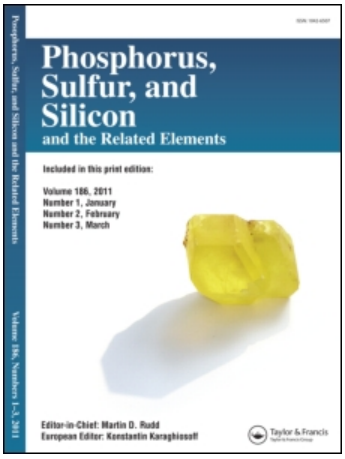

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Chemistry of Substituted Quinolines: Thieno[2,3-b] and Thiopyrano[2,3-b]quinolines

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The reaction of 3-formyl-2-chloroquinolines with thioglycolic acid afforded a mixture of uncyclized [(3-formylquinolin-2-yl)thio]acetic acid in a 60–70% yield and cyclized thieno[2,3-b]quinoline-2-carboxylic acids in a 30–40% yield, respectively. The uncyclized compounds on refluxing with $POCl_3$ in various alcoholic media gave [(3-formylquinolin-2-yl)thio]acetates. Further cyclization was achieved by refluxing them with dimethylformamide (DMF) to produce thieno[2,3-b]quinoline derivatives. On the other hand, the reaction of 3-formyl-2-mercaptoquinolines with chloroacetyl chloride in DMF gave 3-chloro-2H-thiopyrano[2,3-b]quinolin-2-ones. The structures of all the newly synthesized compounds were characterized on the basis of elemental analysis, IR, ^1H NMR, and mass spectral data.

Keywords 3-formyl-2-chloroquinolines; 3-formyl-2-mercaptoquinolines; 3-formyl-(quinolin-2-yl)thio acetic acids; methyl thieno[2,3-b]quinoline-2-carboxylates; thieno[2,3-b]quinolines; thiopyrano[2,3-b]quinolines

INTRODUCTION

Five- and six-membered heterocyclic compounds containing one or two heteroatoms fused to a quinoline ring in a linear fashion are found in natural products as well as in synthetic compounds of biological interest.[1] They are known to exhibit antiallergenic properties[2] and antifungal,[3] hypocholesterolemic, hypolemic,[4] antibacterial,[5] and

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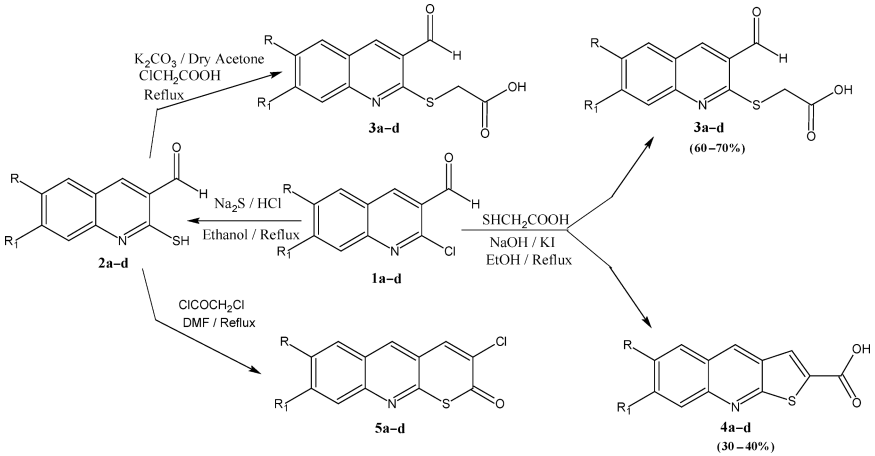
antiviral activity.[6] Numerous thieno[2,3-*b*]quinoline derivatives are well documented for their pharmacological properties exhibiting antibacterial,[7–9] antifungal,[9] antianaphylactic,[10] antiarrhythmic, and anti-inflammatory activity.[11,12]

The synthesis of novel derivatives of quinolines by a convenient method remains an important synthetic task. Many synthetic methods have been developed for the synthesis of thieno quinolines,[13–20] and because of their great importance, this remains an active research. In continuation of our research program,[21–23] which is directed toward the synthesis of potentially bioactive molecules via a simple and practical approach, herein we report the rapid, cost-effective, and efficient method for the synthesis of sulfur-bearing quinoline derivatives. The key intermediate 3-formyl-2-chloroquinolines and 3-formyl-2-mercapto quinolines were prepared from an earlier reported method.[23,24]

RESULTS AND DISCUSSION

Novel condensed heterocycles like thieno[2,3-*b*]quinolines and thiopyrano[2,3-*b*]quinolines can be convceivably obtained by two pathways (Scheme 1). From one pathway, i.e., the reaction of 3-formyl-2-chloroquinolines **1a–d** with thioglycolic acid in the presence of sodium hydroxide in absolute ethanol, two compounds were obtained. They are [(3-formylquinolin-2-yl)thio]acetic acids **3a–d** with a 60–70% yield and thieno[2,3-*b*]quinoline-2-carboxylic acids **4a–d** with 30–40%

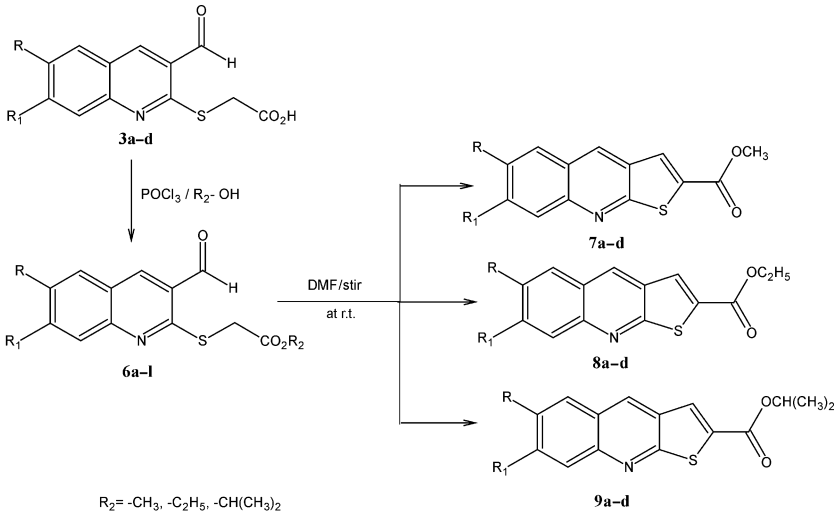


SCHEME 1 General synthetic procedure of [(3-formylquinolin-2-yl)thio]acetic acids, thieno[2,3-*b*], and thiopyrano[2,3-*b*]quinoline derivatives **3a–d**, **4a–d**, and **5a–d**.

yield. Formation of these two products was confirmed by TLC analysis, and they were separated by column chromatography.

Our mechanistic investigations using spectral studies gave proof of cyclized and uncyclized products. A signal that corresponds to $-S-CH_2-$ that appeared at 4.25 δ in ^1H NMR of **3a** revealed the formation of an uncyclized product (>60% column yield is presented). Further, we investigated the other product **4a** (>30%) and found that the signal due to $-S-CH_2-$ group was absent in the ^1H NMR spectrum. This result prompted us to confirm the subsequent cyclization of **3a**. Further, the structure assigned was confirmed by its mass spectrum. It gave a molecular ion peak at m/z 247 for **3a** and 229 for **4a**. Similarly, the spectral details of all other compounds are given in the Experimental section.

The cyclization of thieno[2,3-*b*]quinoline-2-carboxylic acid derivatives **4a–d** prompted us to cyclize [(3-formylquinolin-2-yl)-thio]acetic acid derivatives **3a–d** by converting them into different carboxylic esters derivatives **6a–l**. Thus, 3-formylquinolin-2-yl-thioacetic acid **3a** on refluxing with $POCl_3$ in excess of methanol affords



	R	R_1
a	**H**	**H**
b	**CH_3**	**H**
c	**F**	**Cl**
d	**Cl**	**H**

SCHEME 2 General synthetic procedure of thieno[2,3-*b*]quinoline-2-carboxylates **7a–d**, **8a–d**, and **9a–d**.

methyl(3-formylquinolin-2-yl)thioacetate **6a**. This on stirring with DMF underwent smooth cyclization at r.t. to produce methyl thieno[2,3-*b*]quinoline-2-carboxylate **7a**. In a similar fashion compound **3b–d**, on refluxing with ethanol and isopropyl alcohol, gave **6b–l**. These derivatives upon stirring with DMF resulted in the formation of **7b–d**, **8a–d**, and **9a–d**, respectively.

In the ^{1}H NMR spectrum of **7a**, the signals corresponding to —CHO proton and the signal due to —S—CH_2— group, which was present in **6a**, were found to be absent, whereas other signals remained at the same position in ^{1}H NMR spectrum; this confirms the formation of the thieno ring nucleus. In the IR spectrum, absence of a band at 1640–1644 cm^{-1} corresponds to the —CHO group, and reappearance of band at 1735 cm^{-1} further confirms the ring cyclization. In the mass spectrum of **7a**, presence of the molecular ion peak at m/z 243 confirms the correct structure.

In another pathway, we observed a very interesting result in the reaction of 3-formyl-2-mercaptoquinolines **2a–d** with chloroacetylchloride in DMF media. Here compound **2a–d** underwent cyclization to give thiopyrano[2,3-*b*]quinoline derivatives **5a–d** in a single step under a reflux condition. The ^{1}H NMR spectrum of compound **5a** exhibited a multiplet at 7.53–9.87 δ integrating six aromatic protons corresponding to the quinoline[2,3-*b*]thiopyrano ring nucleus. The IR spectrum of **5a** exhibited absorption bands at 1620–1625 cm^{-1}attributed to thiopyrano ring carbonyl group. This confirms the one-pot condensation of 3-formyl-2-mercaptoquinoline **2a** with chloroacetyl chloride to build thiopyrano nucleus. Further, a cyclized structure was confirmed by recording mass spectra of the compounds **5a**, which gave a molecular ion peak at m/z 247.

EXPERIMENTAL

IR spectra were recorded on a Perkin Elmer 157 infrared spectrophotometer. The ^{1}H NMR spectra (300 MHz) were recorded on a Bruker Supercon FT NMR instrument using TMS as an internal standard and mass spectra on a Jeol JMS-D 300 mass spectrometer operating at 70 eV. Melting points were determined in open capillaries and are uncorrected. The purity of the compounds was checked by TLC and were further purified by column chromatography.

Preparation of [(3-formylquinolin-2-yl)thio]acetic Acid (3a)

Part A

A mixture of **2a** (1.8 g, 0.01 mol), chloroacetic acid (1.4 g, 0.015 mol), and K_2CO_3 (2.7 g, 0.04 mol) in dry acetone (50 mL) was refluxed on a

water bath for about 4–5 h. By using TLC technique, the progress of the reaction was monitored. After completion of the reaction, the reaction mixture was filtered; the solvent was evaporated under reduced pressure and dried. The solid **3a** obtained was purified by column chromatography (1.7 g, 72%). Similarly, the same procedure was followed for the synthesis of **3b–d** (65–72%).

Part B

A mixture of **1a** (1.91 g, 0.01 mol), thioglycolic acid (9.21 g, 0.01 mol), and sodium hydroxide (1.20 g, 0.03 mol) was dissolved in ethanol (30 mL). The mixture was refluxed on a water bath for 4 h. The progress of the reaction was monitored by TLC. The reaction mixture was then poured into water and neutralized with dil HCl. The solid **3a** obtained was filtered, dried, and purified by column chromatography (1.60 g, 70%). Similarly, compounds **3b–d** were prepared in a 65–70% yield.

[(3-Formylquinolin-2-yl)thio]acetic Acid (3a)

Yield: 1.78 g, 72%; m.p. 156–157°C; IR (KBr) ν (cm^{-1}): 1680; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 4.25 (2H, s, —S—CH_2—), 7.59–9.58 (5H, m, Ar—H), 10.31 (1H, s, CHO) 11.6 (1H, s, OH); [M+]: 247. Calcd. (%) for $C_{10}H_{11}NO_3S$: C, 58.29; H, 3.67; N, 5.66; S, 12.97. Found: C, 58.23; H, 3.59; N, 5.57; S, 12.86.

[(3-Formyl-6-methylquinolin-2-yl)thio]acetic Acid (3b)

Yield: 1.69 g, 65%; mp. 161–163°C; IR (KBr) ν (cm^{-1}): 1681; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 2.55 (3H, s, CH_3), 4.26 (2H, s, —S—CH_2—), 7.58–9.56 (4H, m, Ar—H), 10.30 (1H, s, CHO), 11.7 (1H, s, OH); [M+]: 261. Calcd. (%) for $C_{13}H_{11}NO_3S$: C, 59.76; H, 4.24; N, 5.36; S, 12.27. Found: C, 59.68; H, 4.16; N, 5.28; S, 12.23.

[(7-Chloro-6-fluoro-3-formylquinolin-2-yl)thio]acetic Acid (3c)

Yield: 1.88 g, 63%; mp. 164–165°C; IR (KBr) ν (cm^{-1}): 1680; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 4.25 (2H, s, —S—CH_2—), 7.57–9.53 (4H, m, Ar—H), 10.30 (1H, s, CHO), 11.6 (1H, s, OH); [M+]: 299. Calcd. (%) for $C_{12}H_7ClFNO_3S$: C, 48.09; H, 2.35; N, 4.67; S, 10.70. Found: C, 48.01; H, 2.29; N, 4.56; S, 10.61.

[(6-Chloro-3-formylquinolin-2-yl)thio]acetic Acid (3d)

Yield: 1.97 g, 70%; mp. 168–169°C; IR (KBr) ν (cm^{-1}): 1682; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 4.27 (2H, s, —S—CH_2—), 7.54–9.58 (4H,

m, Ar—H), 10.32 (1H, s, CHO), 11.6 (1H, s, OH); [M+]: 281. Calcd. (%) for $C_{12}H_8ClNO_3S$: C, 51.16; H, 2.86; N, 4.97; S, 11.38. Found: C, 51.32; H, 2.75; N, 4.86; S, 11.25.

Preparation of 3-chloro-2*H*-thiopyrano[2,3-*b*]quinolin-2-one

A mixture of 3-formyl-2-mercaptoquinoline **2a** (1.80 g, 0.01 mol) and chloroacetyl chloride (1.68 g, 0.015 mol) in DMF (30 mL) was heated on a water bath for 1 h. After completion of reaction, the reaction mixture was poured into ice-cold water and stirred well, and the solid thus obtained was filtered, dried, and recrystallized from ethyl acetate to give **5a** (1.97 g, 80%). The same procedure was adopted for the synthesis of **5b–d**, and the obtained yield was found to be 70–82%.

3-Chloro-2*H*-thiopyrano[2,3-*b*]quinolin-2-one (5a)

Yield: 1.98 g, 80%; mp. 213–215°C; IR (KBr) ν (cm^{-1}): 1620; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 7.53–9.87 (6H, m, Ar—H), [M+]: 247. Calcd. (%) for $C_{12}H_6ClNOS$: C, 58.19; H, 2.44; N, 5.65; S, 12.95. Found: C, 58.76; H, 2.31; N, 5.65; S, 12.63.

3-Chloro-7-methyl-2*H*-thiopyrano[2,3-*b*]quinolin-2-one (5b)

Yield: 1.98 g, 76%; mp. 223–225°C; IR (KBr) ν (cm^{-1}): 1622; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 2.57 (3H, s, CH_3), 7.54–9.83 (5H, m, Ar—H); [M+]: 261. Calcd. (%) for $C_{13}H_9NO_2S$: C, 59.66; H, 3.08; N, 5.35; S, 12.25. Found: C, 59.56; H, 3.16; N, 5.26; S, 12.17.

3,8-Dichloro-7-fluoro-2*H*-thiopyrano[2,3-*b*]quinolin-2-one (5c)

Yield: 2.16 g, 72%; mp. 203–205°C; IR (KBr) ν (cm^{-1}): 1623; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 7.57–9.86 (4H, m, Ar—H); [M+]: 300. Calcd. (%) for $C_{12}H_4Cl_2FNOS$: C, 48.02; H, 1.34; N, 4.67; S, 10.68. Found: C, 48.08; H, 1.39; N, 4.58; S, 10.58.

3,7-Dichloro-2*H*-thiopyrano[2,3-*b*]quinolin-2-one (5d)

Yield: 2.20 g, 78%; mp. 211–213°C; IR (KBr) ν (cm^{-1}): 1621; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 7.60–9.82 (5H, m, Ar—H); [M+]: 282. Calcd. (%) for $C_{12}H_5Cl_2NOS$: C, 51.08; H, 1.79; N, 4.96; S, 11.37. Found: C, 51.04; H, 1.67; N, 4.89; S, 11.28.

Preparation of [(3-Formylquinolin-2-yl)thio]acetate (6a)

A mixture of **3a** (2.4 g, 0.01 mol) and methanol (50 mL) in the presence of $POCl_3$ (15 mL) was heated on a water bath for 2 h. Completion of the reaction was monitored by TLC. Excess of $POCl_3$ was distilled off under reduced pressure; the residue obtained was washed with water, filtered, and dried. The crude product was purified by column chromatography and gave (1.99 g, 82%) **6a**. In a similar way, **6b–l** were prepared in a 73–82% yield.

[(3-Formylquinolin-2-yl)thio]acetate (6a)

Yield: 2.14 g, 82%; mp. 170–172°C; IR (KBr) ν (cm^{-1}): 1682; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 3.85 (3H, s, OCH_3), 4.23 (2H, s, —S—CH_2—), 7.62–9.63 (5H, m, Ar—H), 10.33 (1H, s, CHO); [M+]: 261. Calcd. (%) for $C_{13}H_{11}NO_3S$: C, 59.76; H, 4.24; N, 5.36; S, 12.27. Found: C, 59.67; H, 4.23; N, 5.28; S, 12.12.

[(3-Formyl-6-methylquinolin-2-yl)thio]acetate (6b)

Yield: 2.00 g, 73%; mp. 168–169°C; IR (KBr) ν (cm^{-1}): 1683; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 2.55 (3H, s, CH_3), 3.83 (3H, s, OCH_3), 4.24 (2H, s, —SCH_2—), 7.64–9.61 (4H, m, Ar—H), 10.33 (1H, s, CHO); [M+]: 275. Calcd. (%) for $C_{14}H_{13}NO_3S$: C, 61.07; H, 4.76; N, 5.09; S, 11.65. Found: C, 61.04; H, 4.62; N, 5.02; S, 11.58.

[(7-Chloro-6-fluoro-3-formylquinolin-2-yl)thio]acetate (6c)

Yield: 2.13 g, 68%; mp. 175–178°C; IR (KBr) ν (cm^{-1}): 1680; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 3.82 (3H, s, OCH_3), 4.26 (2H, s, —S—CH_2—), 7.62–9.64 (3H, m, Ar—H), 10.31 (1H, s, CHO); [M+]: 313. Calcd. (%) for $C_{12}H_7ClFNO_3S$: C, 49.77; H, 2.89; N, 4.46; S, 10.22. Found: C, 49.68; H, 2.78; N, 437; S, 10.14.

[(6-Chloro-3-formylquinolin-2-yl)thio]acetate (6d)

Yield: 2.06 g, 71%; mp. 180–182°C; IR (KBr) ν (cm^{-1}): 1684; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 3.84 (3H, s, OCH_3), 4.25 (2H, s, —S—CH_2—), 7.64–9.61 (4H, m, Ar—H), 10.30 (1H, s, CHO); [M+]: 295. Calcd. (%) for $C_{13}H_{10}ClNO_3S$: C, 52.80; H, 3.41; N, 4.74; S, 10.84. Found: C, 52.71; H, 3.32; N, 4.64; S, 10.73.

Ethyl[(3-formylquinolin-2-yl)thio]acetate (6e)

Yield: 2.06 g, 75%; mp. 174–175°C; IR (KBr) ν (cm^{-1}): 1683; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 1.32 (3H, t, CH_3), 4.33 (2H, q, —OCH_2), 4.21 (2H, s, —S—CH_2—), 7.63–9.61 (5H, m, Ar—H), 10.32 (1H, s, CHO); [M+]: 275. Calcd. (%) for $C_{14}H_{13}NO_3S$: C, 61.07; H, 4.76; N, 5.09; S, 11.65. Found: C, 62.17; H, 4.65; N, 5.13; S, 11.41.

Ethyl [(3-formyl-6-methylquinolin-2-yl)thio]acetate (6f)

Yield: 1.99 g, 69%; mp. 183–185°C; IR (KBr) ν (cm^{-1}): 1682; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 1.31 (3H, t, CH_3), 2.56 (3H, s, CH_3), 4.22 (2H, s, —S—CH_2—), 4.32 (2H, q, —OCH_2), 7.61–9.64 (4H, m, Ar—H), 10.31 (1H, s, CHO); [M+]; 289. Calcd. (%) for $C_{15}H_{15}NO_3S$: C, 62.26; H, 5.23; N, 4.84; S, 11.08. Found: C, 62.18; H, 5.19; N, 4.74; S, 11.02.

Ethyl [(7-chloro-6-fluoro-3-formylquinolin-2-yl)thio]acetate (6g)

Yield: 2.29 g, 70%; mp. 190–192°C; IR (KBr) ν (cm^{-1}): 1682; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 1.32 (3H, t, CH_3), 4.31 (2H, q, —OCH_2), 4.20 (2H, s, —S—CH_2—), 7.63–9.60 (3H, m, Ar—H), 10.33 (1H, s, CHO); [M+], 327. Calcd. (%) for $C_{14}H_{11}ClFNO_3S$: C, 51.30; H, 3.38; N, 4.27; S, 9.78. Found: C, 51.21; H, 3.27; N, 4.18; S, 9.67.

Ethyl [(6-chloro-3-formylquinolin-2-yl)thio]acetate (6h)

Yield: 2.21 g, 70%; mp. 195–197°C; IR (KBr) ν (cm^{-1}): 1680; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 1.30 (3H, t, CH_3), 2.55 (3H, s, CH_3), 4.22 (2H, s, —S—CH_2—), 4.30 (2H, q, —OCH_2), 7.60–9.63 (4H, m, Ar—H), 10.31 (1H, s, CHO); [M+]: 309. Calcd. (%) for $C_{14}H_{12}ClNO_3S$: C, 54.28; H, 3.90; N, 4.52; S, 10.35. Found: C, 54.17; H, 3.79; N, 4.41; S, 10.24.

Isopropyl [(3-formylquinolin-2-yl)thio]acetate (6i)

Yield: 2.22 g, 77%; mp. 188–189°C; IR (KBr) ν (cm^{-1}): 1680; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 1.45 (6H, d, $2CH_3$), 3.55 (1H, h, —CH—), 4.21 (2H, s, —S—CH_2—), 7.61–9.60 (5H, m, Ar—H), 10.30 (1H, s, CHO); [M+]: 289. Calcd. (%) for $C_{15}H_{15}N_3OS$: C, 62.26; H, 5.23; N, 4.84; S, 11.08. Found: C, 62.17; H, 5.16; N, 4.73; S, 11.02.

Isopropyl [(3-formyl-6-methylquinolin-2-yl)thio]acetate (6j)

Yield: 2.12 g, 70%; mp. 176–178°C; IR (KBr) ν (cm^{-1}): 1682; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 1.43 (6H, d, $2CH_3$), 3.54 (1H, h, —CH—), 4.20 (2H, s, —S—CH_2—), 7.63-9.62 (4H, m, Ar—H), 10.31 (1H, s, CHO); [M+]; 303. Calcd. (%) for $C_{16}H_{17}NO_3S$: C, 63.34; H, 5.65; N, 4.62; S, 10.57. Found: C, 63.25; H, 5.53; N, 4.53; S, 10.46.

Isopropyl [(7-chloro-6-fluoro-3-formylquinolin-2-yl)thio] acetate (6k)

Yield: 2.52 g, 74%; mp. 185–186°C; IR (KBr) ν (cm^{-1}): 1682; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 1.40 (6H, d, $2CH_3$), 3.52 (1H, h, —CH—), 4.22 (2H, s, —S—CH_2—), 7.60-9.63 (3H, m, Ar—H), 10.30 (1H, s, CHO); [M+]; 341. Calcd. (%) for $C_{15}H_{13}ClFNO_3S$: C, 52.71; H, 3.83; N, 4.10; S, 9.38. Found: C, 52.64; H, 3.71; N, 4.25, S, 9.50.

Isopropyl [(6-chloro-3-formylquinolin-2-yl)thio]acetate (6l)

Yield: 2.46 g, 76%; mp.197–198°C; IR (KBr) ν (cm^{-1}): 1682; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 1.41 (6H, d, $2CH_3$), 3.52 (1H, h, —CH—), 4.22 (2H, s, —S—CH_2—), 7.60–9.63 (4H, m, Ar—H), 10.30 (1H, s, CHO); [M+]; 323. Calcd. (%) for $C_{15}H_{14}ClNO_3S$: C, 55.64; H, 4.36; N, 4.33; S, 9.90. Found: C, 55.53; H, 4.27; N, 4.24; S, 9.79.

Preparation of methyl thieno[2,3-*b*]quinoline-2-carboxylate (7a)

A mixture of **6a** (2.61 g, 0.01 mol), and DMF (30 mL) was stirred for 4 h. After the completion of the reaction (monitored by TLC), excess DMF was distilled off under reduced pressure. Then the reaction mixture was poured into crushed ice; the solid thus obtained was filtered and dried. The crude product was purified by column chromatography to provide 2.05 g (85%) of pure **7a**. In a similar way, **7b–d**, **8a–d**, and **9a–d** were prepared in a 70–85% yield.

Methyl thieno[2,3-*b*]quinoline-2-carboxylate (7a)

Yield: 1.90 g, 85%, mp. 282–283°C; IR (KBr) ν (cm^{-1}): 1682; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 3.86 (3H, s, OCH_3), 7.62–9.67 (6H, m, Ar—H), [M+]; 243. Calcd. (%) for $C_{13}H_9NO_2S$: C, 64.18; H, 3.73; N, 5.76; S, 13.18. Found: C, 64.26; H, 3.67; N, 63; S, 13.26.

Methyl 6-methylthieno[2,3-b]quinoline-2-carboxylate (7b)

Yield: 1.81 g, 76%; mp. 274–275°C; IR (KBr) ν (cm^{-1}): 1682; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 2.55 (3H, s, CH_3), 3.84 (3H, s, OCH_3), 7.61–9.65 (5H, m, Ar—H); [M+]: 257. Calcd. (%) for $C_{14}H_{11}NO_2S$: C, 65.35; H, 4.31; N, 5.44; S, 12.46. Found: C, 65.26; H, 4.20; N, 5.33; S, 12.35.

Methyl 7-chloro-6-fluorothieno[2,3-*b*]quinoline-2-carboxylate (7c)

Yield: 1.93 g, 70%; mp. 186–189°C; IR (KBr) ν (cm^{-1}): 1680; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 3.81 (3H, s, OCH_3), 7.63–9.62 (4H, m, Ar—H); [M+]: 295. Calcd. (%) for $C_{13}H_7ClFNO_2S$: C, 52.80; H, 2.39; N, 4.74; S, 10.84. Found: C, 52.80; H, 2.39; N, 4.74; S, 10.84.

Methyl 6-chlorothieno[2,3-*b*]quinoline-2-carboxylate (7d)

Yield: 1.86 g, 72%, mp. 294–295°C; IR (KBr) ν (cm^{-1}): 1682; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 3.82 (3H, s, OCH_3), 7.62–9.65 (5H, m, Ar—H); [M+]: 277. Calcd. (%) for $C_{13}H_8ClNO_2S$: C, 56.22; H, 2.90; N, 5.04; S, 11.55. Found: C, 56.32; H, 2.79; N, 5.01; S, 11.47.

Ethyl thieno[2,3-*b*]quinoline-2-carboxylate (8a)

Yield: 1.95 g, 82%; mp. 269–270°C; IR (KBr) ν (cm^{-1}): 1682; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 1.32 (3H, t, CH_3), 4.33 (2H, q, —OCH_2), 7.61–9.68 (6H, m, Ar—H); [M+]: 257. Calcd. (%) for $C_{14}H_{11}NO_2S$: C, 65.35; H, 4.31; N, 5.44; S, 12.46. Found: C, 65.27; H, 4.23; N, 5.36; S, 12.38.

Ethyl 6-methylthieno[2,3-*b*]quinoline-2-carboxylate (8b)

Yield: 1.86 g, 74%; mp. 284–285°C; IR (KBr) ν (cm^{-1}): 1682; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 1.32 (3H, t, CH_3), 2.55 (3H, s, CH_3), 4.33 (2H, q, —OCH_2), 7.61–9.65 (5H, m, Ar—H); [M+]: 271. Calcd. (%) for $C_{15}H_{13}NO_2S$: C, 66.40; H, 4.83; N, 5.16; S, 11.82. Found: C, 66.32; H, 4.73; N, 5.26; S, 11.74.

Ethyl 7-chloro-6-fluorothieno[2,3-*b*]quinoline-2-carboxylate (8c)

Yield: 2.00 g, 69%; mp. 270–272°C; IR (KBr) ν (cm^{-1}): 1682; ^1H NMR (300 MHz, DMSO-d_6)δ (ppm): 1.32 (3H, t, CH_3), 4.33 (2H, q, —OCH_2), 7.61–9.65 (4H, m, Ar—H); [M+]: 309. Calcd. (%) for $C_{14}H_9ClFNO_2S$: C, 54.29; H, 2.93; N, 4.52; S, 10.35. Found: C, 54.17; H, 2.82; N, 4.41; S, 10.46.

Ethyl 6-chlorothieno[2,3-*b*]quinoline-2-carboxylate (8d)

Yield: 1.88 g, 69%; mp. 291–293°C; IR (KBr) ν (cm^{-1}): 1682; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 1.32 (3H, t, CH_3), 4.33 (2H, q, —OCH_2), 7.61–9.65 (5H, m, Ar—H); [M+]: 291. Calcd. (%) for $C_{14}H_{10}ClNO_2S$: C, 57.63; H, 3.45; N, 4.80; S, 10.99. Found: C, 57.52; H, 3.36; N, 4.71; S, 10.84.

Isopropyl thieno[2,3-*b*]quinoline-2-carboxylate (9a)

Yield: 2.01 g, 80%; mp. 257–258°C; IR (KBr) ν (cm^{-1}): 1680; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 1.45 (6H, d, $2CH_3$), 3.55 (1H, h, —CH—), 7.62–9.64 (6H, m, Ar—H); [M+]: 271. Calcd. (%) for $C_{15}H_{13}NO_2S$: C, 66.40; H, 4.83; N, 5.16; S, 11.82. Found: C, 66.33; H, 4.74; N, 5.26; S, 11.73.

Isopropyl 6-methylthieno[2,3-*b*]quinoline-2-carboxylate (9b)

Yield: 2.02 g, 76%; mp. 268–269°C; IR (KBr) ν (cm^{-1}): 1682; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 1.45 (6H, d, $2CH_3$), 2.55 (3H, h, Ar—CH_3) 3.55 (1H, s, —CH—), 7.63–9.64 (5H, m, Ar—H); [M+]: 285. Calcd. (%) for $C_{16}H_{15}NO_2S$: C, 67.34; H, 5.30; N, 4.91; S, 11.24. Found: C, 67.24; H, 5.21; N, 4.82; S, 11.16.

Isopropyl 6-chloro-7-fluorothieno[2,3-*b*]quinoline-2-carboxylate (9c)

Yield: 2.01 g, 66%; mp. 259–261°C; IR (KBr) ν (cm^{-1}): 1682; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 1.45 (6H, d, $2CH_3$), 3.55 (1H, h, —CH—), 7.63–9.64 (4H, m, Ar—H); [M+]: 323. Calcd. (%) for $C_{15}H_{11}ClFNO_2S$: C, 55.64; H, 3.42; N, 4.33; S, 9.90. Found: C, 55.55; H, 3.31; N, 4.21; S, 9.79.

Isopropyl 7-chlorothieno[2,3-*b*]quinoline-2-carboxylate (9d)

Yield: 2.00 g, 70%; mp. 241–245°C; IR (KBr) ν (cm^{-1}): 1680; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 1.46 (6H, d, $2CH_3$), 3.57 (1H, h, —CH—), 7.61–9.67 (5H, m, Ar—H); [M+]: 305. Calcd. (%) for $C_{15}H_{12}ClNO_2S$: C, 58.92; H, 3.96; N, 4.58; S, 10.49. Found: C, 58.81; H, 3.86; N, 4.48; S, 10.38.

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