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Full Paper

# Some reactions of 3-cyano-4-(*p*-methoxyphenyl)-5-oxo-5,6,7,8-tetrahydro-quinoline-2(1*H*)-thione; Synthesis of new tetrahydroquinolines and tetrahydrothieno[2,3-*b*]quinolines

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**Abstract**
In this paper, 3-cyano-4-(*p*-methoxyphenyl)-5-oxo-5,6,7,8-tetrahydroquinoline-2(1*H*)-thione (**2**) was prepared and reacted with methyl iodide to give the corresponding 2-methylthio derivative **3**. Fusion of compound **2** or **3** with hydrazine hydrate produced the aminopyrazolotetrahydroquinoline-5-hydrazone **4**. Reaction of both compounds **2** and **3** with phenylhydrazine or thiosemicarbazide led to the formation of condensation products **6a,b** and **9a,b** respectively. Reaction of cyanoquinolinethione **2** with some α-halocarbonyl compounds namely; ethyl chloroacetate, chloroacetamide, chloro-*N*-(*p*-tolyl)acetamide and phenacyl bromide gave the corresponding alkylated products **10a-d**. On treatment of the latter compounds with sodium ethoxide in boiling ethanol, they underwent intramolecular *Thorpe-Zeigler* cyclization affording the corresponding tetrahydrothieno[2,3-*b*] quinolines **11a-d**. The elemental analyses and spectroscopic data of all compounds are in agreement with their proposed structures.

**Keywords**: hydrazono compounds, thiosemicarbazones, tetrahydroquinolines, tetrahydrothienoquinolines

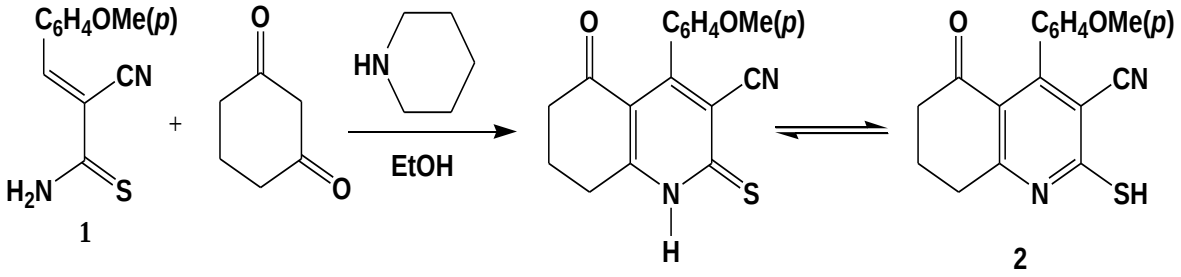
## 1. Introduction

The chemistry of 4-aryl-3-cyano-5,6,7,8-tetrahydroquinoline-2(1*H*)-thiones has been developed intensely during the last three decades [1], which could be attributed, in particular, to the discovery of compounds with antimicrobial activity in this series [2, 3]. The basic methods of their synthesis are: cyclocondensation of 2-arylidenecyclohexanones with cyanothioacetamide [2, 4], reaction of cyclohexanone [5] or its enamine [6] with arylidenecyanothioacetamides and recyclization of enamino nitrile of the 1,3-dithia-4-cyclohexene series [7]. On the other hand, the literature survey

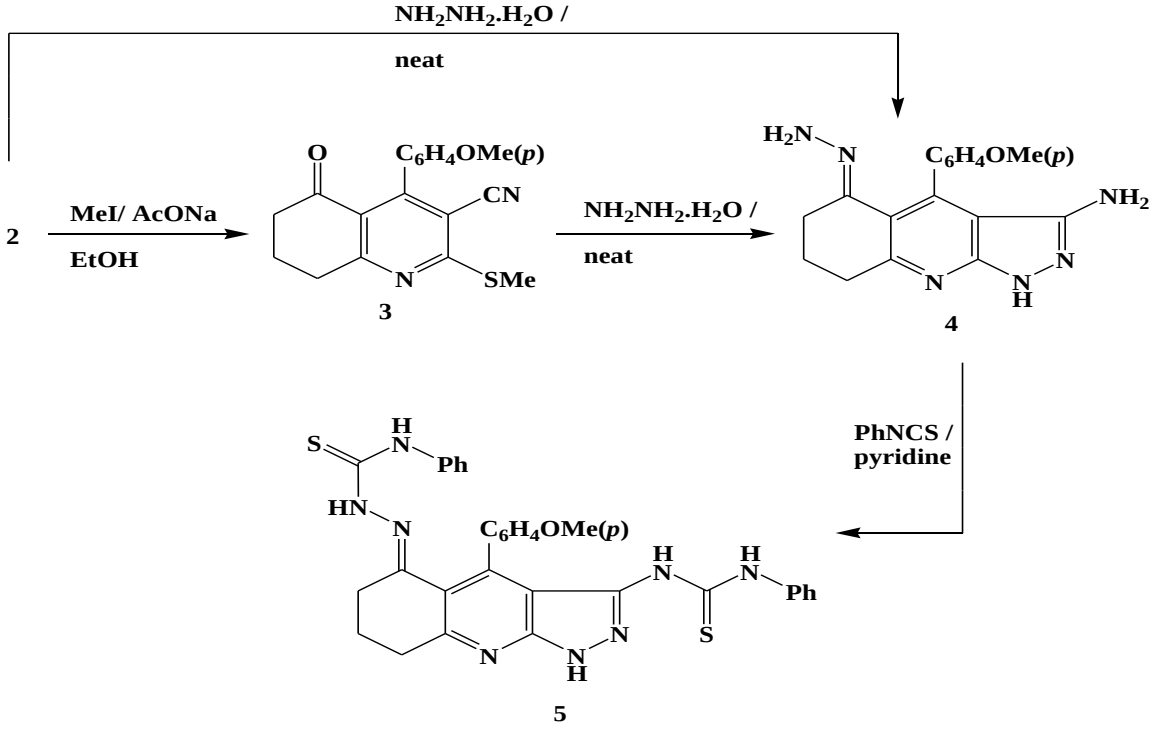
revealed that only few 3-cyano-5-oxo-5,6,7,8-tetrahydroquinoline-2(1*H*)-thiones have been prepared by using 1,3-cyclohexanedione or dimedone [8]. Encouraged by the above finding, we reported herein the synthesis of 3-cyano-4-(*p*-methoxyphenyl)-5-oxo-5,6,7,8-tetrahydroquinoline-2(1*H*)-thione and its reactions with different reagents to obtain other tetrahydroquinolines as well as tetrahydro-thieno[2,3-*b*]quinolines with anticipated biological and medicinal importance.

## 2. Results and discussion

The starting compound **2**, was prepared by refluxing of *p*-methoxbenzylidene-cyanothioacetamide **1** [9] with cyclohexane-1,3-dione in ethanol containing catalytic amount of piperidine (Scheme 1). Reaction of compound **2** with methyl iodide, in the presence of sodium acetate produced the corresponding 2-methylthiotetrahydroquinoline **(3)**. Heating both compounds **2** and **3** with hydrazine hydrate under neat conditions resulted in the formation of 3-aminopyrazolotetrahydroquinoline-hydrazone **4**. The interaction of **3** with two molar amount of phenyl *iso*-thiocyanate in hot pyridine gave the dithiouredo derivative **5** (Scheme 2).

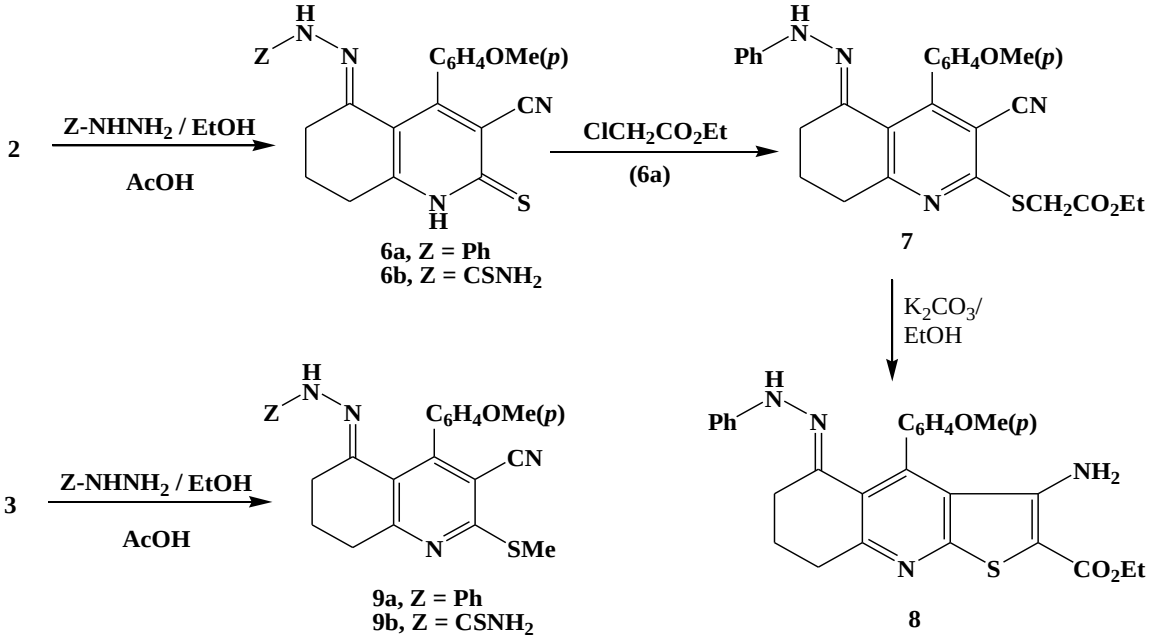



Scheme 1

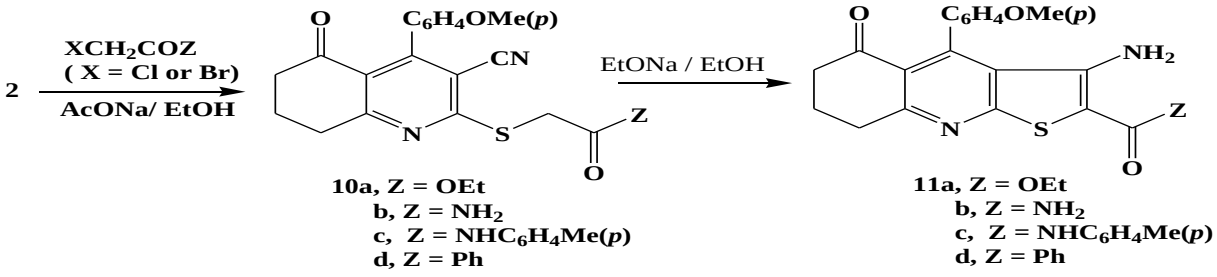



Scheme 2

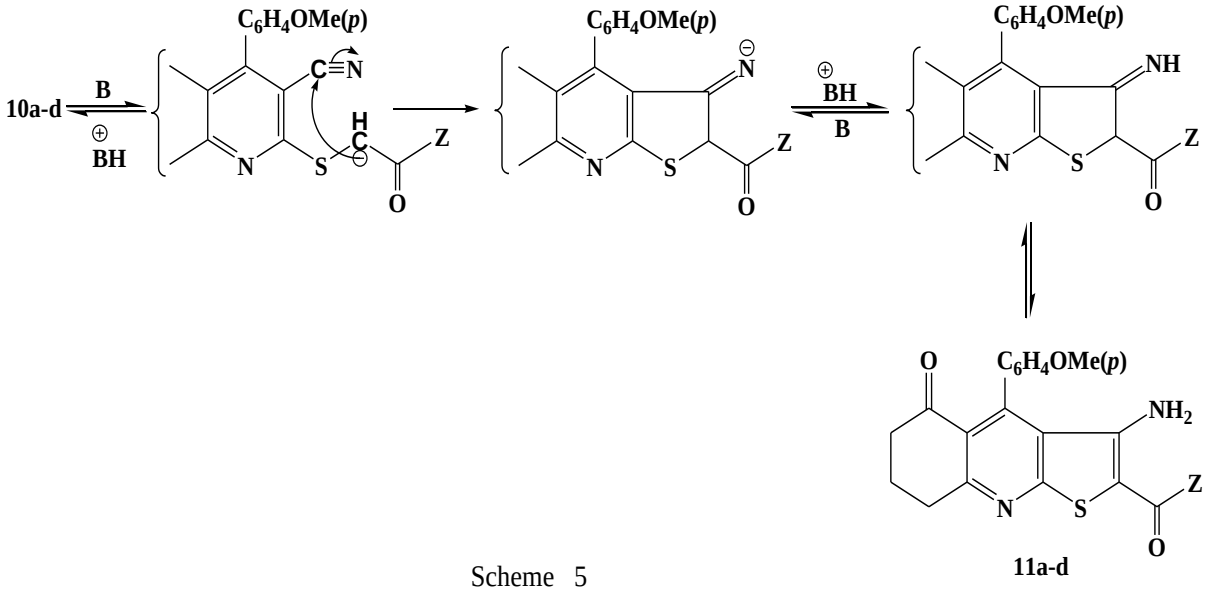
Treatment of compound **2** with phenyl hydrazine or thiosemicarbazide in the presence of glacial acetic acid furnished the corresponding phenylhydrazone 6a or thiosemicarbazone **6b**. The former compound (**6a**) was reacted with ethyl chloroacetate, by refluxing in ethanol containing equimolar amount of sodium acetate to give the open ester **7**. Refluxing of compound **7** with anhydrous $K_2CO_3$ in ethanol led to the formation of tetrahydrothieno[2,3-b]quinoline derivative **8** (Scheme 3). In a similar manner, compound 3 was also reacted with phenyl hydrazine or thiosemicarbazide to afford the corresponding condensation products **9a** and **9b** (Scheme 3). 3-Cyanoquinoline-2(1*H*)-thione **2** underwent *S*-alkylation reactions upon treatment with some α–halocarbonyl compounds namely: ethyl chloroacetate, chloroacetamide, chloro-N-(*p*-tolyl)acetamide and phenacyl bromide, by refluxing in ethanol containing equimolar amount of sodium acetate, to give the corresponding thioethers **10a-d** in high yields (Scheme 4). Upon heating of compounds **10a-d** with sodium ethoxide in ethanol, they underwent intramolecular *Thorpe-Zeigler* cyclization affording the corresponding 3-amino-tetrahydrothieno[2,3-*b*]quinolines **11a-d** (Scheme 4). The mechanism of *Thorpe-Ziegler* cyclization can be represented by Scheme 5 [10]. The elemental analyses and spectroscopic data of all compounds are in agreement with their proposed structures (See: experimental part).




Scheme 3




Scheme 4



Scheme 5

## 3. Experimental

Melting points were measured with Gallan-Kamp melting-point apparatus and are uncorrected. IR Spectra were obtained on a Pye-Unicam SP3-100 spectrophotometer using KBr disc technique. NMR Spectra were recorded on a Bruker 400 MHz Ultrashield TM FT-NMR spectrometer (Universiti Sains Malaysia). Mass spectra were recorded on a Jeol JMS-600 mass spectrometer; Elemental analyses (C, H, N, and S) were conducted using a Vario EL C, H, N, S Analyzer (Assiut University).

### *3.1. 3-cyano-4-(p-methoxyphenyl)-5-oxo-5,6,7,8-tetrahydroquinoline-2(1H)-thione (2).*

To a mixture of compound **1** (2.18 g, 10 mmol), cyclohexane-1,3-dione (1.12 g, 10 mmol) in ethanol (25 ml), few drops of piperidine were added. The reaction mixture was heated under reflux for 4 h and left to stand overnight at room temperature. The resulting precipitate was collected and recrystallized from ethanol as orange plates. Yield: (45 %); m.p.: 305-307 °C. IR: 3414 (NH), 3091 (C-H aromatic), 2838 (C-H aliphatic), 2233 (C≡N), 1678 (C=O) 1605 (C=N) $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$): δ = 14.30 (s, 1H, NH), 7.16-7.18 (d, *J* = 8.0 Hz,, 2H, Ar-H), 7.95-7.97 (d, *J* = 8.0 Hz, 2H, Ar-H), 3.82 (s, 3H, $OCH_3$), 3.01-3.03 (t, *J* = 4.0 Hz, 2H, $CH_2$ at C-6), 2.39-2.41(t, *J* = 4.0 Hz, 2H, $CH_2$ at C-8), 1.99-2.03 (p, *J* = 4.0 Hz, 2H, $CH_2$ at C-7). $^{13}C$ NMR (DMSO-$d_6$): δ =193.25, 180.36, 162.03, 160.42, 156.97, 129.64, 118.58, 117.43, 114.17 (2CH), 129.40 (2CH), 28.63 ($CH_2$), 20.41 ($CH_2$), 55.98 ($OCH_3$). Elemental analysis calculated for $C_{17}H_{14}N_2O_2S$ (%): C, 65.79; H, 4.55; N, 9.03; S, 10.33. Found (%): C, 65.78; H, 4.41; N, 9.18; S, 10.30.

### *3.2. 4-(p-Methoxyphenyl)-2-(methyl-thio)-5-oxo-5,6,7,8-tetrahydroquinoline-3-carbonitrile (3).*

A mixture of compound **2** (3.1 g, 10 mmol), methyl iodide (0.62 ml, 10 mmol) and sodium acetate trihydrate (2 g, 15 mmol) in ethanol (25 ml) was heated under reflux for 2 h. The precipitate product was collected by filtration and washed several times with ethanol followed by distilled water. It was recrystallized from methanol to give **3** in the form of yellow needles. Yield: 79 %; m.p.: 194-195°C. IR: 2962 (C-H aliphatic), 2218 (C≡N), 1685 (C=O), 1610 (C=N) $cm.^{-1}$ $^1H$ NMR (DMSO-$d_6$): δ = 7.20-7.22 (d, *J* = 8.0 Hz,, 2H, Ar-H), 6.99-7.01 (d, *J* = 8.0 Hz, 2H, Ar-H), 3.83 (s, 3H, $OCH_3$), 3.16-3.18 (t, *J* = 4.0 Hz, 2H, $CH_2$ at C-8), 2.69 (s, 3H, $SCH_3$), 2.56-2.58 (t, *J* = 4.0 Hz, 2H, $CH_2$ at C-6), 2.08-2.12 (t, *J* = 4.0 Hz, 2H, $CH_2$ at C-7). $^{13}C$ NMR (DMSO-$d_6$): δ = 195.57,

167.43, 165.30, 159.48, 154.50, 129.28, 122.60, 106.99, 113.41 (2CH), 128.38 (2CH), 33.53 ($CH_2$), 20.35 ($CH_2$), 55.11 ($OCH_3$), 12.98 ($SCH_3$). Elemental analysis calculated for $C_{18}H_{16}N_2O_2S$ (%): C, 66.65; H, 4.97; N, 8.64; S, 9.88. Found (%): C, 66.61; H, 4.92; N, 8.52; S, 9.69.

### *3.3. 5-Hydrazono-4-(p-methoxyphenyl)-5,6,7,8-tetrahydro-1H-pyrazolo[3,4-b] quinoline-3-amine (4).*

A suspension of compound **2** or **3** (10 mmol) in hydrazine hydrate 99 % (12 ml) was gently heated under reflux for 4 h and then allowed to cool. The reaction mixture was triturated with ethanol (15 ml) whereby a canary yellow precipitate formed. It was collected by filtration, washed several times with distilled water, air-dried and recrystallized from dioxane. Yield: 77-82 %, m.p.: 293-295° C. IR: 3437, 3389, 3293, 3193 (NH, $NH_2$), 2937 (C-H aliphatic), 1607, 1595 (C=N) $cm.^{-1}$ $^1$H NMR (DMSO-$d_6$ ): δ = 11.95 (s, 1H, NH), 7.16-7.18 (d, *J* = 8.0 Hz, 2H, Ar-H), a doublet at δ 6.96-7.98 (d, *J* = 8.0 Hz, 2H, Ar-H), 5.83 (s, 2H, $NH_2$ of hydrazone residue), 4.09 (s, 2H, $NH_2$ attached to pyrazole ring), 3.81 (s, 3H, $OCH_3$), 2.76-2.78 (t, 2H, $CH_2$ at C-8), 2.38-2.40 ( t, 2H, $CH_2$ at C-6), 1.86-1.90 (p, 2H, $CH_2$ at C-7). $^{13}$C NMR (DMSO-$d_6$): δ = 150.19, 147.84, 160.56, 158.09, 141.89, 141.71, 130.14, 120.44, 104.45, 113.44 (2CH), 129.78 (2CH), 25.08 ($CH_2$), 20.84 ($CH_2$), 54.96 ($OCH_3$). MS: m/z = 320.96 ($M^+$, 100 %); 304.58 ($M^+$-$NH_2$, 34.9 %). Elemental analysis calculated for $C_{17}H_{18}N_6O$ (%): C, 63.34; H, 5.63; N, 26.07. Found (%): C, 63.16; H, 5.68; N, 25.91.

### *3.4. 4-{4-(p-Methoxyphenyl)-3-(3-phenylthioureido)-7,8-dihydro-1H-pyrazolo[3,4-b]quinolin-5(6H)-ylidene}-N-phenylhydrazinecarbothioamide (5).*

A mixture of compound **4** (3.22 g, 10 mmol) and phenyl *iso*-thiocyanate (2.66 ml, 20 mmol) in pyridine (20 ml) was heated on a water bath for 5 h. The product that formed after cooling was collected and recrystallized from ethanol to give compound **5** in the form of yellow needles. Yield: 81 %, m.p.: 259-261 °C. IR: 3468, 3415, 3383, 3300 (NH), 3034 (C-H aromatic), 2942 (C-H aliphatic), 1638, 1608 (C=N) $cm.^{-1}$ $^1$H NMR (DMSO-$d_6$): δ = 13.55 (s, 1H, NH), 10.43 (s, 1H, NH), 10.30 (br. s, 1H, NH), 8.35 (br. s 1H, NH), 7.94 (s, 1H, NH), 7.14-7.38 (m, 12H, Ar-H), 6.75-6.77 (d, 2H, Ar-H), 3.27 (s, 3H, $OCH_3$), 2.91-2.93 (t, 2H, $CH_2$ at C-8), 2.84-2.86 (t, 2H, $CH_2$ at C-6), 1.95-1.99 (p, 2H, $CH_2$ at C-7). Elemental analysis calculated for $C_{31}H_{28}N_8OS_2$ (%): C, 62.82; H, 4.76; N, 18.90; S, 10.82. Found (%): C, 62.84; H, 4.88; N, 18.91; S, 10.86.

### *3.5. Condensation of ketones 2 or 3 with amino compounds; Formation of compounds 6a,b and 9a,b; General procedure.*

To a mixture of compound **2** or **3** (5 mmol) and phenyl hydrazine or thiosemicarbazide (5 mmol) in ethanol (20 ml), few drops of acetic acid were added. The resulting mixture was heated under reflux for 2 h and left to cool. The precipitated product was collected and recrystallized from the proper solvent to give compounds **6a,b** and **9a,b** respectively.

### *3.5.1. 3-Cyano-4-(p-methoxyphenyl)-5-(2-phenylhydrazono)-5,6,7,8-tetrahydro-quinoline-2(1H)-thione (6a).*

It was obtained by using compound **2** and phenyl hydrazine. Yield: 83 %; m.p.: 300-302 °C (AcOH). IR: 3481, 3414 (NH), 2941 (C-H aliphatic), 2231 (C≡N), 1637, 1603 (C=N) $cm.^{-1}$ $^1$H NMR (DMSO-$d_6$): δ = 14.20 (s, 1H, NH of pyridine ring), 8.97 (s, 1H, NH of phenyl hydrazone), 7.24-7.26 (d, 2H, Ar-H), 7.01-7.03 (d, 2H, Ar-H), 6.92-6.95 (t, 2H, Ar-H), 6.63-6.66 (t, 1H, Ar-H), 6.29-6.31 (d, 2H, Ar-H), 3.80 (s, 3H, $OCH_3$), 2.86-2.88 (t, 2H, $CH_2$ at C-8), 2.54-2.56 (t, 2H, $CH_2$ at C-6), 1.91-1.95 (p, 2H, $CH_2$ at

C-7). $^{13}$C NMR (DMSO-$d_6$): δ =159.78, 154.87, 155.31, 145.08, 136.26, 138.33, 130.68, 124.01, 112.64 (2CH), 113.78 (2CH), 128.10 (2CH), 128.92 (2CH), 118.84 (CH), 27.58 ($CH_2$), 25.21 ($CH_2$), 18.76 ($CH_2$), 55.13 ($OCH_3$). MS: m/z = 400.14 (100%), 308.10 ($M^+$-PhNH, 36%), 92.02 (PhNH, 10 %), 93.02 ($PhNH_2$, 10 %). Elemental analysis calculated for $C_{23}H_{20}N_4OS$ (%): C, 68.98; H, 5.03; N, 13.99; S, 8.01. Found (%): C, 68.91; H, 4.90; N, 13.96; S, 7.81.

### *3.5.2. 2-[3-Cyano-4-(p-methoxyphenyl)-2-thioxo-1,2,7,8-tetrahydroquinolin-5(6H)-ylidene]hydrazinecarbothioamide (6b).*

It was obtained by using compound **2** and thiosemicarbazide. Yield: 77 %; m.p.: 308-310 °C (AcOH). IR: 3389, 3236, 3141 (NH), 3036 (C-H aromatic), 2935 (C-H aliphatic), 2223 (C≡N), 1604 (C=N) cm.$^{-1}$ $^1$H NMR (DMSO-$d_6$) : δ = 14.27 (s, 1H, NH of quinoline ring), 10.04 (s, 1H, NH), 8.05 (s, 1H, NH), 7.23-7.25 (d, 2H, Ar-H), 6.99-7.01 (d, 2H, Ar-H), 5.34 (s, 1H, NH), 3.84 (s, 3H, $OCH_3$), 2.85-2.87 (t, 2H, $CH_2$ at C-8), 2.59-2.61 (t, 2H, $CH_2$ at C-6), 1.84-1.89 (p, 2H, $CH_2$ at C-7).$^{13}$C NMR (DMSO-$d_6$): δ = 154.74, 178.22, 176.36, 159.46, 156.70, 143.15, 130.33, 117.29, 116.68, 113.99 (2CH), 128.40 (2CH), 27.40 ($CH_2$), 25.61 ($CH_2$), 18.58 ($CH_2$), 55.17 ($OCH_3$). MS: m/z = 383.32 (4%), 307.72 ($M^+$-$H_2$NCSNH). Elemental analysis calculated for $C_{18}H_{17}N_5OS_2$ (%): C, 56.38; H, 4.47; N, 18.26; S, 16.72. Found (%): C, 56.31; H, 4.49; N, 18.12; S, 16.58.

### *3.5.3. 4-(p-Methoxyphenyl)-2-methylthio-5-(2-phenylhydrazono)-5,6,7,8-tetrahydroquinoline-3-carbonitrile (9a).*

It was obtained by using compound **3** and phenyl hydrazine. Yield: 72 %, m.p.: 255-256 °C (EtOH). IR: 3476 (NH), 2953 (C-H aliphatic), 2220 (C≡N), 1637, 1602 (C=N) cm.$^{-1}$ $^1$H NMR ( DMSO-$d_6$): δ = 9.10 (s, 1H, NH), 7.24-7.27 (d, 2H, Ar-H), 6.99-7.02 (d, 2H, Ar-H), 6.91-6.96 (t, 2H, Ar-H), 6.63-6.66 (t, 1H, Ar-H), 6.32-6.34 (d, 2H, Ar-H), 3.79 (s, 3H, $OCH_3$), 2.64-2.66 (t, 2H, $CH_2$ at C-6), 2.59 (s, 3H, $SCH_3$), 2.49-2.51 (2H, $CH_2$ at C-8), 1.91-1.95 (p, 2H, $CH_2$ at C-7).$^{13}$C NMR (DMSO-$d_6$): δ = 165.67, 163.94, 160.22, 159.68, 151.70, 145.90, 137.87, 131.71, 107.72, 114.30 (2CH), 114.80 (2CH), 129.00 (2CH), 130.19 (2CH), 119.91 (CH), 34.82 ($CH_2$), 26.77 ($CH_2$), 20.66 ($CH_2$), 56.01 ($OCH_3$), 13.67 ($SCH_3$). MS: m/z = 413.64 (100%), 321.19 ($M^+$-PhNH, 48 %), 107.87 ($C_6H_5OMe$, 26 %), 91.92 (PhNH, 95 %), 92.92 ($PhNH_2$, 25 %). Elemental analysis calculated for $C_{24}H_{22}N_4OS$ (%): C, 69.54; H, 5.35; N, 13.52; S, 7.73. Found (%): C, 69.28; H, 5.36; N, 13.20; S, 7.69.

### *3.5.4. 2-[3-Cyano-4-(p-methoxyphenyl)-2-methylthio-7,8-dihydroquinolin-5(6H)-ylidene]hydrazinecarbothioamide (9b).*

It was obtained by using compound **3** and thiosemicarbazide. Yield: 71 %, m.p.: 264-265 °C (EtOH). IR: 3472, 3398, 3255 (NH), 2952 (C-H aliphatic), 2222 (C≡N), 1637, 1611 (C=N) cm.$^{-1}$ $^1$H NMR (DMSO-$d_6$): δ = 10.18 (s, 1H, NH), 8.08 (s, 1H, NH), 7.23-7.25 (d, 2H, Ar-H), 6.98-7.00 (d, 2H, Ar-H), 5.43 (s, 1H, NH), 3.83 (s, 3H, $OCH_3$), 2.92-2.96 (t, 2H, $CH_2$ at C-6), 2.66-2.700 (t, 2H, $CH_2$ at C-8), 2.6 (s, 3H, $SCH_3$), 1.87-1.92 (p, 2H, $CH_2$ at C-7).$^{13}$C NMR (DMSO-$d_6$): δ = 179.96, 171.35, 164.11, 159.60, 155.67, 153.59, 122.99, 131.88, 105.44, 114.35 (2CH), 128.60 (2CH), 28.52 ($CH_2$), 25.97 ($CH_2$), 19.21 ($CH_2$), 56.03 ($OCH_3$), 14.11 ($SCH_3$). MS: m/z = 397.40 ($M^+$, 5.4 %), 323 [$M^+$-($NHCSNH_2$)]. Elemental analysis calculated for $C_{19}H_{19}N_5OS_2$ (%): C, 57.41; H, 4.82; N, 17.62; S, 16.13. Found (%): C, 57.37; H, 4.60; N, 17.35; S, 16.00.

***3.6. Reaction of thiones 6a or 2 with some halo compounds; Formation of thioethers 7 or 10a-d; General procedure.***

To a suspension of compound **6a** or **2** (10 mmol) and sodium acetate trihydrate (1.63 g, 12 mmol) in ethanol (30 ml), the appropriate halo compound (10 mmol) was added. The resulting mixture was heated under reflux for 3 h and then allowed to cool. The formed solid was filtered off, washed with water, dried in air and recrystallized from ethanol to give compounds **7** or **10a-d** respectively.

***3.6.1. Ethyl [3-cyano-4-(p-methoxyphenyl)-5-(2-phenylhydrazono)-5,6,7,8-tetra hydroquinolin-2-ylthio]acetate (7).***

It was prepared by using compound **6a** and ethyl chloroacetate. Yield: 66 %; m.p.: 239-241°C. IR: 3332 (NH), 2216 (C≡N), 1742 (C=O, ester), 1631 (C=N) cm.$^{-1}$ $^{1}$H NMR: ($CDCl_3$): δ = 6.80-7.28 (m, 10H, Ar-H and NH), 4.27 (s, 2H, $SCH_2$), 3.90-4.20 (q, 2H, $OCH_2$), 3.86 (s, 3H, $OCH_3$), 2.94-2.96 (t, 2H, $CH_2$ at C-8), 2.58-2.61 (t, 2H, $CH_2$ at C-6), 2.06-2.10 (p, 2H, $CH_2$ at C-7), 1.33 (t, 3H, $CH_3$ of ester). Elemental analysis calculated for $C_{27}H_{26}N_4O_3S$ (%): C, 66.65; H, 5.39; N, 11.51; S, 6.59. Found (%): C, 66.47; H, 5.36; N, 11.54; S, 6.64.

***3.6.2. Ethyl (3-cyano-4-(p-methoxyphenyl)-5-oxo-5,6,7,8-tetrahydroquinolin-2-ylthio)acetate (10a).***

It was prepared by using compound **2** and ethyl chloroacetate. Yield: 68 %; m.p.: 119-121 °C. IR: 2969 (C-H aliphatic), 2221 (C≡N), 1745 (C=O, ester), 1693 (C=O, ketone), 1637, 1608 (C=N) cm.$^{-1}$ $^{1}$H NMR (DMSO-$d_6$): δ = 7.21-7.24 (d, *J* = 12.0 Hz, 2H, Ar-H), 6.98-7.01 (d, *J* = 12.0 Hz, 2H, Ar-H), 4.15-4.19 (m, 4H, $SCH_2$ and $OCH_2$), δ 3.83 (s, 3H, $OCH_3$), 3.05-3.07 (t, 2H, $CH_2$ at C-6), 2.50-2.52 (t, 2H, $CH_2$ at C-8), 2.09-2.13 (p, 2H, $CH_2$ at C-7), 1.21-1.24 (t, 3H, $CH_3$ of ester).$^{13}$C NMR (DMSO-$d_6$): δ = 196.35, 169.07, 168.15, 164.43, 160.46, 155.61, 130.19, 123.93, 107.59, 114.35 (2CH), 129.08 (2CH), 84.15 ($CH_2$), 62.09 ($CH_2$), 34.16 ($CH_2$), 33.46 ($CH_2$), 21.16 ($CH_2$), 56.01 ($OCH_3$), 14.99 ($CH_3$). Elemental analysis calculated for $C_{21}H_{20}N_2O_4S$ (%): C, 63.62; H, 5.08; N, 7.07; S, 8.09. Found (%): C, 63.45; H, 5.29; N, 7.00; S, 8.16.

***3.6.3. [3-Cyano-4-(p-methoxyphenyl)-5-oxo-5,6,7,8-tetrahydroquinolin-2-ylthio] acetamide (10b).***

It was prepared by using compound **2** and chloroacetamide. Yield: 65 %; m.p.: 190-192°C. IR: 3485, 3367 ($NH_2$), 2220 (C≡N), 1682 (C=O, ketone), 1652 (C=O, amide) cm.$^{-1}$ $^{1}$H NMR ($CDCl_3$): δ = 7.15-7.17 (d, 2H, Ar-H), 7.00-7.02 (d, 2H, Ar-H), 6.55 (br. s, 1H, NH), 5.45 (br. s, 1H, NH), 4.01 (s, 2H, $SCH_2$), 3.89 (s, 3H, $OCH_3$), 3.21-3.23 (t, 2H, $CH_2$ at C-8), 2.64-2.66 (t, 2H, $CH_2$ at C-6), 2.19-2.23 (p, 2H, $CH_2$ at C-7). Elemental analysis calculated for $C_{19}H_{17}N_3O_3S$ (%): C, 62.11; H, 4.66; N, 11.44; S, 8.73. Found (%): C, 62.16; H, 4.68; N, 11.19; S, 8.50.

***3.6.4. 3-Cyano-4-(p-methoxyphenyl)-5-oxo-2-[N-(p-tolyl)carbamoylmethylthio]-5,6,7,8-tetrahydroquinoline (10c).***

It was prepared by using compound **2** and chloro *N*-(*p*-tolyl)acetamide. Yield: 77 %; m.p.: 182-183 °C. IR: 3323 (NH), 2222 (C≡N), 1686 (C=O, ketone), 1660 (C=O, anilide) cm.$^{-1}$ $^{1}$H NMR (DMSO-$d_6$) : δ = 11.31 (br. s, 1H, NH), 7.63-7.65 (d, 2H, Ar-H), 7.32-7.34 (d, 2H, Ar-H), 7.21-7.23 (d, 2H, Ar-H), 7.11-7.13 (d, 2H, Ar-H), 4.45 (s, 2H, $SCH_2$), 3.91 (s, 3H, $OCH_3$), 3.20-3.22 (t, 2H, $CH_2$ at C-8), 2.61-2.63 (t, 2H, $CH_2$ at C-6), 2.18-2.22 (p, 2H, $CH_2$ at C-7), 2.15 (s, 3H, $CH_3$). Elemental analysis calculated for $C_{26}H_{23}N_3O_3S$ (%): C, 68.25; H, 5.07; N, 9.18; S, 7.01. Found (%): C, 68.11; H, 5.08; N, 9.00; S, 6.78.

***3.6.5. 4-(p-Methoxyphenyl)-5-oxo-2-(phenacylthio)-5,6,7,8-tetrahydroquinoline-3-carbonitrile (10d).***

It was prepared by using compound **2** and phenacyl bromide. Yield: 74 % ; m.p.: 220-221 °C. IR: 2219 (C≡N), 1693 (C=O, cyclic ketone), 1672 (C=O, phenacyl residue) $cm.^{-1}$ $^1$H NMR ($CDCl_3$): δ = 8.00-8.02 (d, *J* = 8.0 Hz,, 2H, Ar-H), 7.56-7.60 (t, *J* = 8.0 Hz, 1H, Ar-H), 7.45-7.49 (t, *J* = 8.0 Hz, 2H, Ar-H), 7.03-7.05 (d, *J* = 8.0 Hz,, 2H, Ar-H), 6.88-6.90 (d, *J* = 8.0 Hz,, 2H, Ar-H), 4.63 (s, 2H, $SCH_2$), 3.78 (s, 3H, $OCH_3$), 2.76-2.79 (t, 2H, $CH_2$ at C-6), 2.45-2.48 (t, 2H, $CH_2$ at C-8), 1.94-1.98 (p, , 2H, $CH_2$ at C-7). Elemental analysis calculated for $C_{25}H_{20}N_2O_3S$ (%): C, 70.07; H, 4.70; N, 6.54; S, 7.48. Found (%): C, 70.01; H, 4.72; N, 6.68; S, 7.80.

***3.7. Ethyl 3-amino-4-(p-methoxyphenyl)-5-(2-phenylhydrazono)-5,6,7,8-tetrahydro-thieno[2,3-b]quinoline-2-carboxylate (8).***

To a suspension of compound **7** (1.0 g) in ethanol, 0.5 g of anhydrous $K_2CO_3$ was added. The reaction mixture was heated under reflux for 3 h and filtered while hot to remove $K_2CO_3$. The product that forming on cooling of the filtrate was collected by filtration, washed with water and recrystallized from ethanol to give yellow needles of compound **8**. Yield: 71 %; m.p.: 267-268°C. IR: 3482, 3351 ($NH_2$), 2954 (C-H aliphatic), 1690 (C=O, cyclohexanone residue) 1661 (C=O, ester) $cm.^{-1}$ $^1$H NMR: ($CDCl_3$): δ = 6.85-7.30 (m, 10H, Ar-H and NH), 5.30 (s, 2H, $NH_2$), 3.93-4.21 (q, 2H, $OCH_2$), 3.86 (s, 3H, $OCH_3$), 2.96-2.98 (t, 2H, $CH_2$ at C-8), 2.60-2.63 (t, 2H, $CH_2$ at C-6), 2.10-2.14 (p, 2H, $CH_2$ at C-7), 1.10-1.40 (t, 3H, $CH_3$ of ester). Elemental analysis calculated for $C_{27}H_{26}N_4O_3S$ (%): C, 66.65; H, 5.39; N, 11.51; S, 6.59. Found (%): C, 66.40; H, 5.31; N, 11.63; S, 6.74.

***3.8. Cyclization of compounds 10a-d; Formation of thienoquinolines 11a-d; General procedure.***

Compound **10a-d** (5 mmol) was suspended in sodium ethoxide solution (0.05 g sodium in 30 ml absolute ethanol) and heated under reflux for 5 mins. The solid that formed after cooling was collected and recrystallized from ethanol as canary yellow needles of **11a-d**.

***3.8.1. Ethyl 3-amino-4-(p-methoxyphenyl)-5-oxo-5,6,7,8tetrahydrothieno [2,3-b]quinoline-2-carboxylate (11a).***

It was obtained by cyclization of compound **10a**. Yield: 64 %, m.p.: 200-202 °C. IR: 3482, 3351 ($NH_2$), 2954 (C-H aliphatic), 1681 (C=O, ketone) 1661 (C=O, ester) $cm^{-1}$.$^1$H NMR ($CDCl_3$): δ = 7.28-7.30 (2H, Ar-H), 7.00-7.02 (d, 2H, Ar-H), 5.3 (br. s, 2H, $NH_2$), 4.32 (q, 2H, $OCH_2$), 3.89 (s, 3H, $OCH_3$), 3.26-3.28 (t, 2H, $CH_2$ at C-6), 2.66-2.68 (t, 2H, $CH_2$ at C-8), 2.20-2.24 (p, 2H, $CH_2$ at C-7), 1.29-1.32 (t, 3H, $CH_3$ of ester group). Elemental analysis calculated for $C_{21}H_{20}N_2O_4S$ (%): C, 63.62; H, 5.08; N, 7.07; S, 8.09. Found (%): C, 63.91; H, 5.05; N, 6.90; S, 8.41.

***3.8.2. 3-Amino-4-(p-methoxyphenyl)-5-oxo-5,6,7,8-tetrahydrothieno[2,3-b] quinoline-2-carboxamide (11b).***

It was obtained by cyclization of compound **10b**. Yield: 61 %; m.p.: 292-293 °C. IR: 3469, 3373 ($NH_2$), 2946 (C-H aliphatic), 1686 (C=O, ketone), 1646 $cm^{-1}$ (C=O, amide), 1637, 1608 (C=N) $cm^{-1}$. $^1$H NMR (DMSO-$d_6$): δ = 7.19-7.21 (d, 4H, $CONH_2$ and Ar-H), 7.04-7.06 (d, 2H, Ar-H), 5.68 (s, 2H, $NH_2$ attached to thiophene ring), 3.85 (s, 3H, $OCH_3$), 3.19-3.21 (t, 2H, $CH_2$ at C-6), 2.55-2.57 (t, 2H, $CH_2$ at C-8), 2.07-2.11 (p, 2H, $CH_2$ at C-7). $^{13}$C NMR: δ = 146.70, 196.94, 163.64, 166.68, 161.18, 158.93, 147.80, 127.85, 123.16, 122.52, 96.84, 113.69 (2CH), 128.51 (2CH), 33.35 ($CH_2$), 20.74 ($CH_2$), 18.53 ($CH_2$), 55.14

($OCH_3$). Elemental analysis calculated for $C_{19}H_{17}N_3O_3S$ (%): C, 62.11; H, 4.66; N, 11.44; S, 8.73. Found (%): C, 62.18; H, 4.68; N, 11.61; S, 8.69.

***3.8.3. 3-Amino-4-(p-methoxyphenyl)-5-oxo-2-[N-(p-tolyl)carbamoyl]-5,6,7,8-tetra- hydrothieno[2,3-b]quinoline (11c).***

It was obtained by cyclization of compound **10c**. Yield: 75 %. m.p.: 211-213 °C. IR: 3464, 3335 (NH, $NH_2$), 2925 (C-H aliphatic), 1693 (C=O, cyclohexanone residue), 1650 (C=O, acetanilide residue) $cm.^{-1}$ $^1H$ NMR (DMSO-$d_6$): δ = 10.22 (br. s, 1H, CONH), 7.61-7.63 (d, 2H, Ar-H), 7.58-7.60 (d, 2H, Ar-H), 7.18-7.20 (d, 2H, Ar-H), 7.12-7.14 (d, 2H, Ar-H), 5.66 (br. s, 2H, $NH_2$), 3.72 (s, 3H, $OCH_3$), 2.63-2.65 (t, 2H, $CH_2$ at C-8), 2.36-2.38 (t, 2H, $CH_2$ at C-6), 2.16-2.20 (p, 2H, $CH_2$ at C-7), 2.23 (s, 3H, $CH_3$). MS: m/z = 457.43 ($M^+$, 42.7 %). Elemental analysis calculated for $C_{26}H_{23}N_3O_3S$ (%): C, 68.25; H, 5.07; N, 9.18; S, 7.01. Found (%): C, 68.49; H, 5.02; N, 9.17; S, 7.24.

***3.8.4. 3-Amino-2-benzoyl-4-(p-methoxy-phenyl)-5-oxo-5,6,7,8-tetrahydrothieno [2,3-b]quinoline (11d).***

It was obtained by cyclization of compound **10d**. Yield: 71 %; m.p.: 216-218 °C. IR: 3460, 3272 ($NH_2$), 2926 $cm^{-1}$ (C-H aliphatic), 1688 (C=O, cyclohexanone residue), 1640 (C=O, benzoyl residue) $cm.^{-1}$ $^1H$ NMR ($CDCl_3$): δ =7.81-7.83 (d, 2H, Ar-H), 7.52-7.54 (t, 1H, Ar-H), 7.50-7.52 (t, 2H, Ar-H), 7.27-7.29 (d, 2H, Ar-H), 7.10-7.13 (d, 2H, Ar-H), δ 5.72 (s, 2H, $NH_2$ attached to thiophene ring), 3.94 (s, 3H, $OCH_3$), 3.36-3.38 (t, 2H, $CH_2$ at C-6), 2.66-2.68 (t, 2H, $CH_2$ at C-8), 2.21-2.25 (p, 2H, $CH_2$ at C-7)ppm. Elemental analysis calculated for $C_{25}H_{20}N_2O_3S$ (%): C, 70.07; H, 4.70; N, 6.54; S, 7.48. Found (%): C, 70.09; H, 4.44; N, 6.40; S, 7.52.

## 4. Conclusion

The starting compound, 3-cyano-4-(*p*-methoxyphenyl)-5-oxo-5,6,7,8-tetrahydro-quinoline-2(1*H*)-thione (**2**) was prepared and converted it into the corresponding 2-methylthio derivative **3.** The synthetic utility of both **2** and **3** for preparation of new tetrahydroquinolines, tetrahydropyrazoloquinolines and tetrahydrothienoquinolines was evaluated.

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