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ARTICLE

Synthesis of thieno[2,3–*b*]quinoline and selenopheno[2,3–*b*]quinoline derivatives *via* iodocyclization reaction and DFT mechanistic study

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In this letter, we report the regioselective iodocyclization reaction of 3-alkynyl-2-(methylthio)quinolines and 3-alkynyl-2-(methylseleno)quinolines for the synthesis of thieno[2,3–*b*]quinoline and selenopheno[2,3–*b*]quinoline derivatives. Further, the resulting halides derivatives were allowed for structural diversification by employing various palladium-catalyzed Sonogashira, Suzuki, and Heck reactions, which can act as the important intermediates for building other valuable compounds. All compounds were fully characterized by the FT-IR, mass, ^{1}H NMR, and ^{13}C NMR spectral data. Finally, the structure of the thieno[2,3–*b*]quinoline derivative was confirmed by X–ray crystallography. This methodology provided a novel pathway to access quinoline fused heterocycles via iodocyclization reaction. Further, the reaction process was well elucidated by density functional theory calculations.

Introduction

Nitrogen-containing heterocycles are gaining more importance as being the centre of activity.[1] Among the *N*–heterocycles, quinoline subunits are prevalent in natural products[2] and pharmaceutical molecules[3] and are important intermediates for asymmetric synthesis.[4] Further, the synthesis of quinoline fused heterocycles has attracted considerable attention because of their interesting properties and biological activities.[5] In this regard, little is known about annulated furoquinoline and thienoquinoline heterocycles with different features and applications in the literature.[6] However, to the best of our knowledge, selenophenoquinoline heterocycles have never been described thus far due to difficulties involved in their synthesis. Therefore, the development of new synthetic methodologies to access quinoline–fused heterocycles becomes an important objective. In this regard, the iodocyclization of acetylenic substrates bearing a suitably placed nucleophilic group has become a powerful synthetic tool for the synthesis of structurally diverse heterocycles.[7,8] In our continuing efforts toward the synthesis of heterocycles, we used this iodocyclization methodology for the synthesis of 4-alkyl-2-imino-1,3-oxaselenolanes,[9] 3-aryl-5,6-dihydrothiazolo[2,3–*c*][1,2,4]triazoles or 2-aryl-5*H*-[1,2,4]triazolo[5,1–*b*][1,3]thiazines[10] and for the construction of bicyclic β–lactams starting from allyl–thioureas,[11] alkyne–thioureas,[12] alkyne–selenoureas,[13] allene–selenoureas[13] and allene–thioureas.[14] These results prompted us to investigate the applicability of iodocyclization reaction for the synthesis of thieno[2,3–*b*]quinoline and selenopheno[2,3–*b*]quinoline heterocycles. To the best of our knowledge such iodocyclization approach was never described for the synthesis of thieno[2,3–*b*]quinoline or selenopheno[2,3–*b*]quinoline heterocycles. Moreover, the quinoline fused S/Se-heterocycles synthesized *via* electrophilic iodocyclization will be useful for the development of polycyclic aromatic hydrocarbons/acenes.[15] Herein, we describe for the first time, the synthesis of thieno[2,3–*b*]quinoline and selenopheno[2,3–*b*]quinoline derivatives *via* iodine-mediated electrophilic cyclization of 3-alkynyl-2-(methylthio)quinolines and 3-alkynyl-2-(methylseleno)quinolines respectively and their density functional theory (DFT) mechanistic study.

Results and discussion

Our investigations in this direction were began with 2-(methylthio)- and 2-(methylseleno)-quinoline-3-carbaldehydes **1a-1h** which were readily prepared from corresponding 2-chloroquinoline-3-carbaldehydes using a literature procedure (see Supporting Information).[16] In recent years, the preparation of alkynes from carbonyl compounds *via* a one-carbon homologation by Corey–Fuchs reaction[17] has become a very useful pathway for the synthesis of acetylenes.[18] The quinoline-3-carbaldehydes **1a-1h** were converted to the corresponding dibromo olefin which on treatment with *n*-butyl

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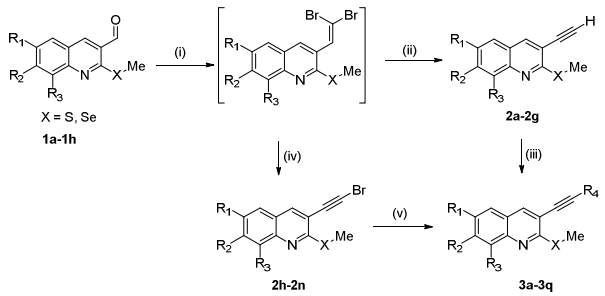
lithium readily yielded the terminal alkynes **2a–2g** in good yields (Table 1, entries 1–7). However, the dibromo intermediate on treatment with DBU in DMSO at room temperature *via* dehydrohalogenation afforded the bromoalkyne compounds **2h–2n** in 75–86% yields (Table 1, entries 8–13). Next, under Sonogashira coupling conditions, the terminal alkynes **2a–2g** were alkylated to with aryl halides to give substituted alkynes **3a–3j** in good yields (Table 1, entries 14–23). Further, to study the effect of substitution at the alkyne part, the bromoalkyne derivatives **2h–2n** were converted to the corresponding dialkynes **3k–3q** under Sonogashira coupling reaction conditions (Table 1, entries 24–30).[19] The structures of **2a–2n** and **3a–3q** were confirmed by the IR, ^{1}H NMR, ^{13}C NMR and HRMS spectral analysis.

Table 1. Synthesis of 3-alkynyl-2-(methylthio)quinoline and 3-alkynyl-2-(methylseleno)quinoline derivatives **2** and **3**.[a]

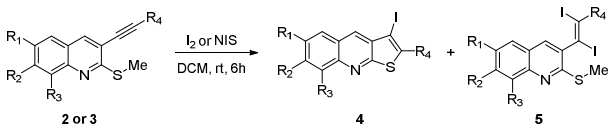


Entry	X	R^1	R^2	R^3	R^4	**2** or **3** yield (%)[b]
1	S	$-CH_3$	-H	-H	-H	**2a** (67%)
2	S	-H	$-CH_3$	-H	-H	**2b** (69%)
3	S	-H	-H	$-CH_3$	-H	**2c** (72%)
4	S	-H	-H	-H	-H	**2d** (75%)
5	Se	$-CH_3$	-H	-H	-H	**2e** (65%)
6	Se	-H	$-CH_3$	-H	-H	**2f** (66%)
7	Se	-H	-H	-H	-H	**2g** (71%)
8	S	$-CH_3$	-H	-H	-Br	**2h** (77%)
9	S	-H	$-CH_3$	-H	-Br	**2i** (86%)
10	S	-H	-H	-H	-Br	**2j** (84%)
11	Se	$-CH_3$	-H	-H	-Br	**2k** (81%)
12	Se	-H	$-CH_3$	-H	-Br	**2l** (77%)
13	Se	-H	-H	$-CH_3$	-Br	**2m** (71%)
14	Se	-H	-H	-H	-Br	**2n** (75%)
15	S	$-CH_3$	-H	-H	$-C_6H_5$	**3a** (76%)
16	S	-H	$-CH_3$	-H	$-C_6H_5$	**3b** (79%)
17	S	-H	-H	-H	$-C_6H_5$	**3c** (87%)
18	S	$-CH_3$	-H	-H	-*m*-$CH_3C_6H_4$	**3d** (80%)
19	S	-H	$-CH_3$	-H	-*m*-$CH_3C_6H_4$	**3e** (75%)
20	S	-H	-H	-H	-*m*-$CH_3C_6H_4$	**3f** (72%)
21	S	$-CH_3$	-H	-H	-*p*-$CH_3OC_6H_4$	**3g** (70%)
22	Se	$-CH_3$	-H	-H	$-C_6H_5$	**3h** (70%)
23	Se	-H	$-CH_3$	-H	$-C_6H_5$	**3i** (72%)
24	Se	-H	-H	-H	$-C_6H_5$	**3j** (67%)
25	S	$-CH_3$	-H	-H	$-CCC_6H_5$	**3k** (65%)
26	S	-H	$-CH_3$	-H	$-CCC_6H_5$	**3l** (71%)
27	S	-H	-H	-H	$-CCC_6H_5$	**3m** (67%)
28	Se	$-CH_3$	-H	-H	$-CCC_6H_5$	**3n** (70%)
29	Se	-H	$-CH_3$	-H	$-CCC_6H_5$	**3o** (73%)
30	Se	-H	-H	$-CH_3$	$-CCC_6H_5$	**3p** (76%)
31	Se	-H	-H	-H	$-CCC_6H_5$	**3q** (70%)

[a]**Reaction conditions:** (i) CBr_4, PPh_3, DCM, 0 °C, 1 h (ii) *n*-BuLi, -78 °C, Et_2O, 1 h (iii) aryl iodide, $Pd(PPh_3)_2Cl_2$, CuI, NEt_3, THF, rt, 12 h; or Phenylboronic acid, 2M Na_2CO_3, $Pd(PPh_3)_2Cl_2$, DME, 90 °C (iv) DBU, DMSO, 1 h (v) Phenyl acetylene, CuI, $Pd(PPh_3)_2Cl_2$, NEt_3, PPh_3, 70 °C, 5 h. [b]Isolated yields.

We first examined the iodocyclization reaction of unsubstituted alkyne **2a** with 2 equiv of iodine in DCM at room temperature. The reaction resulted in the formation of thieno[2,3–*b*]quinoline derivative **4a** in 25% yield along with the diiodo compound **5a** in 23% yield. Further, the use of K_2CO_3 as a base with 2 equiv of iodine in the iodocyclization reaction provided the desired thieno[2,3–*b*]quinoline **4a** in 32% yield along with traces of diiodo compound **5a**. To improve the yield of cyclization product, different reaction conditions were screened (see Supporting Information). Best result was obtained, when the iodocyclization reaction was carried out using 2 equiv of NIS in CH_2Cl_2 at room temperature to afford desired thieno[2,3–*b*]quinoline **4a** in 69% yield with traces of diiodo compound **5a** (Table 2, entry 1).

Table 2. Synthesis of thieno[2,3–b]quinoline derivatives **4** *via* iodocyclization,[a] and calculated activation Gibbs free energies (ΔG^a) [kcal/mol].



Entry	R^1	R^2	R^3	R^4	**4** yield (%)[b]	ΔG^{ad}
1	$-CH_3$	-H	-H	-H	**4a** (69%)[c]	21.2
2	-H	$-CH_3$	-H	-H	**4b** (70%)[c]	21.5
3	-H	-H	$-CH_3$	-H	**4c** (72%)[c]	21.4
4	-H	-H	-H	-H	**4d** (61%)[c]	21.5
5	$-CH_3$	-H	-H	-Br	**4e** (81%)[c]	17.7
6	-H	$-CH_3$	-H	-Br	**4f** (85%)[c]	17.9
7	-H	-H	-H	-Br	**4g** (84%)[c]	18.0
8	$-CH_3$	-H	-H	$-C_6H_5$	**4h** (90%)	7.7
9	-H	$-CH_3$	-H	$-C_6H_5$	**4i** (79%)	7.7
10	-H	-H	-H	$-C_6H_5$	**4j** (86%)	8.8
11	$-CH_3$	-H	-H	-*m*-$CH_3C_6H_4$	**4k** (83%)	5.9
12	-H	$-CH_3$	-H	-*m*-$CH_3C_6H_4$	**4l** (80%)	6.9
13	-H	-H	-H	-*m*-$CH_3C_6H_4$	**4m** (86%)	7.2
14	$-CH_3$	-H	-H	-*p*-$CH_3OC_6H_4$	**4n** (77%)	5.0
15	$-CH_3$	-H	-H	$-CCC_6H_5$	**4o** (81%)	9.5
16	-H	$-CH_3$	-H	$-CCC_6H_5$	**4p** (84%)	9.0

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17	-H	-H	-H	$-CCC_6H_5$	**4q** (91%)	9.5

[a]All iodocyclization reactions were conducted at room temperature with 2.0 equiv of I_2 in CH_2Cl_2 unless and otherwise stated. [b]Isolated yields. [c]Reaction was carried out using 2 equiv of NIS in CH_2Cl_2 at room temperature. [d]Calculated by M06-2X/6-311+G**+Midi!//M06-2X/6-31G*+Midi! method. Thermal correction was calculated at T = 298 K and solvent effect (CH_2Cl_2) was taken into account by SCRF-PCM method.

Under optimal conditions, the iodocyclization reaction of other unsubstituted alkyne **2b–2d** and bromoalkyne **2h–2j** was carried out and the corresponding thieno[2,3–*b*]quinoline derivatives **4b–4g** were obtained in good yields (entries 2–7). Next, the iodocyclization reaction of substituted alkyne **3a** under similar reaction conditions afforded desire product **4h** in 83% yield (see Supporting Information). However, when the iodocyclization reaction of **3a** was carried out using 2 equiv of iodine in CH_2Cl_2 at room temperature, the thieno[2,3–*b*]quinoline **4h** was obtained in 90% yield (Table 2, entry 8). To further expand the application scope of this reaction, the iodocyclization reaction of other substituted alkynes **3b–3g** and **3k–3m** was carried out using 2 equiv of iodine in CH_2Cl_2 at room temperature and the corresponding thieno[2,3–*b*]quinoline derivatives **4i–4q** were obtained in good to excellent yields (Table 2, entries 9–17). The present iodocyclization reaction was found to be highly dependent on the type of iodinating reagent used in the cyclization reaction. The nature of R^1–R^3 groups on quinoline ring system had very little effect on the iodocyclization reaction and a variety of functional groups were well tolerated under the present reaction conditions. The structure of thieno[2,3–*b*]quinoline derivatives **4** was confirmed by the studies of IR, ^{1}H NMR, ^{13}C NMR, and HRMS spectral analysis. Finally, the molecular structure of the representative thieno[2,3–*b*]quinoline compound **4a** was determined by the X–ray crystallography (see Supporting Information).[20]

To investigate the reaction mechanism of iodocyclization of **2** or **3**, we performed DFT calculations. The relative Gibbs free energy profiles and the stationary point structures of the reactions leading to **4a–4d** (R^4 = -H) are presented in Figure 1, and those for the other reactions are in Figures S2–S6 in Supporting Information. All reactions proceed by a stepwise mechanism and have two transition states (TSs) corresponding to iodine addition (TS1) and elimination of CH_3I or *N*-methylsuccinimide (TS2). The rate-determining step is iodine addition process (TS1) in all reactions, since the relative Gibbs free energy of TS1 is always higher than that of TS2. We can see that energy profiles for reactions **2a-2d** are similar to each other. For instance, relative energies of TS1 in reactions **2a-2d** are 21.2, 21.5, 21.4, and 21.5 kcal/mol, respectively. The shapes of the potential energy profiles of iodocyclization reactions depend only on R^4 on alkynyl group, and are hardly affected by R^1-R^3 groups on quinoline ring system. Figure 2 shows the optimized TS structures with the characteristic interatomic distances (C···I, I···N, and C···S distances in TS1, and

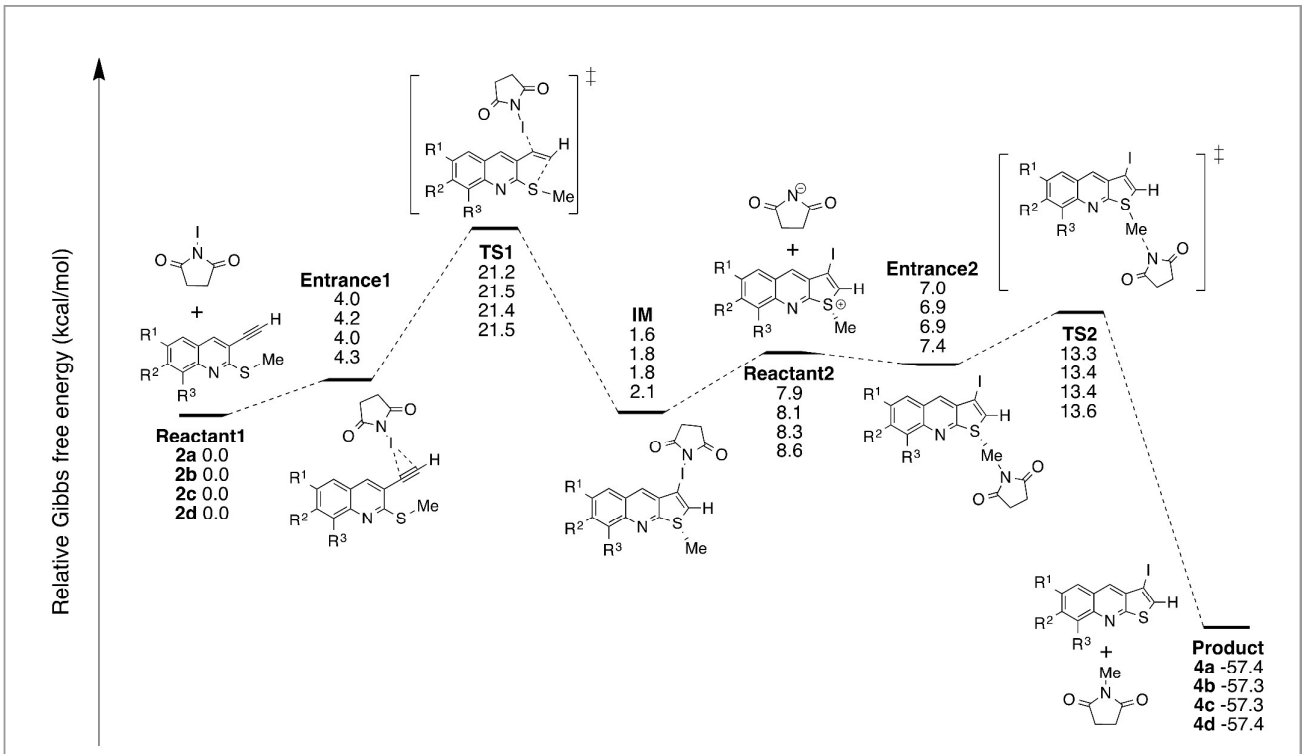

Figure 1. Relative Gibbs free energy profiles at T = 298K of the reactions leading to **4a-4d** obtained by M06-2X/6-311+G**+Midi!//M06-2X/6-31G*+Midi! calculations. Solvent effect (solvent = CH_2Cl_2) was taken into account by SCRF-PCM method.

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S···C and C···N ones in TS2) in reactions **2a-2d**. (See Supporting Information Figures S2-S6 for reactions leading to **4e-4q**). Clearly, R^1-R^3 groups on quinoline ring hardly affect the TS structures, as well as the potential energy profiles.

Next, to explain the reactivity of **2** or **3** for iodocyclization, we focus on the charge of the carbon atom in alkynyl group, which forms a new C–S bond in the reaction. Figure 3 shows the relationship between natural charge of the carbon atom

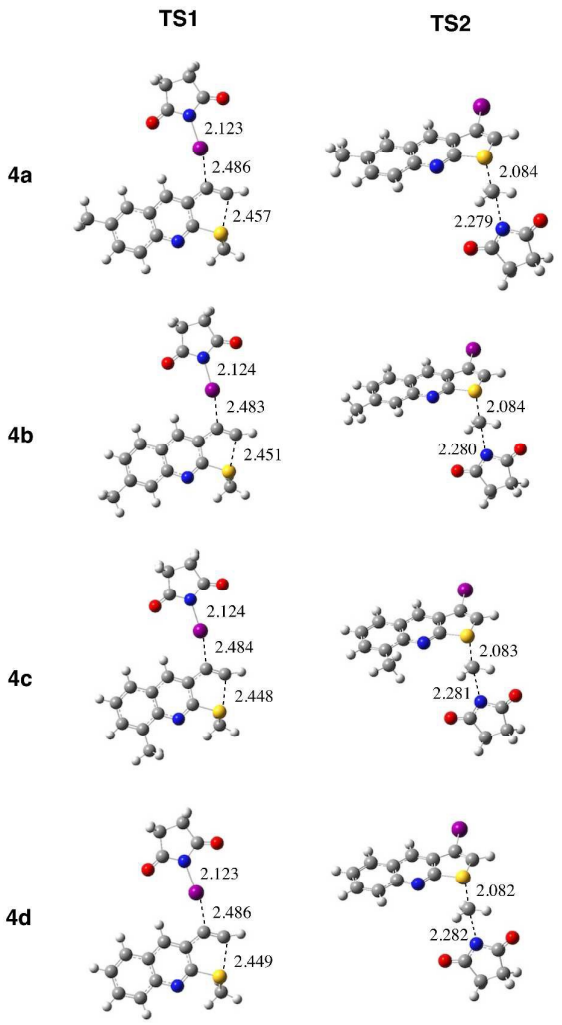


Figure 2. **Optimized transition state structures with characteristic interatomic distances [Å] of** TS1 **and** TS2 **in reactions leading to** 4a-4d.

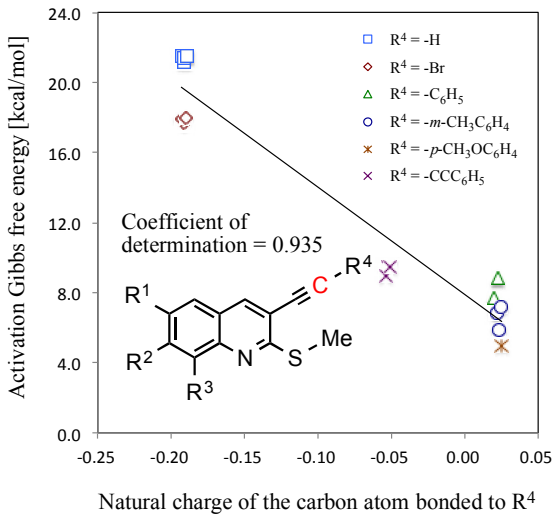
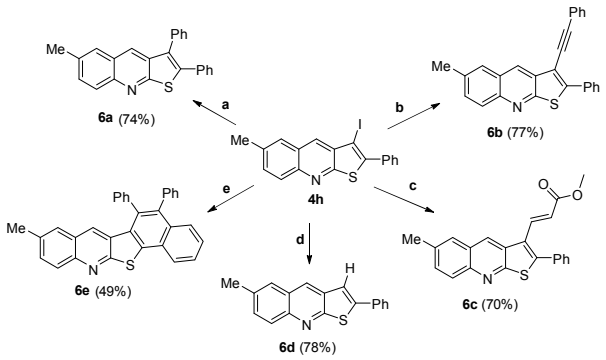


Figure 3. Relationship between natural charge of the carbon atom bonded to R^4 group (red-marked) and ΔG^a values of sulfur-containing systems.

and the activation Gibbs free energy (ΔG^a), which correspond to the highest relative Gibbs free energy in each reaction. Since the relative Gibbs free energy of TS1 (iodine addition process) is always higher than that of TS2, as stated above, ΔG^a values correspond to the relative Gibbs free energies of TS1. A clear linear relationship (Coefficient of determination = 0.935) between these values can be found. Iodocyclization reaction proceeds more easily with the less electron-rich carbon atom. In addition, the charge of the carbon atom in alkynyl group clearly depends on R^4 group. Therefore, our DFT results indicated that R^4 group was important to determine the reactivity for iodocyclization, which fact was consistent with experimental results.

Further, the presence of iodine on the thieno[2,3–b]quinoline product **4h** is an interesting feature of the iodocyclization which allowed us further structural elaboration, most notable by Suzuki coupling,[21] Sonogashira coupling,[22] Heck reaction,[23] dehydroiodination[24] and alkyne annulation reaction[25] to afford the corresponding diversified quinoline moieties **6a–6e** (Scheme 1).

Scheme 1. Functionalization of the 3-iodo-6-methyl-2-phenylthieno[2,3–b]quinoline 4h**.**



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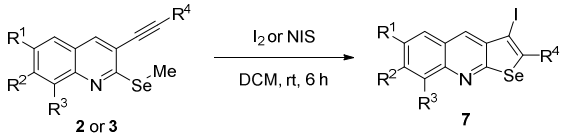
Reaction conditions: (a) Phenylboronic acid, $Pd(OAc)_2$, Cs_2CO_3, DMF, 110 ^{0}C. (b) Phenyl acetylene, $Pd(PPh_3)_2Cl_2$, CuI, NEt_3, THF, room temperature. (c) Methyl acrylate, PPh_3, $Pd(OAc)_2$, K_2CO_3 DMF, 110 ^{0}C. (d) $Pd(PPh_3)_2Cl_2$, NEt_3, HCOOH, DMF, 60 ^{0}C. (e) Diphenylacetylene, $Pd(OAc)_2$, NaOAc, LiCl, DMF, 100 ^{0}C.

Interest in the synthesis of selenium-containing heterocycles has increased in recent years because of their interesting reactivities and their potential biological activities.[26] With the optimized reaction conditions in hand, we next investigated the scope of this reaction for the iodocyclization reaction of 3-alkynyl-quinoline derivatives having methylseleno group at 2-position (Table 3). Under standard conditions, the iodocyclization of unsubstituted alkynes **2e–2g** and bromoalkynes **2k–2m** sing 2 equiv of NIS in CH_2Cl_2 at room temperature readily afforded the corresponding selenopheno[2,3–*b*]quinoline derivatives **7a–7f** in good yields (Table 3, entries 1–6). However, the iodocyclization of substituted alkyne compounds **3h–3j** and **3n–3q** was carried out using 2 equiv of iodine in CH_2Cl_2 at room temperature to afford the corresponding selenopheno[2,3–*b*]quinoline derivatives **7g–7m** in good yields (entries 7–13). The structure of selenopheno[2,3–*b*]quinoline derivatives **7** was confirmed by the studies of IR, ^{1}H NMR, ^{13}C NMR, and HRMS spectral analysis. The calculated ΔG^a values are listed in Table 3, and the relative Gibbs free energy profiles and the stationary point structures of the reactions leading to **7a–7m** are presented in Figures S8–S11 in Supporting Information. As in the case of sulfur-containing systems, we can find similar observation for selenium-containing system that only R^4 group affects the ΔG^a value and determines the reactivity of molecules (see Figures S8-S13 in Supporting Information for details).

Table 3. Synthesis of selenopheno[2,3–b]quinoline derivatives **7**,[a] and calculated activation Gibbs free energies (ΔG^a) [kcal/mol].



Entry	R^1	R^2	R^3	R^4	7 yield (%)[b]	ΔG^{ad}
1	$-CH_3$	-H	-H	-H	**7a** (64%)[c]	20.0
2	-H	$-CH_3$	-H	-H	**7b** (54%)[c]	20.1
3	-H	-H	-H	-H	**7c** (60%)[c]	20.1
4	$-CH_3$	-H	-H	-Br	**7d** (75%)[c]	16.5
5	-H	$-CH_3$	-H	-Br	**7e** (61%)[c]	16.6
6	-H	-H	-H	-Br	**7f** (71%)[c]	17.0
7	$-CH_3$	-H	-H	$-C_6H_5$	**7g** (79%)	4.5
8	-H	$-CH_3$	-H	$-C_6H_5$	**7h** (86%)	4.2
9	-H	-H	-H	$-C_6H_5$	**7i** (85%)	4.7
10	$-CH_3$	-H	-H	$-CCC_6H_5$	**7j** (79%)	8.5
11	-H	$-CH_3$	-H	$-CCC_6H_5$	**7k** (80%)	8.2
12	-H	-H	$-CH_3$	$-CCC_6H_5$	**7l** (87%)	8.4
13	-H	-H	-H	$-CCC_6H_5$	**7m** (85%)	8.4

[a]All iodocyclization reactions were conducted at room temperature with 2.0 equiv of I_2 in CH_2Cl_2 unless and otherwise stated. [b]Isolated yields. [c]Reaction was carried out using 2 equiv of NIS in CH_2Cl_2 at room temperature. [d]Calculated by M06-2X/6-311+G**+Midi!//M06-2X/6-31G*+Midi! method. Thermal correction was calculated at T = 298 K and solvent effect (CH_2Cl_2) was taken into account by SCRF-PCM method.

Summary and Conclusions

In summary, we have developed a new, simple and general synthetic route for the construction of thieno[2,3–*b*]quinoline and selenopheno[2,3-*b*]quinoline derivatives *via* iodocyclization reaction. The structures of the products were confirmed by IR, NMR and HRMS, as well as X-ray diffraction experiments. DFT calculations were also carried out to study the effect of iodinating reagent and substituents on the reactivity of the iodocyclization. Finally, the structural elaboration was done by Suzuki coupling, Sonogashira coupling, Heck reaction, dehydroiodination and alkyne annulation reaction. Further expansion of current strategies and evaluation of biological activity is in progress.

Experimental

General Methods: All solvents and reagents were purchased from the suppliers and used without further purification. IR spectra were recorded on a JASCO FT/IR-460 Plus spectrophotometer. Reactions were monitored by TLC on silica plates using UV-light or Iodine chamber for visualization. Evaporation and condensation were carried out in vacuo. NMR spectra were recorded with JEOL JNM-ECS 400 spectrometers with tetramethylsilane as an internal standard. Chemical shifts δ and coupling constants J are given in ppm (parts per million) and Hz (hertz) respectively. The following abbreviations were used as follows: s: singlet, d: doublet, t: triplet, m: multiplet. All known compounds data are in consistent with the given literature reports. Scale up reactions also performed as per the given general procedure without any deviation. Melting points were measured by a Yanaco micromelting point apparatus.

General procedure for synthesis of compounds 4a-4g, 5a, 5b, 5d and 7a-7f:

To a stirred solution of 3-ethynyl-6-methyl-2-(methylthio)quinoline **2a** (30 mg, 0.140 mmol, 1 equiv.), NIS (63 mg, 0.281 mmol, 2 equiv.) in dry DCM (5 mL) was stirred for 6 h, After completion of reaction (monitored by TLC), reaction mixture was quenched by saturated sodium thiosulfate and extracted with DCM (15 mL). Solvent was evaporated under reduced pressure to afford a crude residue. The crude was purified by silica gel chromatography using hexane/ethyl acetate (98:2) as eluent to afford **4a** 32 mg as white solid, Yield: 69%; Melting point: 176-178 ^{0}C; IR (neat): 3086, 1595, 1548, 1488, 1330, 1136, 1055, 912, 790, 773, 699, 628, 562, 504 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 8.06 (d, *J* = 9.0 Hz, 1H), 7.78 (s, 1H), 7.75 (s, 1H), 7.62 (d, *J* = 9.0 Hz, 1H), 2.58 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 159.59, 146.03, 135.95, 132.74, 131.77, 131.16, 127.84,

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127.07, 126.08, 75.15, 21.76; HRMS (ESI): m/z = 325.9500 calcd. For $C_{12}H_9NSI$, found 325.9511 $[M+H]^+$.

(E)-3-(1,2-diiodovinyl)-6-methyl-2-(methylthio)quinoline (5a)
Yield: 23%; Sticky; IR (KBr): 2923, 2367, 2341, 1554, 1490, 1334, 1155, 1052, 824 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 9.4 Hz, 1H), 7.69 (s, 1H), 7.52 (d, *J* = 6.7 Hz, 2H), 7.49 (s, 1H), 2.70 (s, 3H), 2.51 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 155.29, 146.40, 136.07, 135.60, 134.13, 132.71, 127.75, 126.95, 125.32, 91.41, 87.37, 21.54, 13.40; HRMS (ESI): m/z = 467.8780 calcd. For $C_{13}H_{12}NSI_2$, found 467.8780 $[M+H]^+$.

3-Iodo-7-methylthieno[2,3-b]quinoline (4b)
Yield: 70%; Melting point: 130-133 ^{0}C; IR (neat): 2931, 1931, 1732, 1619, 1604, 1573, 1385, 1360, 1259, 1091, 1049, 1040, 809, 797, 779, 766, 697, 574 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.38 (s, 1H), 7.92 (d, *J* = 8.5 Hz, 2H), 7.73 (s, 1H), 7.43 (d, *J* = 9.9 Hz, 1H), 2.62 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 160.52, 147.56, 140.74, 132.23, 132.12, 130.63, 128.62, 128.15, 127.00, 124.19, 75.14, 22.24; HRMS (ESI): m/z = 325.9500 calcd. For $C_{12}H_9NSI$, found 325.9496 $[M+H]^+$.

(E)-3-(1,2-diiodovinyl)-7-methyl-2-(methylthio)quinoline (5b)
Yield: 21%; Melting point: 99-102 ^{0}C; IR (neat): 3076, 2915, 1904, 1730, 1693, 1605, 1625, 1395, 1327, 1311, 1258, 1088, 1057, 1010, 816, 795, 780, 688 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.72 (s, 1H), 7.64 (d, *J* = 8.1 Hz, 1H), 7.49 (s, 1H), 7.30 (s, 1H), 2.70 (s, 3H), 2.54 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 156.31, 147.97, 141.10, 135.31, 134.40, 127.94, 127.67, 127.28, 123.30, 91.51, 87.41, 22.05, 13.40; HRMS (ESI): m/z = 467.8780 calcd. For $C_{13}H_{12}NSI_2$, found 467.8759 $[M+H]^+$.

3-Iodo-8-methylthieno[2,3-b]quinoline (4c)
Yield: 72%; Melting point: 179-182 ^{0}C; IR (neat): 2917, 2551, 1971, 1944, 1684, 1614, 1592, 1562, 1544, 1330, 1165, 1093, 889, 762, 558, 488 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.40 (s, 1H), 7.88 (d, *J* = 8.5 Hz, 1H), 7.77 (s, 1H), 7.63 (d, *J* = 6.7 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 1H), 2.88 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 159.56, 146.60, 136.25, 132.64, 132.36, 131.31, 130.00, 126.53, 125.97, 125.83, 74.96, 18.53; HRMS (ESI): m/z = 325.9500 calcd. For $C_{12}H_9INS$, found 325.9529 $[M+H]^+$.

3-Iodothieno[2,3-b]quinoline (4d)
Yield: 61%; Melting point: 152-154 ^{0}C; IR (neat): 3084, 1798, 1586, 1542, 1388, 1325, 1051, 948, 901, 769, 742, 701, 594, 503 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.44 (s, 1H), 8.18 (d, *J* = 8.1 Hz, 1H), 8.04 (d, *J* = 7.6 Hz, 1H), 7.79 (m, 2H), 7.61 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 160.52, 147.23, 132.74, 132.55, 131.41, 130.18, 128.57, 128.25, 126.09, 125.99, 75.10; HRMS (ESI): m/z = 311.9344 calcd. For $C_{11}H_7NSI$, found 311.9362 $[M+H]^+$.

(E)-3-(1,2-diiodovinyl)-2-(methylthio)quinoline (5d)
Yield: 20%; Melting point: 135-138 ^{0}C; IR (neat): 2922, 1732, 1603, 1549, 1309, 1380, 1139, 1043, 952, 963, 813, 778, 747, 596, 477 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.1 Hz, 1H), 7.74-7.77 (m, 2H), 7.69 (m, 1H), 7.51 (s, 1H), 7.46 (t, *J* = 6.7 Hz, 1H), 2.71 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 156.50, 147.77, 136.16, 134.62, 130.53, 128.06, 128.02, 125.76, 125.34, 91.12, 87.51, 13.43; HRMS (ESI): m/z = 453.8624 calcd. For $C_{12}H_{10}NSI_2$, found 453.8594 $[M+H]^+$.

2-Bromo-3-iodo-6-methylthieno[2,3-b]quinoline (4e)
Yield: 81%; Melting point: 134-136 ^{0}C; IR (neat): 2920, 1584, 1551, 1389, 1323, 1136, 1066, 951, 905, 813, 565, 519, 749 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H), 8.01 (d, *J* = 8.5 Hz, 1H), 7.76 (s, 1H), 7.62 (d, *J* = 8.5 Hz, 1H), 2.58 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 161.00, 146.01, 136.38, 133.89, 132.85, 131.97, 127.84, 127.04, 126.62, 122.04, 83.97, 21.76; HRMS (ESI): m/z = 403.8606 calcd. For $C_{12}H_8NSBrI$, found 403.8595 $[M+H]^+$.

2-Bromo-3-iodo-7-methylthieno[2,3-b]quinoline (4f)
Yield: 85%; Melting point: 201-203 ^{0}C; IR (neat): 1996, 2011, 1705, 1627, 1588, 1549, 1478, 1331, 1308, 1145, 1082, 895, 870, 797, 614, 586, 537, 466 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.24 (s, 1H), 7.88 (d, *J* = 8.5 Hz, 2H), 7.42 (d, *J* = 8.5 Hz, 1H), 2.60 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 161.91, 147.53, 140.96, 133.28, 132.40, 128.94, 128.08, 127.03, 124.69, 121.43, 83.94, 22.26; HRMS (ESI): m/z = 403.8606 calcd. For $C_{12}H_8NSBrI$, found 403.8590 $[M+H]^+$.

2-Bromo-3-iodothieno[2,3-b]quinoline (4g)
Yield: 84%; Melting point: 178-180 ^{0}C; IR (neat): 2357, 1919, 1801, 1614, 1587, 1547, 1479, 1391, 1321, 1228, 1133, 945, 927, 900, 834, 779, 742, 719, 546, 510 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 8.07 (dd, *J* = 44.2, 7.9 Hz, 2H), 7.79 (s, 1H), 7.59 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 161.94, 147.22, 133.91, 132.68, 130.32, 128.49, 128.24, 126.51, 126.45, 122.36, 83.93; HRMS (ESI): m/z = 389.8449 calcd. For $C_{11}H_6NSBrI$, found 389.8420 $[M+H]^+$.

3-Iodo-6-methylselenopheno[2,3-b]quinoline (7a)
Yield: 64%; Melting point: 181-183 ^{0}C; IR (neat): 3083, 2162, 1778, 1731, 1586, 1527, 1549, 1329, 1263, 1035, 911, 815, 766, 757, 716, 621, 517, 479 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 1H), 8.28 (s, 1H), 8.03 (d, *J* = 9.0 Hz, 1H), 7.77 (s, 1H), 7.62 (d, *J* = 9.0 Hz, 1H), 2.58 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 161.42, 145.71, 136.09, 135.05, 133.87, 132.78, 132.32, 127.66, 127.21, 126.12, 76.79, 21.76; ^{77}Se-NMR (400 MHz, $CDCl_3$) δ 582.01; HRMS (ESI): m/z = 373.8945 calcd. For $C_{12}H_9NSeI$, found 373.8925 $[M+H]^+$.

3-Iodo-7-methylselenopheno[2,3-b]quinoline (7b)
Yield: 54%; Sticky; IR (KBr): 2362, 2347, 1616, 1585, 1555, 1486, 1317, 1132, 753, 669 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 1H), 8.27 (s, 1H), 7.92-7.94 (m, 2H), 7.45 (d, *J* = 8.5 Hz, 1H), 2.62 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 141.04, 134.54, 134.39, 131.86, 128.75, 128.24, 127.23, 126.73, 126.70, 124.22, 77.65, 22.24; ^{77}Se-NMR (75 MHz, $CDCl_3$) δ 631.83; HRMS (ESI): m/z = 373.8945 calcd. For $C_{12}H_9NSeI$, found 373.8959 $[M+H]^+$.

3-Iodoselenopheno[2,3-b]quinoline (7c)
Yield: 60%; Sticky; IR (KBr): 2927, 2854, 2378, 2158, 1676, 1616, 1486, 1137, 1048, 956, 914, 860, 752, 668, 583 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.48 (s, 1H), 8.32 (s, 1H), 8.16 (d, *J* = 8.5 Hz, 1H), 8.04 (d, *J* = 8.1 Hz, 1H), 7.79-7.83 (m, 1H), 7.61 (t, *J* = 7.6 Hz, 1H); ^{13}C-

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NMR (100 MHz, $CDCl_3$) δ 162.49, 146.92, 135.13, 134.57, 132.58, 130.29, 128.65, 128.05, 126.23, 126.06, 76.77; ^{77}Se-NMR (400 MHz, $CDCl_3$) δ 584.41; HRMS (ESI): m/z = 359.8788 calcd. For $C_{11}H_7NSeI$, found 359.8797 $[M+H]^+$.

2-Bromo-3-iodo-6-methylselenopheno[2,3-b]quinoline (7d)

Yield: 75%; Melting point: 187-188 ^{0}C; IR (neat): 2917, 1682, 1584, 1567, 1548, 1488, 1392, 1329, 1259, 1099, 1061, 1028, 909, 813, 782, 763, 631, 480 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.92 (d, *J* = 8.5 Hz, 1H), 7.69 (s, 1H), 7.55 (d, *J* = 9.0 Hz, 1H), 2.51 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 163.58, 146.02, 136.50, 136.30, 134.38, 132.89, 127.64, 127.20, 126.78, 120.54, 87.58, 21.75; ^{77}Se-NMR (400 MHz, $CDCl_3$) δ 661.99; HRMS (ESI): m/z = 451.8050 calcd. For $C_{12}H_8NSeBrI$, found 451.8061 $[M+H]^+$.

2-Bromo-3-iodo-7-methylselenopheno[2,3-b]quinoline (7e)

Yield: 61%; Melting point: 203-206 ^{0}C; IR (neat): 1800, 1614, 1587, 1547, 1322, 1134, 945, 900, 774, 741, 597, 546, 473 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$ and Acetone-d_6) δ 8.27 (d, *J* = 4.6 Hz, 1H), 7.78-7.85 (m, 2H), 7.38 (d, *J* = 8.2 Hz, 1H), 2.53 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$ and Acetone-d_6) δ 147.19, 141.34, 135.80, 135.02, 129.07, 128.16, 128.12, 126.33, 124.82, 119.90, 87.43, 22.07; ^{77}Se-NMR (400 MHz, $CDCl_3$ and Acetone-d_6) δ 664.55; HRMS (ESI): m/z = 451.8050 calcd. For $C_{12}H_8NSeBrI$, found 451.8031 $[M+H]^+$.

2-Bromo-3-iodoselenopheno[2,3-b]quinoline (7f)

Yield: 71%; Melting point: 178-182 ^{0}C; IR (neat): 2923, 2028, 1733, 1613, 1581, 1551, 1326, 1316, 1140, 1129, 1070, 900, 892, 823, 752, 742, 496, 474 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 8.11 (d, *J* = 8.5 Hz, 1H), 8.02 (d, *J* = 8.5 Hz, 1H), 7.81 (t, *J* = 7.0 Hz, 1H), 7.61 (t, *J* = 8.1 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 164.66, 147.25, 136.39, 135.04, 130.43, 128.59, 128.04, 126.72, 126.58, 120.89, 87.48; ^{77}Se-NMR (400 MHz, $CDCl_3$) δ 664.24; HRMS (ESI): m/z = 437.7894 calcd. For $C_{11}H_6NSeBrI$, found 437.7906 $[M+H]^+$.

General procedure for the synthesis of 4h-4q and 7g-7m:

To a stirred solution of 6-methyl-2-(methylthio)-3-(phenylethynyl)quinoline **3a** (10 mg, 0.034 mmol, 1 equiv.) and iodine (18 mg, 0.069 mmol, 2 equiv.) in dry DCM (5 mL) was stirred for 6 h, After completion of reaction (monitored by TLC), reaction mixture was quenched by saturated sodium thiosulfate and extracted with DCM (15 mL). Solvent was evaporated under reduced pressure to afford a crude residue. The crude was purified by silica gel chromatography using hexane/ethyl acetate (97:3) as eluent to afford **4h** as white crystal, Yield: 90%; Melting point: 183-186 ^{0}C; IR (neat): 2916, 1674, 1629, 1588, 1575, 1550, 1488, 1440, 1181, 1093, 1074, 902, 839, 814, 754, 693, 569, 558 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 8.07 (d, *J* = 9.0 Hz, 1H), 7.81 (s, 1H), 7.76 (dd, *J* = 7.9, 1.6 Hz, 2H), 7.62 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.48-7.54 (m, 3H), 2.59 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 160.44, 146.29, 143.53, 135.83, 135.23, 134.41, 133.18, 132.55, 132.48, 130.41, 130.00, 129.52, 128.75, 127.81, 127.09, 126.67, 75.93, 21.76; HRMS (ESI): m/z = 401.9813 calcd. For $C_{18}H_{13}NSI$, found 401.9842 $[M+H]^+$.

3-Iodo-7-methyl-2-phenylthieno[2,3-b]quinoline (4i)

Yield: 79%; Melting point: 143-146 ^{0}C; IR (neat): 2914, 2373, 1631, 1530, 1474, 1440, 1304, 1144, 1073, 897, 868, 795, 758, 737, 691, 616, 598, 465 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.44 (s, 1H), 7.93-7.95 (m, 2H), 7.76 (dd, *J* = 7.9, 1.6 Hz, 2H), 7.48-7.54 (m, 3H), 7.43 (d, *J* = 9.9 Hz, 1H), 2.63 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 161.35, 147.82, 142.93, 140.58, 134.63, 134.42, 132.92, 130.00, 129.48, 128.74, 128.50, 128.13, 127.00, 124.76, 75.91, 22.24; HRMS (ESI): m/z = 401.9813 calcd. For $C_{18}H_{13}NSI$, found 401.9835 $[M+H]^+$.

3-Iodo-2-phenylthieno[2,3-b]quinoline (4j)

Yield: 86%; Melting point: 163-166 ^{0}C; IR (neat): 2922, 1613, 1583, 1548, 1476, 1327, 1143, 1075, 891, 853, 836, 762, 748, 738, 694, 599, 470 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.48 (s, 1H), 8.18 (d, *J* = 8.5 Hz, 1H), 8.05 (d, *J* = 8.1 Hz, 1H), 7.76-7.81 (m, 3H), 7.59 (t, *J* = 7.0 Hz, 1H), 7.49-7.55 (m, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 161.36, 147.49, 143.69, 135.25, 134.33, 133.21, 130.01, 129.59, 128.77, 128.54, 128.19, 126.56, 125.99, 75.86; HRMS (ESI): m/z = 387.9657 calcd. For $C_{17}H_{11}NSI$, found 387.9656 $[M+H]^+$.

3-Iodo-6-methyl-2-(m-tolyl)thieno[2,3-b]quinoline (4k)

Yield: 83%; Melting point: 156-160 ^{0}C; IR (neat): 2913, 1809, 1771, 1582, 1548, 1487, 1335, 1138, 1083, 1075, 904, 815, 793, 728, 698, 565, 478 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.38 (s, 1H), 8.06 (d, *J* = 9.0 Hz, 1H), 7.80 (s, 1H), 7.59 (q, *J* = 9.0 Hz, 3H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.29 (d, *J* = 7.6 Hz, 1H), 2.59 (s, 3H), 2.47 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 160.45, 146.25, 143.67, 138.55, 135.78, 135.24, 134.30, 132.49, 132.39, 130.56, 130.30, 128.62, 127.80, 127.10, 126.66, 75.75, 21.76, 21.54; HRMS (ESI): m/z = 415.9970 calcd. For $C_{19}H_{15}NSI$, found 415.9976 $[M+H]^+$.

3-Iodo-7-methyl-2-(m-tolyl)thieno[2,3-b]quinoline (4l)

Yield: 80%; Melting point: 104-107 ^{0}C; IR (neat): 2918, 1732, 1624, 1451, 1478, 1333, 1144, 1085, 893, 885, 873, 790, 779, 768, 621, 468 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 1H), 7.87 (t, *J* = 4.0 Hz, 2H), 7.50 (d, *J* = 9.0 Hz, 2H), 7.34 (q, *J* = 7.5 Hz, 2H), 7.22 (d, *J* = 7.6 Hz, 1H), 2.55 (s, 3H), 2.40 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 161.37, 147.78, 143.15, 140.52, 138.55, 134.64, 134.30, 132.84, 130.57, 130.26, 128.61, 128.47, 128.12, 127.10, 126.99, 124.75, 75.72, 22.24, 21.54; HRMS (ESI): m/z = 415.9970 calcd. For $C_{19}H_{15}INS$, found 415.9969 $[M+H]^+$.

3-Iodo-2-(m-tolyl)thieno[2,3-b]quinoline (4m)

Yield: 86%; Melting point: 131-134 ^{0}C; IR (neat): 3052, 1806, 1615, 1600, 1548, 1329, 1128, 1084, 899, 851, 805, 771, 746, 694, 736, 599, 475 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 8.17 (d, *J* = 8.5 Hz, 1H), 8.04 (d, *J* = 9.0 Hz, 1H), 7.75-7.79 (m, 1H), 7.56-7.60 (m, 3H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.30 (d, *J* = 7.6 Hz, 1H), 2.47 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 161.37, 147.45, 143.91, 138.59, 135.26, 134.21, 133.11, 130.56, 130.38, 129.96, 128.65, 128.52, 128.18, 127.11, 126.56, 125.95, 75.67, 21.55; HRMS (ESI): m/z = 401.9813 calcd. For $C_{18}H_{13}NSI$, found 401.9803 $[M+H]^+$.

3-Iodo-2-(4-methoxyphenyl)-6-methylthieno[2,3-b]quinoline (4n)

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Yield: 77%; Melting point: 178-180 ^{0}C; IR (neat): 2988, 1775, 1731, 1605, 1490, 1459, 1435, 1295, 1252, 1178, 1112, 1087, 1027, 825, 813, 792, 764, 559, 525 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 8.06 (d, *J* = 9.0 Hz, 1H), 7.80 (s, 1H), 7.72 (d, *J* = 8.5 Hz, 2H), 7.61 (d, *J* = 9.0 Hz, 1H), 7.04 (d, *J* = 8.5 Hz, 2H), 3.90 (s, 3H), 2.59 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 160.60, 146.12, 143.40, 135.77, 135.41, 132.40, 132.13, 131.36, 127.75, 127.06, 126.69, 126.64, 114.17, 75.09, 55.52, 21.76; HRMS (ESI): m/z = 431.9919 calcd. For $C_{19}H_{15}NOS$, found 431.9924 $[M+H]^+$.

3-Iodo-6-methyl-2-(phenylethynyl)thieno[2,3-b]quinoline (4o)

Yield: 81%; Melting point: 208-211 ^{0}C; IR (neat): 2206, 1728, 1678, 1588, 1548, 1488, 1440, 1331, 1135, 1070, 907, 864, 816, 792, 757, 690, 560, 554 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.28 (s, 1H), 8.04 (d, *J* = 8.5 Hz, 1H), 7.77 (s, 1H), 7.64-7.67 (m, 2H), 7.61 (d, *J* = 9.0 Hz, 1H), 7.40-7.42 (m, 3H), 2.58 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 159.94, 146.81, 136.13, 133.59, 132.92, 132.23, 131.95, 129.59, 128.64, 127.83, 127.17, 126.54, 126.20, 122.05, 101.17, 84.71, 84.36, 21.75; HRMS (ESI): m/z = 425.9813 calcd. For $C_{20}H_{13}NSI$, found 425.9788 $[M+H]^+$.

3-Iodo-7-methyl-2-(phenylethynyl)thieno[2,3-b]quinoline (4p)

Yield: 84%; Melting point: 212-215 ^{0}C; IR (neat): 2920, 2163, 1911, 1688, 1625, 1590, 1545, 1439, 1331, 1148, 1071, 895, 888, 878, 787, 760, 693, 593, 545 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.30 (s, 1H), 7.90 (t, *J* = 4.0 Hz, 2H), 7.64-7.66 (m, 2H), 7.40-7.42 (m, 4H), 2.61 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 160.86, 148.30, 141.05, 132.96, 132.67, 131.93, 129.56, 128.74, 128.63, 128.22, 127.01, 125.66, 124.63, 122.08, 101.01, 84.75, 84.36, 22.29; HRMS (ESI): m/z = 425.9813 calcd. For $C_{20}H_{13}NSI$, found 425.9827 $[M+H]^+$.

3-Iodo-2-(phenylethynyl)thieno[2,3-b]quinoline (4q)

Yield: 91%; Melting point: 222-224 ^{0}C; IR (neat): 2964, 2201, 1813, 1614, 1586, 1546, 1329, 1146, 1128, 1070, 900, 778, 753, 723, 687, 540, 472 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 8.15 (d, *J* = 8.5 Hz, 1H), 8.02 (d, *J* = 8.5 Hz, 1H), 7.78 (t, *J* = 7.2 Hz, 1H), 7.64-7.67 (m, 2H), 7.59 (t, *J* = 7.2 Hz, 1H), 7.40-7.43 (m, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 160.88, 147.99, 133.62, 132.97, 131.97, 130.37, 129.65, 128.65, 128.22, 126.45, 126.24, 121.99, 101.41, 84.63, 84.29, 76.78; HRMS (ESI): m/z = 411.9657 calcd. For $C_{19}H_{11}NSI$, found 411.9632 $[M+H]^+$

3-Iodo-6-methyl-2-phenylselenopheno[2,3-b]quinoline (7g)

Yield: 79%; Melting point: 179-182 ^{0}C; IR (neat): 2920, 2345, 1805, 1718,1674, 1571, 1549, 1488, 1438, 1333, 1301, 902, 814, 767, 704, 745, 692,556, 513 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.44 (s, 1H), 8.04 (d, *J* = 8.5 Hz, 1H), 7.80 (s, 1H), 7.68 (dd, *J* = 8.1, 1.3 Hz, 2H), 7.62 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.46-7.52 (m, 3H), 2.59 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 162.82, 146.16, 145.59, 137.86, 136.81, 136.04, 134.74, 132.69, 130.07, 129.36, 128.76, 127.68, 127.32, 126.86, 76.85, 21.84; ^{77}Se-NMR (400 MHz, $CDCl_3$) δ 628.19; HRMS (ESI): m/z = 449.9258 calcd. For $C_{18}H_{13}NSeI$, found 449.9253 $[M+H]^+$.

3-Iodo-7-methyl-2-phenylselenopheno[2,3-b]quinoline (7h)

Yield: 86%; Melting point: 129-132 ^{0}C; IR (neat): 2915, 1748, 1622, 1575, 1474, 1440, 1331, 1223, 1057, 898, 798, 761, 692, 593, 468 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.91 (d, *J* = 7.6 Hz, 2H), 7.66-7.68 (m, 2H), 7.45-7.51 (m, 3H), 7.42 (d, *J* = 8.5 Hz, 1H), 2.62 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 163.79, 147.58, 144.96, 140.72, 137.18, 136.72, 135.03, 130.00, 129.25, 128.69, 128.56, 128.21, 126.85, 124.84, 79.03, 22.26; ^{77}Se-NMR (400 MHz, $CDCl_3$) δ 629.89; HRMS (ESI): m/z = 449.9258 calcd. For $C_{18}H_{13}NSeI$, found 449.9255 $[M+H]^+$.

3-Iodo-2-phenylselenopheno[2,3-b]quinoline (7i)

Yield: 85%; Melting point: 139-142 ^{0}C; IR (neat): 2922, 1847, 1819, 1731, 1614, 1577, 1551, 1479, 1441, 1328, 1261, 1133, 1076, 1056, 1027, 760, 742, 690, 606, 465 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.53 (s, 1H), 8.15 (d, *J* = 8.5 Hz, 1H), 8.04 (d, *J* = 8.1 Hz, 1H), 7.77-7.81 (m, 1H), 7.68 (dd, *J* = 7.9, 1.6 Hz, 2H), 7.60 (t, *J* = 7.0 Hz, 1H), 7.47-7.52 (m, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 163.81, 147.28, 145.76, 137.85, 136.64, 135.32, 130.14, 130.00, 129.35, 128.72, 128.62, 127.98, 126.70, 126.11, 78.96; ^{77}Se-NMR (400 MHz, $CDCl_3$) δ 630.59; HRMS (ESI): m/z = 435.9101 calcd. For $C_{17}H_{11}NSeI$, found 435.9128 $[M+H]^+$.

3-Iodo-6-methyl-2-(phenylethynyl)selenopheno[2,3-b]quinoline (7j)

Yield: 79%; Melting point: 200-203 ^{0}C; IR (neat): 2920, 1913, 1722, 1579, 1549, 1479, 1439, 1331, 1136, 902, 856, 814, 753, 697,686, 517, 479 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.30 (s, 1H), 8.00 (d, *J* = 8.5 Hz, 1H), 7.75 (s, 1H), 7.59-7.64 (m, 3H), 7.41 (t, *J* = 2.7 Hz, 3H), 2.57 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 162.17, 146.57, 136.24, 136.17, 134.43, 132.93, 131.85, 129.53, 128.64, 127.62, 127.32, 126.64, 125.74, 122.28, 102.77, 87.42, 86.55, 21.75; ^{77}Se-NMR (400 MHz, $CDCl_3$) δ 648.77; HRMS (ESI): m/z = 473.9258 calcd. For $C_{20}H_{13}NSeI$, found 473.9250 $[M+H]^+$.

3-Iodo-7-methyl-2-(phenylethynyl)selenopheno[2,3-b]quinoline (7k)

Yield: 80%; Melting point: 183-186 ^{0}C; IR (neat): 3006, 2364, 2348, 2341, 1714, 1427, 1364, 1223, 1093, 895, 798, 687, 529 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.34 (s, 1H), 7.88 (d, *J* = 8.2 Hz, 2H), 7.62-7.65 (m, 2H), 7.41 (q, *J* = 2.9 Hz, 4H), 2.60 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 163.22, 148.05, 141.17, 135.56, 134.82, 131.84, 129.49, 128.79, 128.63, 128.32, 126.88, 125.25, 124.72, 122.32, 102.60, 87.40, 86.56, 22.28; ^{77}Se-NMR (400 MHz, $CDCl_3$) δ 650.19; HRMS (ESI): m/z = 473.9258 calcd. For $C_{20}H_{13}NSeI$, found 473.9262 $[M+H]^+$.

3-Iodo-8-methyl-2-(phenylethynyl)selenopheno[2,3-b]quinoline (7l)

Yield: 87%; Melting point: 231-234 ^{0}C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 7.85 (d, *J* = 8.1 Hz, 1H), 7.61-7.66 (m, 3H), 7.48 (d, *J* = 8.1 Hz, 1H), 7.41 (t, *J* = 2.7 Hz, 3H), 2.86 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 162.13, 147.12, 136.15, 135.89, 135.27, 131.85, 130.37, 129.50, 128.63, 126.68, 126.58, 126.08, 122.34, 102.68, 87.31, 86.65, 18.43; ^{77}Se-NMR (400 MHz, $CDCl_3$) δ 651.94.

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3-Iodo-2-(phenylethynyl)selenopheno[2,3-b]quinoline (7m)

Yield: 85%; Melting point: 194-197 ^{0}C; IR (neat): 2961, 2191, 1729, 1546, 1478, 1439, 1332, 1258, 1069, 1013, 852, 792, 773, 748, 694, 685, 589 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 1H), 8.13 (d, *J* = 8.5 Hz, 1H), 8.03 (d, *J* = 7.6 Hz, 1H), 7.78 (d, *J* = 6.7 Hz, 1H), 7.63-7.66 (m, 2H), 7.60 (s, 1H), 7.42 (q, *J* = 2.4 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 147.79, 136.27, 135.12, 131.86, 130.45, 129.59, 128.75, 128.66, 128.65, 128.03, 126.59, 126.37, 126.04, 122.22, 103.02, 87.24, 86.48; ^{77}Se-NMR (400 MHz, $CDCl_3$) δ 651.01; HRMS (ESI): m/z = 459.9101 calcd. For $C_{19}H_{11}NSeI$, found 459.9104 $[M+H]^+$.

General procedure for the synthesis of 6-methyl-2,3-diphenylthieno[2,3-b]quinoline (6a)

To a solution of 3-iodo-6-methyl-2-phenylthieno[2,3-b]quinoline **4h** (20 mg, 0.050 mmol) the phenyl boronic acid (9.1 mg, 0.075 mmol) in 4 ml DMF, Pd $(OAc)_2$ (1.1 mg, 1 mol %), Cs_2CO_3 (48.7 mg, 0.150 mmol) were added. The resulting mixture was then heated at 60 ^{0}C for 12 h. The solvent was removed under reduced pressure, the residue was extracted with ethyl acetate: brine; The crude was purified by silica gel chromatography using hexane/ethyl acetate (95:5) as eluents to afford **6a** 13 mg, Yield: 74%; Melting point: 186-188 ^{0}C; IR (neat): 2917, 1978, 1626, 1599, 1584, 1556, 1491, 1442, 1298, 1357, 1090, 908, 820, 755, 698, 559, 478 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 1H), 8.05 (d, *J* = 9.0 Hz, 1H), 7.62 (s, 1H), 7.56-7.58 (m, 1H), 7.42-7.48 (m, 3H), 7.39 (td, *J* = 3.9, 1.9 Hz, 4H), 7.28 (t, *J* = 3.1 Hz, 3H), 2.53 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 161.42, 145.65, 140.23, 135.23, 134.84, 134.10, 133.84, 131.98, 130.38, 130.25, 129.85, 129.13, 129.05, 128.57, 128.43, 127.94, 127.92, 127.08, 126.09, 21.71; HRMS (ESI): m/z = 352.1160 calcd. For $C_{24}H_{18}NS$, found 352.1159 $[M+H]^+$.

General procedure for synthesis of 6-methyl-2-phenyl-3-(phenylethynyl)thieno[2,3-b]quinoline (6b)

To a solution of the corresponding 3-iodo-6-methyl-2-phenylthieno[2,3-b]quinoline **4h** (0.062 mmol) and the phenyl acetylene (0.080 mmol, 1.3 equiv) in 5ml THF; Et_3N (1 mL), $PdCl_2(PPh_3)_2$ (4.4 mg, 1 mol %) and copper(I) iodide (1.19 mg, 1 mol %) were added. The resulting mixture was then stirred under nitrogen atmosphere for 14 h. The solvent was removed under reduced pressure, the residue was extracted with ethyl acetate and purified by silica gel column chromatography using hexane: ethyl acetate (97:3) as eluent to afford **6b** 18 mg, Yield: 77%; Melting point: 129-132 ^{0}C; IR (neat): 2919, 1791, 1732, 1624, 1587, 1478, 1451, 1333, 1261, 1445, 897, 790, 778, 768, 694, 621, 468 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 8.14 (d, *J* = 7.2 Hz, 2H), 8.05 (d, *J* = 8.5 Hz, 1H), 7.78 (s, 1H), 7.62-7.64 (m, 2H), 7.59 (d, *J* = 9.0 Hz, 1H), 7.52 (t, *J* = 7.4 Hz, 2H), 7.41-7.47 (m, 4H), 2.58 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 159.82, 147.11, 146.11, 135.69, 133.71, 133.66, 132.25, 131.75, 129.59, 129.18, 128.88, 128.76, 128.64, 128.04, 127.11, 126.78, 126.24, 123.10, 110.78, 95.36, 83.41, 21.75; HRMS (ESI): m/z = 376.1160 calcd. For $C_{26}H_{18}NS$, found 376.1154 $[M+H]^+$.

General procedure for the synthesis of methyl (E)-3-(6-methyl-2-phenylthieno[2,3-b]quinolin-3-yl)acrylate (6c)

To a solution of the corresponding 3-iodo-6-methyl-2-phenylthieno[2,3-b]quinoline **4h** (20 mg, 0.037 mmol) and the methyl acrylate (6.5 mg, 0.074 mmol) in 4 ml DMF; Pd $(OAc)_2$ (0.4 mg, 0.5 mol %), PPh_3 (9.8 mg, 0.037 mmol) and K_2CO_3 (10.3 mg, 0.074 mmol) were added. The resulting mixture was then heated under nitrogen atmosphere for 12 h. The solvent was removed under reduced pressure, the residue was extracted with ethyl acetate and purified by silica gel column chromatography using hexane: ethyl acetate (97:3) as eluent to afford **6c** 12 mg, along with 23% **6d**; Yield: 70%; Melting point: 186-190 ^{0}C; IR (neat): 2917, 1716, 1627, 1587, 1491, 1443, 1423, 1305, 1283, 1222, 1174, 1158, 1080, 1095, 1013, 898, 817, 691, 563 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.70 (s, 1H), 8.05 (d, *J* = 8.5 Hz, 1H), 7.90 (d, *J* = 16.2 Hz, 1H), 7.78 (s, 1H), 7.58-7.63 (m, 3H), 7.51 (t, *J* = 7.4 Hz, 3H), 6.66 (d, *J* = 16.6 Hz, 1H), 3.85 (s, 3H), 2.60 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 167.65, 161.09, 148.79, 145.54, 137.42, 135.89, 133.14, 132.52, 130.87, 130.28, 129.73, 129.33, 129.07, 127.94, 127.22, 126.06, 124.18, 119.96, 51.95, 21.76; HRMS (ESI): m/z = 360.1058 calcd. For $C_{22}H_{18}NO_2S$, found 360.1057 $[M+H]^+$.

General procedure for the synthesis of 6-methyl-2-phenylthieno[2,3-b]quinoline (6d)

To a solution of the corresponding 3-iodo-6-methyl-2-phenylthieno[2,3-b]quinoline **4h** (30 mg, 0.074 mmol) the formic acid (6.9 mg, 0.149 mmol) in 5 ml DMF, Pd $(PPh_3)_2Cl_2$ (2.6 mg, 0.5 mol %), NEt_3 (22.7 mg, 0.224 mmol) were added. The resulting mixture was then heated at 60^{0}C for 12 h. The solvent was removed under reduced pressure, the residue was extracted with ethyl acetate: brine and purified by silica gel column chromatography using hexane: ethyl acetate (98:2) as eluent to afford **6d** 16 mg, Yield: 78%; Melting point: 239-243 ^{0}C; IR (neat): 1738, 1646, 1625, 1587, 1552, 1533, 1489, 1444, 1341, 1217, 1068, 913, 903, 817, 750, 680, 700, 691, 560, 473 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 1H), 8.02 (d, *J* = 9.0 Hz, 1H), 7.76-7.78 (m, 2H), 7.68 (s, 1H), 7.54-7.57 (m, 2H), 7.47 (dd, *J* = 8.1, 6.7 Hz, 2H), 7.41 (d, *J* = 7.2 Hz, 1H), 2.56 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 162.35, 145.45, 145.24, 135.35, 133.95, 133.45, 131.79, 129.15, 128.86, 128.05, 126.88, 126.79, 126.21, 116.24, 21.72; HRMS (ESI): m/z = 275.0769 calcd. For $C_{18}H_{13}NS$, found 275.0746 $[M+H]^+$.

General procedure for the synthesis of 9-methyl-1,2-diphenylbenzo[4,5]thieno[2,3-b]quinoline (6e)

To a solution of 3-iodo-6-methyl-2-phenylthieno[2,3-b]quinoline 4h (20 mg, 0.049 mmol), Pd $(OAc)_2$ (0.6 mg, 5 mol %), NaOAc (8 mg, 0.099 mmol), LiCl (6 mg, 0.149 mmol), in 4 mL DMF; Diphenylacetylene (9 mg, 0.049 mmol) were added. The resulting mixture was heated at 100 °C for 4 days. The mixture was allowed to cool to room temperature, diluted with diethyl ether (15 mL); dried over sodium sulfate, and filtered. The solvent was removed under reduced pressure and the residue was purified by column chromatography using hexane: ethyl acetate (98:2) as eluent to afford 6e 11 mg (49%) as a yellow solid; Melting point: >300 ^{0}C; IR (neat): 1961, 1801, 1601, 1585, 1548, 1493, 1439, 1327, 1256, 1103, 1070, 1030, 911, 823, 813, 755, 726, 698, 564 cm^{-1}; ^{1}H-NMR

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(400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.1 Hz, 1H), 7.99 (d, *J* = 8.5 Hz, 1H), 7.65 (d, *J* = 8.5 Hz, 1H), 7.61 (d, *J* = 8.1 Hz, 1H), 7.52 (d, *J* = 8.5 Hz, 2H), 7.39 (d, *J* = 5.8 Hz, 3H), 7.26-7.29 (m, 5H), 7.20-7.24 (m, 2H), 7.16 (s, 1H), 6.99 (s, 1H), 2.47 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 162.09, 145.48, 139.61, 138.41, 137.11, 136.88, 135.89, 135.10, 132.22, 132.16, 131.35, 131.31, 130.37, 130.24, 128.66, 128.26, 128.15, 128.07, 127.72, 127.63, 127.50, 127.48, 127.32, 126.82, 126.81, 125.23, 125.20, 21.54; HRMS (ESI): m/z = 452.1496 calcd. For $C_{32}H_{22}NS$, found 452.1473 $[M+H]^+$.

Conflicts of interest

"There are no conflicts to declare".

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Supporting Information:

Experimental procedures, characterization data for the new compounds, and copies of ^{1}H and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.rsc.org.

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