulfate (**5j**).* White solid; mp 223 °C(decomposed) (EtOH); R_f=0.54 (DCM/EtOH, 9:1); IR (KBr): 3463 (OH), 1713 (CO_2CH_3) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ=8.68 (1H, s, ArH), 7.94 (1H, s, ArH), 7.91 (1H, d, *J*=8.0 Hz, ArH), 7.69–7.73 (1H, m, ArH), 7.63 (2H, dd, *J*=8.0, 1.6 Hz, ArH), 7.55–7.59 (1H, m, ArH), 7.48 (1H, t, *J*=7.6 Hz, ArH), 7.39 (1H, t, *J*=7.6 Hz, ArH), 4.55 (2H, s, CH_2), 3.82 (3H, s, OCH_3), 3.36 (2H, s, OH×2); ^{13}C NMR (100 MHz, DMSO-d_6) δ=166.1, 156.0, 146.8, 138.1, 137.4, 137.2, 136.5, 131.0, 130.8, 130.5, 129.8, 129.0, 128.7, 127.7, 127.3, 126.4, 126.1, 125.7, 60.4, 52.4; MS (ESI) *m*/*z*=464.1 (M^+–1, 100); HRMS (ESI) calcd for $C_{20}H_{16}ClNO_6S_2$ (M^+): 465.0118; found: 367.0131.

*4.4.16. (E)-Methyl 3-bromo-5H-benzo[7,8]thiocino[2,3-b]quinoline-6-carboxylate sulfate (**5k**).* White solid; mp 235 °C(decomposed) (EtOH); R_f=0.51 (DCM/EtOH, 9:1); IR (KBr): 3458 (OH), 1712 (CO_2CH_3) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ=8.65 (1H, s, ArH), 7.94 (1H, s, ArH), 7.90 (1H, d, *J*=8.0 Hz, ArH), 7.69–7.73 (1H, m, ArH), 7.64–7.66 (2H, m, ArH), 7.51–7.58 (3H, m, ArH), 4.56 (2H, s, CH_2), 3.82 (3H, s, OCH_3), 3.34 (2H, s, OH×2); ^{13}C NMR (100 MHz, DMSO-d_6) δ=166.1, 156.5, 146.6, 137.9, 137.3, 136.1 (2C), 131.9 (2C), 130.9, 130.6, 129.0, 128.7, 127.2, 126.3, 125.8, 125.6, 122.3, 60.4, 52.4; MS (ESI) *m*/*z*=508.1 (M^+–1, 100); HRMS (ESI) calcd for $C_{20}H_{16}BrNO_6S_2$ (M^+): 508.9689; found: 508.9672.

*4.4.17. (E)-Methyl 1,3-dichloro-5H-benzo[7,8]thiocino[2,3-b]quinoline-6-carboxylate sulfate (**5l**).* White solid; mp 246 °C(decomposed) (EtOH); R_f=0.52 (DCM/EtOH, 9:1); IR (KBr): 3458 (OH), 1710 (CO_2CH_3) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ=8.68 (1H, s, ArH), 7.91 (2H, m, ArH), 7.84 (1H, d, *J*=2.4 Hz, ArH), 7.68 (1H, d, *J*=8.4 Hz, ArH), 7.62 (1H, d, *J*=8.4 Hz, ArH), 7.57–7.59 (1H, m, ArH), 7.50 (1H, dd, *J*=8.4, 2.4 Hz, ArH), 4.57 (2H, s, CH_2), 3.82 (3H, s, OCH_3), 3.35 (2H, s, OH×2); ^{13}C NMR (100 MHz, DMSO-d_6) δ=166.1, 155.5, 146.7, 138.4, 138.1, 137.7, 137.0, 134.7, 131.0, 130.8, 129.4, 128.7, 128.2, 127.9, 127.3, 126.5, 125.9, 125.7, 60.4, 52.4; MS (ESI) *m*/*z*=498.2 (M^+–1, 100); HRMS (ESI) calcd for $C_{20}H_{15}Cl_2NO_6S_2$ (M^+): 498.9787; found: 498.9774.

*4.4.18. (E)-Methyl 1,3-dichloro-12-methyl-5H-benzo[7,8]thiocino[2,3-b]quinoline-6-carboxylate sulfate (**5m**).* White solid; mp 257 °C (decomposed) (EtOH); R_f=0.58 (DCM/EtOH, 9:1); IR (KBr): 3447 (OH), 1716 (CO_2CH_3) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ=8.65 (1H, s, ArH), 7.94 (1H, s, ArH), 7.87 (1H, d, *J*=2.4 Hz, ArH), 7.78 (1H, d, *J*=8.0 Hz, ArH), 7.73 (1H, d, *J*=8.0 Hz, ArH), 7.54 (1H, d, *J*=8.0 Hz, ArH), 7.42 (1H, t, *J*=8.0 Hz, ArH), 4.61 (2H, s, CH_2), 3.84 (3H, s, OCH_3), 3.35 (2H, d, *J*=2.4 Hz, OH×2), 2.22 (3H, s, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ=166.1, 154.5, 145.4, 139.5, 138.5, 138.1, 136.6, 135.0, 134.6, 131.0, 130.8, 129.2, 128.7, 127.7, 126.6, 126.0, 125.4, 125.0, 60.4, 52.4, 16.4; MS (ESI) *m*/*z*=512.1 (M^+–1, 1); HRMS (ESI) calcd for $C_{21}H_{17}Cl_2NO_6S_2$ (M^+): 512.9796; found: 512.9787.

*4.4.19. (E)-Methyl 3,12-dimethyl-5H-benzo[7,8]thiocino[2,3-b]quinoline-6-carboxylate sulfate (**5n**).* White solid; mp 215 °C(decomposed) (EtOH); R_f=0.64 (DCM/EtOH, 9:1); IR (KBr): 3465 (OH), 1709 (CO_2CH_3) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ=8.59 (1H, s, ArH), 7.96 (1H, s, ArH), 7.71 (1H, d, *J*=8.0 Hz, ArH), 7.51 (2H, d, *J*=8.0 Hz, ArH), 7.40 (1H, t, *J*=7.6 Hz, ArH), 7.29 (2H, d, *J*=8.0 Hz, ArH), 4.61 (2H, s, CH_2), 3.83 (3H, s, OCH_3), 3.35 (2H, s, OH×2), 2.38(3H, s, CH_3), 2.28 (3H, s, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ=166.2, 156.5, 145.5, 138.5, 137.8, 137.1, 134.9 (2C), 134.7, 130.6, 130.4, 129.4 (2C), 126.5, 125.7, 125.5, 125.3, 125.0, 60.4, 52.3, 20.9, 16.6; MS (ESI) *m*/*z*=458.1 (M^+–1, 100); HRMS (ESI) calcd for $C_{22}H_{21}NO_6S_2$ (M^+): 459.0732; found: 459.0717.

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Supplementary data

Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2011.03.039.

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