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Some reactions of 3-cyano-4-(p-methoxyphenyl)-5-oxo-5,6,7,8-tetrahydroquinoline-2(1H)-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(1H)-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(1H)-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-arylidene cyclohexanones 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(1H)-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(1H)-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-methoxybenzylidene-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-methyltetrahydroquinoline (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 isothiocyanate in hot pyridine gave the dithiouredo derivative 5 (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$_2$CO$_3$ 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(1H)-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-Ziegler 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](image)

![Scheme 4](image)
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-d6): 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, OCH₃), 3.01-3.03 (t, J = 4.0 Hz, 2H, CH₂ at C-6), 2.39-2.41 (t, J = 4.0 Hz, 2H, CH₂ at C-8), 1.99-2.03 (p, J = 4.0 Hz, 2H, CH₂ at C-7). ¹³C NMR (DMSO-d6): 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 (CH₃), 20.41 (CH₂), 55.98 (OCH₃). Elemental analysis calculated for C₁₇H₁₄N₂O₅S (%): 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-(methylthio)-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-d6): 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, OCH₃), 3.16-3.18 (t, J = 4.0 Hz, 2H, CH₂ at C-8), 2.69 (s, 3H, S(CH₃), 2.56-2.58 (t, J = 4.0 Hz, 2H, CH₂ at C-6), 2.08-2.12 (t, J = 4.0 Hz, 2H, CH₂ at C-7). ¹³C NMR (DMSO-d6): δ = 195.57,

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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 aliphatic), 2942 (C-H aromatic), 1638, 1608 (C=N) cm⁻¹. ¹H NMR (DMSO-d₆): 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, OCH₃), 2.91-2.93 (t, 2H, CH₂ at C-8), 2.84-2.86 (t, 2H, CH₂ at C-6), 1.95-1.99 (p, 2H, CH₂ at C-7). Elemental analysis calculated for C₃₁H₂₈N₈O₅S (%): 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-tetrahydroquinoline-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. ¹H NMR (DMSO-d₆): 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, OCH₃), 2.86-2.88 (t, 2H, CH₂ at C-8), 2.54-2.56 (t, 2H, CH₂ at C-6), 1.91-1.95 (p, 2H, CH₂ at
C-7). $^{13}$C NMR (DMSO-<sub>d6</sub>): $\delta$ = 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<sub>2</sub>), 25.21 (CH<sub>2</sub>), 18.76 (CH<sub>2</sub>), 55.13 (OCH<sub>3</sub>). MS: m/z = 400.14 (100%), 308.10 (M<sup>+</sup>-PhNH, 36%), 92.02 (PhNH, 10 %), 93.02 (PhNH<sub>2</sub>, 10 %). Elemental analysis calculated for C<sub>23</sub>H<sub>26</sub>N<sub>2</sub>O<sub>3</sub> (%): 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<sup>-1</sup>. $^{1}$H NMR (DMSO-<sub>d6</sub>): $\delta$ = 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<sub>3</sub>), 2.85-2.87 (t, 2H, CH<sub>2</sub> at C-8), 2.59-2.61 (t, 2H, CH<sub>2</sub> at C-6), 1.84-1.89 (p, 2H, CH<sub>2</sub> at C-7). $^{13}$C NMR (DMSO-<sub>d6</sub>): $\delta$ = 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<sub>3</sub>), 25.61 (CH<sub>2</sub>), 18.58 (CH<sub>2</sub>), 55.17 (OCH<sub>3</sub>). MS: m/z = 383.32 (4%), 307.72 (M<sup>+</sup>-H<sub>2</sub>NCSNH). Elemental analysis calculated for C<sub>18</sub>H<sub>19</sub>N<sub>3</sub>O<sub>2</sub> (%): 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<sup>-1</sup>. $^{1}$H NMR (DMSO-<sub>d6</sub>): $\delta$ = 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<sub>3</sub>), 2.64-2.66 (t, 2H, CH<sub>2</sub> at C-6), 2.59 (s, 3H, SCH<sub>3</sub>), 2.49-2.51 (2H, CH<sub>2</sub> at C-8), 1.91-1.95 (p, 2H, CH<sub>2</sub> at C-7). $^{13}$C NMR (DMSO-<sub>d6</sub>): $\delta$ = 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<sub>2</sub>), 26.77 (CH<sub>3</sub>), 20.66 (CH<sub>2</sub>), 56.01 (OCH<sub>3</sub>), 13.67 (SCH<sub>3</sub>). MS: m/z = 413.64 (100%), 321.19 (M<sup>+</sup>-PhNH, 48 %), 107.87 (C<sub>6</sub>H<sub>5</sub>OMe, 26 %), 91.92 (PhNH, 95 %), 92.92 (PhNH<sub>2</sub>, 25 %). Elemental analysis calculated for C<sub>24</sub>H<sub>22</sub>N<sub>2</sub>O<sub>3</sub> (%): 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<sup>-1</sup>. $^{1}$H NMR (DMSO-<sub>d6</sub>): $\delta$ = 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<sub>3</sub>), 2.92-2.96 (t, 2H, CH<sub>2</sub> at C-6), 2.66-2.70 (t, 2H, CH<sub>2</sub> at C-8), 2.6 (3H, SCH<sub>3</sub>), 1.87-1.92 (p, 2H, CH<sub>2</sub> at C-7). $^{13}$C NMR (DMSO-<sub>d6</sub>): $\delta$ = 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<sub>2</sub>), 25.97 (CH<sub>2</sub>), 19.21 (CH<sub>2</sub>), 56.03 (OCH<sub>3</sub>), 14.11 (SCH<sub>3</sub>). MS: m/z = 397.40 (M<sup>+</sup>, 5.4 %), 323 [M<sup>+</sup>-NHCSNH]<sub>2</sub>]. Elemental analysis calculated for C<sub>19</sub>H<sub>19</sub>N<sub>3</sub>O<sub>3</sub>S (%) : 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.


It was prepared by using compound 6a and ethyl chloroacetate. Yield: 66 %; m.p.: 239-241°C. IR: 3332 (NH), 2216 (C=O, ester), 1631 (C=N) cm⁻¹.

¹H NMR: (CDCl₃): δ = 6.80-7.28 (m, 10H, Ar-H and NH), 4.27 (s, 2H, SCH₂), 3.90-4.20 (q, 2H, OCH₂), 3.86 (s, 3H, OCH₃), 2.94-2.96 (t, 2H, CH₂ at C-8), 2.58-2.61 (t, 2H, CH₂ at C-6), 2.06-2.10 (p, 2H, CH₂ at C-7), 1.33 (t, 3H, CH₃ of ester). Elemental analysis calculated for C₂₇H₂₆N₄O₃S (%): C, 62.16; H, 4.68; N, 11.19; S, 8.50. Found (%): 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.

3.6.2. Ethyl (3-cyano-4-(p-methoxy-phenyl)-5-oxo-5,6,7,8-tetrahydroquinolin-2-ylid]acetate (10a).

It was prepared by using compound 2 and ethyl chloroacetate. Yield: 68 %; m.p.: 119-121 ºC. IR: 2969 (C-H aliphatic), 2221 (C=N), 1745 (C=O, ester), 1693 (C=O, ketone), 1637, 1608 (C=N) cm⁻¹.

¹H NMR (DMSO-d₆): 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, SCH₂ and OCH₂), δ 3.83 (s, 3H, OCH₃), 3.05-3.07 (t, 2H, CH₂ at C-6), 2.50-2.52 (t, 2H, CH₂ at C-8), 2.09-2.13 (p, 2H, CH₂ at C-7), 1.21-1.24 (t, 3H, CH₃ of ester).¹³C NMR (DMSO-d₆): 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 (CH₂), 62.09 (CH₂), 34.16 (CH₂), 33.46 (CH₂), 21.16 (CH₂), 56.01 (OCH₃), 14.99 (CH₃).

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

It was prepared by using compound 2 and chloroacetamide. Yield: 65 %; m.p.: 190-192ºC. IR: 3485, 3367 (NH₂), 2220 (C=N), 1682 (C=O, ketone), 1652 (C=O, amide) cm⁻¹.¹H NMR (CDCl₃): 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, SCH₂), 3.89 (s, 3H, OCH₃), 3.21-3.23 (t, 2H, CH₂ at C-8), 2.64-2.66 (t, 2H, CH₂ at C-6), 2.19-2.23 (p, 2H, CH₂ at C-7). Elemental analysis calculated for C₁₉H₁₇N₂O₃S (%): C, 62.11; H, 4.66; N, 11.44; S, 8.73. Found (%): C, 62.16; H, 4.68; N, 11.29; S, 8.50.

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

It was prepared by using compound 2 and chloro-N-(p-toly)acetamide. Yield: 77 %; m.p.: 182-183 ºC. IR: 3323 (NH₂), 2222 (C=N), 1686 (C=O, ketone), 1660 (C=O, anilide) cm⁻¹.¹H NMR (DMSO-d₆): 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, SCH₂), 3.91 (s, 3H, OCH₃), 3.20-3.22 (t, 2H, CH₂ at C-8), 2.61-2.63 (t, 2H, CH₂ at C-6), 2.18-2.22 (p, 2H, CH₂ at C-7), 2.15 (s, 3H, CH₃). Elemental analysis calculated for C₂₃H₂₃N₂O₃S (%): 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. ¹H NMR (CDCl₃): 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, SCH₂), 3.78 (s, 3H, OCH₃), 2.76-2.79 (t, 2H, CH₂ at C-6), 2.45-2.48 (t, 2H, CH₂ at C-8), 1.94-1.98 (p, 2H, CH₂ at C-7). Elemental analysis calculated for C₂₅H₂₇N₂O₃S: (%) 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 K₂CO₃ was added. The reaction mixture was heated under reflux for 3 h and filtered while hot to remove K₂CO₃. 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 (NH₂), 2954 (C-H aliphatic), 1690 (C=O, cyclohexanone residue) 1661 (C=O, ester) cm⁻¹. ¹H NMR: (CDCl₃): δ = 6.85-7.30 (m, 10H, Ar-H and NH), 5.30 (s, 2H, NH₂), 3.93-4.21 (q, 2H, OCH₂), 3.86 (s, 3H, OCH₃), 2.96-2.98 (t, 2H, CH₂ at C-8), 2.60-2.63 (t, 2H, CH₂ at C-6), 2.10-2.14 (p, 2H, CH₂ at C-7), 1.10-1.40 (t, 3H, CH₃ of ester). Elemental analysis calculated for C₂₁H₂₆N₂O₃S: (%) 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.


It was obtained by cyclization of compound 10a. Yield: 64%; m.p.: 200-202°C. IR: 3482, 3351 (NH₂), 2954 (C-H aliphatic), 1681 (C=O, ketone) 1661 (C=O, ester) cm⁻¹. ¹H NMR: (CDCl₃): δ = 7.28-7.30 (2H, Ar-H), 7.00-7.02 (d, 2H, Ar-H), 5.3 (br. s, 2H, NH₂), 4.32 (q, 2H, OCH₂), 3.89 (s, 3H, OCH₃), 3.26-3.28 (t, 2H, CH₂ at C-6), 2.66-2.68 (t, 2H, CH₂ at C-8), 2.20-2.24 (p, 2H, CH₂ at C-7), 1.29-1.32 (t, 3H, CH₃ of ester group). Elemental analysis calculated for C₂₁H₂₆N₂O₃S: (%) 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 (NH₂), 2946 (C-H aliphatic), 1686 (C=O, ketone), 1646 cm⁻¹ (C=O, amide), 1637, 1608 (C=N) cm⁻¹. ¹H NMR: (DMSO-d₆): δ = 7.19-7.21 (d, 4H, CONH₂ and Ar-H), 7.04-7.06 (d, 2H, Ar-H), 5.68 (s, 2H, NH₂ attached to thiophene ring), 3.85 (s, 3H, OCH₃), 3.19-3.21 (t, 2H, CH₂ at C-6), 2.55-2.57 (t, 2H, CH₂ at C-8), 2.07-2.11 (p, 2H, CH₂ at C-7). ¹³C 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 (CH₂), 20.74 (CH₂), 18.53 (CH₂), 55.14.
3.8.3. 3-Amino-4-(p-methoxyphenyl)-5-oxo-2-[N-(p-tolyl)carbamoyl]-5,6,7,8-tetrahydrothieno[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, acetonilide residue) cm$^{-1}$.

Elemental analysis calculated for C$_{29}$H$_{26}$N$_2$O$_4$S (%): 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-tetrahydroquinoline-2(1H)-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, tetrahydropyrrozoloquinolines and tetrahydrothienoquinolines was evaluated.

References