

---

**SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF SOME NEW COUMARIN, PYRIDINE, 1,2,3-TRIAZOLE, THIAZOLIDINONE, PYRAZOLOTRIAZINE, THIOPHENE AND THIAZOLE DERIVATIVES BEARING CARBONYLHYDRAZONOETHYLPHENYLTOSYLATE MOIETY**

---

MAHMOUD M. ABDELALL<sup>a</sup>, SHABAN I. MOHAMED<sup>b</sup>, AHMED H. HALAWA<sup>a</sup>, AHMED A. HASSAN<sup>a</sup> AND MOHAMED A. ELNASSAG<sup>a</sup>

- a) *Chemistry Department, Faculty of Science, Al-Azhar University, Nasr City, Cairo, Egypt.*  
b) *Technology Engineering Institute, Tamoh, Giza, Egypt.*
- 

**Abstract**

A number of novel coumarin (**4**), pyridinone (**5a,b**), thiophenopyridinone (**6**), 1,2,3-triazole (**7**), pyrazolotriazine (**10**), thiazole (**11,14a,b,15**), thiophene (**12**), thiazolidinone (**20,21,23**) derivatives were synthesized via interaction of 4-(1-(2-(2-cyanoacetyl)hydrazono)ethyl)phenyltosylate (**3**) with different nucleophilic reagents. The structures of the newly synthesized compounds were confirmed by elemental analyses IR, <sup>1</sup>H-NMR and mass spectral data. All compounds were evaluated for their antimicrobial activities.

**Keywords:** Cyanoacetylhydrazonoethylphenyltosylate, pyridine, thiazole, coumarin, thiophene, pyrazolotriazine and thiazolidinone

**Introduction**

Several organosulphur heterocycles such as thiazole, thiazolidine, thiazolidinone and thiophene<sup>1-3</sup> show diverse biological and physiological activities which exhibit pesticidal<sup>4</sup>, anticonvulsant<sup>5</sup>, nematocidal<sup>6</sup>, herbicidal<sup>7</sup>, antiviral<sup>8</sup>, fungicidal<sup>9</sup>, bactericidal, <sup>10</sup>antiprotazoal<sup>11</sup> and hypoglycemic activity. They also act as chemotherapeutic agents due to the presence of the N-C-S fragment. In addition, pyridine derivatives are known to possess interesting biological properties that show anticancer<sup>12-15</sup> and antimicrobial activities<sup>16,17</sup>. This encouraged us to design a specific work aimed at synthesizing several new derivatives of these ring systems incorporated with carbonylhydrazonoethylphenyltosylate moiety.

**Results and Discussion**

The present work is designed to synthesize some new heterocycles carrying biologically active phenyltosylate moiety. Thus, 4-acetylphenyltosylate (**2**) was prepared by the reaction of 4-hydroxyacetophenone with tosyl chloride in acetone in the presence of potassium carbonate. Compound **2** was characterized by the presence of strong absorption bands at 1680 and 1376, 1166 cm<sup>-1</sup> due to CO and

SO<sub>2</sub> groups, respectively. Its <sup>1</sup>H-NMR spectrum displayed two singlet signals at 2.45 and 2.57 ppm, due to CH<sub>3</sub> of tolyl and acetyl groups respectively.

Condensation of compound **2** with cyanoacetohydrazide in ethanol afforded 4-(1-(2-(2-cyanoacetyl)hydrazono)ethyl)phenyltosylate (**3**), **Eq.1** The structure of compound **3** was proved on the basis of analytical and spectral data. Thus, IR spectrum showed bands at 3186, 2260 and 1680 cm<sup>-1</sup> due to NH, CN and CO groups respectively and its <sup>1</sup>H-NMR spectrum revealed the presence of a characteristic signal due to methylene protons at 3.88 ppm.

2-Cyanoacetohydrazide **3** is a versatile reagent and have been extensively used as synthetic starting material for the synthesis of several substituted heterocyclic compounds. Thus, compound **3** was allowed to react with salicylaldehyde in ethanol in the presence of piperidine to give a product identified as 4-(1-(2-(2-oxo-2H-chromene-3-carbonyl)hydrazono)ethyl)phenyltosylate (**4**), **Scheme 1**. The reactivity of compound **3** towards dicarbonyl compounds was studied. Thus, cyclocondensation of **3** with acetylacetone and benzoylacetone in ethanol in the presence of piperidine as a catalyst furnished the pyridine-2-one derivatives **5a,b** respectively. **Scheme 1**, Analytical and spectral data are consistent with the proposed structures.

Also, interaction of compound **5a** with elemental sulfur via Gewald reaction produced 4-(1-(3-amino-6-methyl-4-oxothieno[3,4-c]pyridin-5(4H)-ylimino)ethyl)phenyltosylate (**6**), **Scheme 1**. The structure of the latter product was confirmed by the presence of the characteristic absorption of the amino group in its IR spectrum.

On the other hand, coupling of compound **3** with 4-chlorophenylazide in ethanolic sodium ethoxide afforded 4-(1-(2-(5-amino-1-(4-chlorophenyl)-1H-1,2,3-triazole-4-carbonyl)hydrazono)ethyl)phenyltosylate (**7**), **Scheme 1**. Moreover, compound **3** underwent coupling with equimolar amount of 4-fluorophenyldiazonium chloride in ethanolic sodium acetate at 0°C affording the aryl hydrazone derivative **8a**, <sup>1</sup>H-NMR spectrum provided a firm support for structure **8a** and ruled out the other possible structure **8b**, **Scheme 2**.

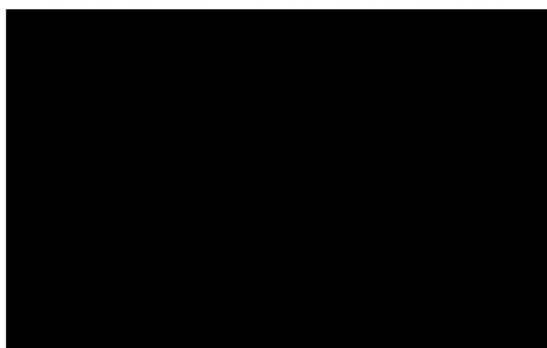
In continuation of our interest in the synthesis of bridged head nitrogen heterocyclic systems<sup>18</sup>, we have found that diazotized heterocyclic amine is an excellent building block for the synthesis of the target compound. Thus, coupling of compound **3** with 5-(chlorodiazonyl)-3-(methylthio)-1H-pyrazole-4-carbonitrile<sup>19</sup> in pyridine at 0°C afforded non-isoluble intermediate **9**, which undergoes intramolecular cyclization into the corresponding pyrazolotriazine derivative **10**, **Scheme 2**

The reaction of compound **3** with elemental sulfur and phenyl isothiocyanate afforded the 2-thioxothiazole derivative **11**. The formation of the latter product can be explained on the basis of the reported Hanzesch reaction<sup>20</sup>, **Scheme 3**. Similarly, the reaction of compound **3** with cyclopentanone and elemental sulfur yielded 4-(1-(2-(2-amino-5,6-dihydro-4H-cyclopenta[b]thiophene-3-carbonyl)hydrazono)ethyl)phenyltosylate (**12**), **Scheme 3**

The reactivity of cyanoacetohydrazide **3** towards phenyl isothiocyanate in the presence of potassium hydroxide followed by in situ heterocyclization with  $\alpha$ -halo compounds was studied. Thus, treatment of 2-cyanoacetohydrazide derivative **3** with phenyl isothiocyanate in dimethylformamide in the presence of potassium hydroxide at room temperature yielded the non-isolable intermediate potassium sulfide salt **13**. On treatment of intermediate **13** with chloroacetone and phenacyl bromide at room temperature afforded the corresponding thiazole derivatives **14a,b** respectively, **Scheme 4**. The formation of **14a,b** were assumed to proceed through the initial alkylation by loss of potassium halide followed by in situ heterocyclization via Dieckmann type<sup>21</sup> cyclization. Also, cyclocondensation of the non-isolable intermediate **13** in situ with the 2-oxo-N',2-diphenylacetohydrazonoyl bromide afforded 4-(1-(2-(2-cyano-2-(3,4-diphenyl-5-(phenyldiazonyl)thiazol-2(3H)-ylidene)acetyl)hydrazono)ethyl)phenyltosylate (**15**), **Scheme 4**. Furthermore, the non-isolable potassium salt **13** was allowed to react with chloroacetonitrile at

room temperature to give the open chain product **16**, **Scheme 4**, However, from these expected products (**16-18**), only the 4-(1-(2-(2-cyano-3-(cyanomethyl-thio)-3-(phenylamino)acryloyl)hydrazono)ethyl)phenyltosylate (**16**) manifested to be the reasonable as confirmed by elemental analysis and spectroscopic data.

On the other hand, reaction of potassium sulfide intermediate **13** in situ with ethyl chloroacetate at room temperature furnished the S-alkyl intermediate (**19**) which underwent intramolecular cyclization to give 4-(1-(2-(2-cyano-2-(4-oxo-3-phenylthiazolidin-2-ylidene)acetyl)hydrazono)ethyl)phenyltosylate (**20**), **Scheme 5**. Condensation of compound **20** with 4-methoxybenzaldehyde in refluxing ethanol in the presence of catalytic amount of piperidine gave 4-(1-(2-(2-cyano-2-(5-(4-methoxybenzylidene-4-oxo-3-phenylthiazolidin-2-ylidene)acetyl)hydrazono)ethyl)phenyltosylate (**21**), **Scheme 5**. Finally, treatment of non-isolable potassium salt **13** in situ with chloroacetyl chloride at room temperature afforded the S-acyl intermediate (**22**) which underwent intramolecular cyclization to give 4-(1-(2-(2-cyano-2-(5-oxo-3-phenylthiazolidin-2-ylidene)acetyl)hydrazono)ethyl)phenyltosylate (**23**), **Scheme 5**.



### Antimicrobial Screening:

The synthesized compounds were tested for their antimicrobial activities in vitro by agar diffusion method using "Mueller–Hinton" agar medium for bacteria and "Sabouraud's" agar medium for yeasts.

The assayed collection included two gram-positive bacteria: *Bacillus subtilis* (NCIB 3610) and *Staphylococcus aureus* (NCTC 7447); two gram-negative bacteria: *Escherichia coli* (NCTC 10416) and *Pseudomonas aeruginosa* (NCIB 9016); and fungi namely *Candida albicans* (IMRU 3669), using Ampicillin 25 µg/ml as a reference compound. The inhibition zone diameters were recorded and rounded up to the nearest whole number (mm) for analysis. The inhibitory effects of the synthesized compounds against these organisms are given in **Table (1)** and depicted graphically in **Figures (1-2)**

**Table (1)** : Biological activity of the newly synthesized compounds

Inhibition-zone diameter (mm/mg sample)		
Gram-positive	Gram-negative	Fungi

0 Compound No.	<i>B. Subtilis</i> (NCIB 3610)	<i>S. aureus</i> (NCTC 7447)	<i>E. Coli</i> (NCTC 10416)	<i>P. aeruginosa</i> (NCIB 9016)	<i>C. albicans</i> (IMRU 3669)
2	8	6	8	8	8
3	6	8	8	8	6
4	6	6	6	6	7
5a	7	7	7	7	8
5b	7	6	6	8	8
6	8	8	8	15	6
7	7	5	8	6	7
8a	15	17	8	12	8
10	6	6	7	7	6
11	6	7	6	8	6
12	8	8	8	15	8
14a	15	17	8	15	15
14b	8	7	8	8	6
15	7	6	8	8	7
16	8	8	9	8	6
20	8	8	6	6	8
21	6	6	6	8	8
23	6	6	6	8	8
Ampicillin	19	18	19	21	17

**Inhibition zone diameter** : weak activity (6-11mm), moderate activity (12-15), strong activity (<15), MICs (mg/ml) showed in parentheses

The screening results from **Table (1)** and **Figure (1)** indicate that: all compounds under investigation were less active against all the tested bacterial strains than the standard drug Ampicillin. In other words, all synthesized compounds showed weak activity against the tested gram-positive bacteria except compounds (**8a**, **14a**) which showed moderate activities against *Bacillus subtilis* (NCIB 3610) and strong activities against *Staphylococcus aureus* (NCTC 7447). Furthermore, all synthesized compounds showed weak activity against *Escherichia coli* (NCTC 10416). In addition, compounds (**6**, **8a**, **12**, **14a**) in the series were found to have moderate activities against *Pseudomonas aeruginosa* (NCIB 9016).

Also, from **Table (1)** and **Figure (2)** it's evident that: all the synthesized compounds showed a weak in vitro antifungal activity against the tested organism except compound (**14a**) which showed moderate activity against *Candida albicans* (IMRU 3669).

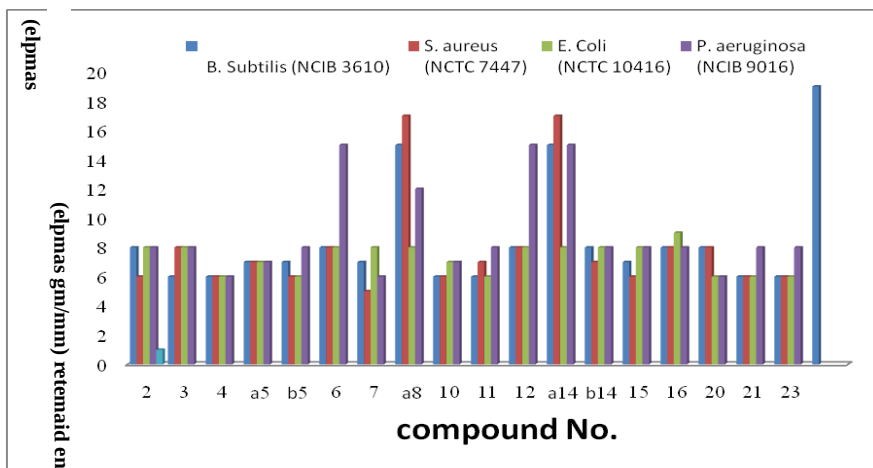


Figure (1) : Graphical representation of the antibacterial activity of tested compounds, compared with Ampicillin.

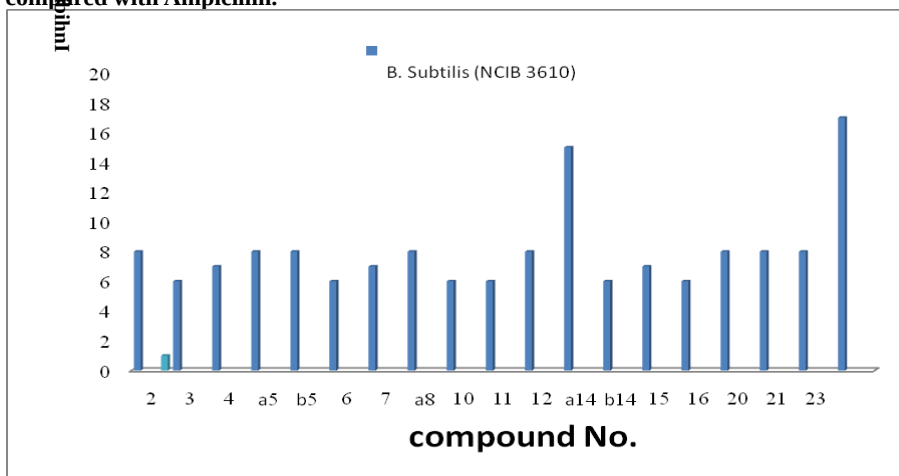


Figure (2) : Graphical representation of the antifungal activity of tested compounds, compared with Ampicillin.

**Experimental Section:**

Melting points (°C, uncorrected) were determined in open capillaries on a Gallen Kamp melting point apparatus (Sanyo GallenKemp, Southborough, UK). Pre-coated silica gel plates (silica gel 0.25 mm, 60 G F 254; Merck, Germany) were used for thin layer chromatography, dichloromethane/methanol (9.5:0.5 mL) mixture was used as a developing solvent system and the spots were recorded. IR spectra (KBr) were recorded on a FTIR 5300 spectrometer ( $\nu$ ,  $\text{cm}^{-1}$ ).  $^1\text{H-NMR}$  spectra were recorded at 300 MHz on a Varian Gemini NMR spectrometer ( $\delta$ , ppm) using TMS as an internal standard. Mass spectra were obtained on GC Ms-QP 1000 EX mass spectrometer at 70 eV. Elemental analyses were performed on Carlo Erba 1108 Elemental Analyzer (Heraeus, Hanau, Germany). All compounds were within  $\pm 0.4$  % of the theoretical values.

#### **4-Acetylphenyltosylate (2)**

A mixture of 4-hydroxyacetophenone (0.01 mol), tosyl chloride (0.01 mol) and potassium carbonate (0.02 mol) in acetone (30 ml) was stirred for 2hr. The separated product was filtered off, washed with water, dried and recrystallized to give **2**, (**Table 2**). IR ( $\text{cm}^{-1}$ ): 1680 (CO), 1376, 1166 ( $\text{SO}_2$ ),  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ):  $\delta$  2.45(s, 3H,  $\text{CH}_3$  of p-tolyl), 2.57(s, 3H,  $\text{CH}_3$  of acetyl), 7.07-7.91 (m, 8H, Ar-H).

#### **4-(1-(2-(2-Cyanoacetyl)hydrazono)ethyl)phenyltosylate (3)**

To a solution of 2-cyanoacetohydrazide (1.0 g, 0.01 mol) in ethanol (20 mL), 4-acetylphenyltosylate (**2**; 0.01 mol) was added. The reaction mixture was heated under reflux for 2 hr, then left to cool. The solid product formed was collected by filtration and recrystallized to give **3**, (**Table 2**). IR ( $\text{cm}^{-1}$ ): 3186 (NH), 2260 (CN), 1680 (CO), 1382, 1170 ( $\text{SO}_2$ ).  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ):  $\delta$  2.28 (s, 3H,  $\text{CH}_3$  of p-tolyl), 2.46 (s, 3H,  $\text{CH}_3$  of  $\text{CH}_3\text{-C=N}$ ), 3.88 (s, 2H,  $\text{CH}_2$ ), 7.02-7.74 (m, 8H, Ar-H), 9.57 (s, 1H, NH).

#### **4-(1-(2-(2-Oxo-2H-chromene-3-carbonyl)hydrazono)ethyl)phenyltosylate (4)**

To a solution of compound (**3**; 0.01mol) in absolute ethanol (20 mL) containing piperidine (0.3 mL), salicylaldehyde (0.01 mol) was added. The reaction mixture was heated under reflux for 3hr and then allowed to cool. The precipitate that formed was filtered off, washed with ethanol, dried and recrystallized to give **4**, (**Table 2**). IR ( $\text{cm}^{-1}$ ): 3223 (NH), 1685 (CO), 1361, 1154 ( $\text{SO}_2$ ).  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ ):  $\delta$  2.29 (s, 3H,  $\text{CH}_3$  of p-tolyl), 2.46(s, 3H,  $\text{CH}_3$  of  $\text{CH}_3\text{-C=N}$ ), 7.06-8.00 (m, 12H, Ar-H), 8.98 (s, 1H, CH-coumarin), 11.60(s, 1H, NH).



**Reaction of 4-(1-(2-(2-cyanoacetyl)hydrazono)ethyl)phenyltosylate (3) with 1,3-dicarbonyl compounds**

**General procedure:** A mixture of compound (3; 0.01 mol) and an equimolar amount of the appropriate 1,3-dicarbonyl compounds (acetylacetone or benzoylacetone) in ethanol (20 mL) was refluxed for 3hr, after cooling, the separated solid was filtered off, dried well and recrystallized to give compounds **5a,b**, (Table 2).

**4-(1-(3-Cyano-4,6-dimethyl-2-oxopyridin-1(2H)-ylimino)ethyl)phenyltosylate (5a)**

IR (cm<sup>-1</sup>): 2218 (CN), 1654 (CO), 1362, 1156 (SO<sub>2</sub>). <sup>1</sup>H-NMR (CDCl<sub>3</sub>): δ 2.39 (s, 3H, CH<sub>3</sub> of p-tolyl), 2.46 (s, 3H, CH<sub>3</sub>-pyridine), 2.50 (s, 3H, CH<sub>3</sub>-pyridine), 2.58 (s, 3H, CH<sub>3</sub> of CH<sub>3</sub>-C=N), 6.07 (s, 1H, H-pyridine), 7.07-7.91 (m, 8H, ArH).

**4-(1-(3-Cyano-4-methyl-2-oxo-6-phenylpyridin-1(2H)-ylimino)ethyl)phenyltosylate (5b)**

IR (cm<sup>-1</sup>): 2218 (CN), 1654 (CO), 1362, 1156 (SO<sub>2</sub>). <sup>1</sup>H-NMR (CDCl<sub>3</sub>): δ 2.19 (s, 3H, CH<sub>3</sub> of p-tolyl), 2.43 (s, 3H, CH<sub>3</sub>-pyridine), 2.51 (s, 3H, CH<sub>3</sub> of CH<sub>3</sub>-C=N), 6.23 (s, 1H, H-pyridine), 6.95-7.67 (m, 13H, ArH).

**4-(1-(3-Amino-6-methyl-4-oxothieno[3,4-c]pyridin-5(4H)-ylimino)ethyl)phenyltosylate (6)**

To a solution of compound (5a; 0.01 mol) in absolute ethanol (30 mL) containing triethylamine, elemental sulfur (0.32 g, 0.01 mol) was added. The reaction mixture was heated under reflux for 1hr. After cooling the solid obtained was recrystallized to give **6**, (Table 2). IR (cm<sup>-1</sup>): 3412, 3350 (NH<sub>2</sub>), 1642 (CO), 1366, 1162 (SO<sub>2</sub>). Mass, m/z (intensity %): M 467 (0.75), 91 (100).

**4-(1-(2-(5-Amino-1-(4-chlorophenyl)-1H-1,2,3-triazole-4-carbonyl)hydrazono)ethyl)phenyltosylate (7)**

A mixture of compound (3; 0.01 mol), sodium ethoxide( 0.01mol) and 4-chlorophenylazide (0.01 mol) in ethanol (20 ml) was refluxed for 2hr, the contents of the flask were poured onto crushed ice. The solid obtained was filtered, dried and recrystallized to give **7**, (Table 2). IR (cm<sup>-1</sup>): 3428, 3356, 3144 (NH<sub>2</sub>, NH), 1648 (CO), 1388, 1158 (SO<sub>2</sub>). Mass, m/z (intensity %): M 489 (0.13), 119(100).

**4-(1-(2-(2-Cyano-2-(2-(4-fluorophenyl)hydrazono)acetyl)hydrazono)ethyl)phenyltosylate (8a)**

To a cold solution of compound (3; 0.01 mol) in pyridine (25 mL) 4-flourobenzenediazonium chloride (0.01 mol) [prepared by diazotization of 4-flouroaniline (0.01 mol) in HCl (6M, 6ml) with sodium nitrite (0.7g) at 0-5°C] was

added portionwise over 30 min with constant stirring. After complete addition, the reaction mixture was stirred for a further 2hr at 0-5°C. The solid product was filtered off, washed with water, dried and finally recrystallized to give **8a**, (Table 2). IR (cm<sup>-1</sup>): 3192 (NH), 2197 (CN), 1660 (CO), 1361, 1152 (SO<sub>2</sub>). <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>): δ 2.37 (s, 3H, CH<sub>3</sub> of p-tolyl), 2.46 (s, 3H, CH<sub>3</sub> of CH<sub>3</sub>-C=N), 7.13-7.93 (m, 13H, Ar-H and NH), 11.03 (s, 1H, NH).

**4-(1-(2-(4-Amino-8-cyano-7-(methylthio)pyrazolo[5,1-c][1,2,4]triazine-3-carbonyl)hydrazono)ethyl)phenyltosylate (10)**

To a solution of compound (3; 0.01 mol) in pyridine (10 mL), an ice cooled solution of 4-cyano-3-(methylsulfanyl)-1H-pyrazole-5-diazonium chloride [ prepared by addition solution of sodium nitrite (0.01 mol) in water (5 mL) to the hetero cyclic amine (0.01 mol) in hydrochloric acid (12 mL) at [0-5°C] was added dropwise with stirring. Stirring was continued for 30 min. The precipitated product was filtered off, washed with water, dried and recrystallized to give **10**, (Table 2). IR (cm<sup>-1</sup>): 3307, 3274, 3259 (NH<sub>2</sub>, NH), 2199 (CN), 1680 (CO), 1364, 1155 (SO<sub>2</sub>). <sup>1</sup>H-NMR (CDCl<sub>3</sub>): δ 2.21 (s, 3H, CH<sub>3</sub> of p-tolyl), 2.42 (s, 3H, CH<sub>3</sub> of CH<sub>3</sub>-C=N), 2.51 (s, 3H, CH<sub>3</sub> of SCH<sub>3</sub>), 4.23 (s, 2H, NH<sub>2</sub>), 7.05-7.82 (m, 8H, Ar-H), 11.08(s, 1H, NH).

**4-(1-(2-(4-Amino-3-phenyl-2-thioxo-2,3-dihydrothiazole-5-carbonyl)hydrazono)ethyl)phenyltosylate (11)**

A mixture of compound (3; 0.01 mol) and elemental sulfur (0.01 mol) and phenyl isothiocyanate (0.01 mol) in dioxane (30 mL) containing triethylamine (1mL) was refluxed for 3hr, then left to cool. The solid product formed upon pouring onto ice/water was recrystallized to give 11, (Table 2). IR (cm-1): 3421, 3311, 3163 (NH<sub>2</sub>, NH), 1661 (CO), 1358, 1163 (SO<sub>2</sub>). <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>): δ 2.23 (s, 3H, CH<sub>3</sub> of p-tolyl), 2.38 (s, 3H, CH<sub>3</sub> of CH<sub>3</sub>-C=N), 3.54 (s, 2H, NH<sub>2</sub>), 7.06-7.78 (m, 13H, Ar-H), 10.54 (s, 1H, NH).

**4-(1-(2-(2-Amino-5,6-dihydro-4H-cyclopenta[b]thiophene-3-carbonyl)hydrazono)ethyl)phenyltosylate (12)**

To a solution of compound (3; 0.01 mol) in dioxane (30 mL) containing triethylamine (1 mL), cyclopentanone (0.01 mol) together with elemental sulfur (0.01 mol) were added. The reaction mixture was refluxed for 2hr, then poured onto ice/water. The solid obtained was collected and recrystallized to give **12**, (Table 2). IR (cm<sup>-1</sup>): 3400, 3358, 3170 (NH<sub>2</sub>, NH), 1676 (CO), 1366, 1154 (SO<sub>2</sub>). <sup>1</sup>H-NMR

(DMSO-d<sub>6</sub>):  $\delta$  1.46-1.63 (m, 6H, 3CH<sub>2</sub> of H-cyclopentane), 2.43 (s, 3H, CH<sub>3</sub> of p-tolyl), 2.45 (s, 3H, CH<sub>3</sub> of CH<sub>3</sub>-C=N), 3.42(s, 2H, NH<sub>2</sub>), 6.94-7.69 (m, 9H, Ar-H and NH).

**Reaction of 4-(1-(2-(2-cyanoacetyl)hydrazono)ethyl)phenyltosylate (3) with  $\alpha$ -halo compounds**

**General procedure:** To a cooled suspension of finely grounded KOH (0.01 mol) in dry DMF (40 ml), 2-cyanoacetohydrazide derivative (3; 0.01 mol) and subsequently phenyl isothiocyanate (0.01 mol) were added, the reaction mixture was stirred overnight at room temperature, then treated with the appropriate halo compounds (0.01 mol) and left at room temperature for an additional 24 hr. The reaction mixture was then treated with cold H<sub>2</sub>O (50 ml) and neutralized with 1N HCl. The resulting precipitate was collected by filtration, washed with water, dried and recrystallized from an appropriate solvent.

**4-(1-(2-(2-Cyano-2-(4-methyl-3-phenylthiazol-2(3H)-ylidene)acetyl)hydrazono)ethyl)phenyltosylate (14a), (Table 2).**

IR (cm<sup>-1</sup>): 3364 (NH), 2172 (CN), 1666 (CO), 1368, 1152 (SO<sub>2</sub>). <sup>1</sup>H-NMR (CDCl<sub>3</sub>):  $\delta$  1.85 (s, 3H, CH<sub>3</sub> of thiazole), 2.08 (s, 3H, CH<sub>3</sub> of p-tolyl), 2.42 (s, 3H, CH<sub>3</sub> of CH<sub>3</sub>-C=N), 6.96-7.75 (m, 14H, Ar-H and H-thiazole), 9.27 (s, 1H, NH).

**4-(1-(2-(2-Cyano-2-(3,4-diphenylthiazol-2(3H)-ylidene)acetyl)hydrazono)ethyl)phenyltosylate (14b), (Table 2).**

IR (cm<sup>-1</sup>): 3310 (NH), 2184 (CN), 1640 (CO), 1362, 1150 (SO<sub>2</sub>). Mass, m/z (intensity %): M 606 (0.82), 302 (100).

**4-(1-(2-(2-Cyano-2-(3,4-diphenyl-5-(phenyldiazenyl)thiazol-2(3H)-ylidene)acetyl)hydrazono)ethyl)phenyltosylate (15), (Table 2).**

IR (cm<sup>-1</sup>): 3166 (NH), 2184 (CN), 1654 (CO), 1342, 1166 (SO<sub>2</sub>). Mass, m/z (intensity %): M 710 (0.75), 77(100).

**4-(1-(2-(2-Cyano-3-(cyanomethylthio)-3-(phenylamino)acryloyl)hydrazono)ethyl)phenyltosylate (16), (Table 2).**

IR (cm<sup>-1</sup>): 3353 (NH), 2210 (CN), 1674 (CO), 1344, 1160 (SO<sub>2</sub>). <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>):  $\delta$  2.28 (s, 3H, CH<sub>3</sub> of p-tolyl), 2.41 (s, 3H, CH<sub>3</sub> of CH<sub>3</sub>-C=N), 4.03 (s, 2H, CH<sub>2</sub>), 6.90-7.79 (m, 14H, Ar-H and NH), 9.15 (br, 1H, NH).

**4-(1-(2-(2-Cyano-2-(4-oxo-3-phenylthiazolidin-2-ylidene)acetyl)hydrazono)ethyl)phenyltosylate (20), (Table 2).**

IR (cm<sup>-1</sup>): 3368 (NH), 2188 (CN), 1746, 1670 (2CO), 1366, 1172 (SO<sub>2</sub>). <sup>1</sup>H-NMR (CDCl<sub>3</sub>): δ 2.46 (s, 3H, CH<sub>3</sub> of p-tolyl), 2.59 (s, 3H, CH<sub>3</sub> of CH<sub>3</sub>-C=N), 4.07 (s, 2H, CH<sub>2</sub>), 7.08-7.92 (m, 14H, Ar-H and NH).

**4-(1-(2-(2-Cyano-2-(5-oxo-3-phenylthiazolidin-2-ylidene)acetyl)hydrazono)ethyl)phenyltosylate (23), (Table 2).**

IR (cm<sup>-1</sup>): 3352 (NH), 2183 (CN), 1665 (CO), 1351, 1164 (SO<sub>2</sub>). Mass, m/z (intensity %): M 546 (100), M+1(29).

**4-(1-(2-(2-Cyano-2-(5-(4-methoxybenzylidene)-4-oxo-3-phenylthiazolidin-2-ylidene)acetyl)hydrazono)ethyl)phenyltosylate (21)**

A mixture of (**20**; 0.01mol) and 4-methoxybenzaldehyde (0.01 mol) in absolute ethanol (30 mL) containing few drops of piperidine was refluxed for 3hr until the solid was formed. The reaction mixture was allowed to cool, the solid was filtered off, washed and recrystallized to give **21**, (**Table 2**). IR (cm<sup>-1</sup>): 3352 (NH), 2183 (CN), 1665 (CO), 1351, 1164 (SO<sub>2</sub>). <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>): δ 2.13 (s, 3H, CH<sub>3</sub> of p-tolyl), 2.39 (s, 3H, CH<sub>3</sub> of CH<sub>3</sub>-C=N), 3.83 (s, 3H, OCH<sub>3</sub>), 7.02-7.76 (m, 18H, Ar-H and NH).

**Antimicrobial Assay :**

In the agar diffusion method<sup>22,23</sup>, compounds dissolved in dimethylsulfoxide (DMSO) at a concentration of 100 mg/mL were used. Agar media seeded with the tested microorganisms were poured in Petri dishes and were allowed to solidify, and then holes of about 7 mm were punched in the agar using a sterile cork porrer. A 50-μl volume of the dissolved compounds were added to the pores and DMSO without any compound was included as solvent control. Plates were allowed to stand in a refrigerator for two hours before incubation to allow the tested compounds to diffuse through the agar. The plates containing bacterial cultures were incubated at 37°C for 24 h and those containing yeasts were incubated at 30°C for 48h. After incubation, the growth inhibition zones around the holes were observed, indicating that the examined compound inhibits the growth of microorganism. The tested microorganisms were obtained from the Regional Center for Mycology & Biotechnology (RCMP), Al-Azhar University.

Table (2) : Physical and analytical data of the newly Prepared compounds

Comp.	m.p.°C (Solvent of recrystallization)	Colour (Yield%)	M.formula (M.Wt.)	Calculated / Found (%)				
				C	H	N	O	S
2	65-67 (Et.)	White (85)	C <sub>15</sub> H <sub>14</sub> O <sub>4</sub> S (290.33)	62.05	4.86	-----	22.04	11.04
				62.00	4.80	-----	22.00	11.00
3	165-168 (Et.)	White (84)	C <sub>18</sub> H <sub>17</sub> N <sub>3</sub> O <sub>4</sub> S (371.41)	58.21	4.61	11.31	17.23	8.63
				58.18	4.58	11.30	17.20	8.61
4	262-265 (D.)	Yellow (60)	C <sub>25</sub> H <sub>20</sub> N <sub>2</sub> O <sub>6</sub> S (476.50)	63.02	4.23	5.88	20.15	6.73
				62.99	4.21	5.80	20.12	6.71
5a	195-198 (Et.)	Yellow (77)	C <sub>23</sub> H <sub>21</sub> N <sub>3</sub> O <sub>4</sub> S (435.50)	63.43	4.86	9.65	14.70	7.36
				63.40	4.85	9.63	14.67	7.35
5b	200-202 (B.)	Yellow (70)	C <sub>28</sub> H <sub>23</sub> N <sub>3</sub> O <sub>4</sub> S (497.56)	67.59	4.66	8.45	12.86	6.44
				67.57	4.63	8.42	12.84	6.41
6	350-355 (D.)	Brown (60)	C <sub>23</sub> H <sub>21</sub> N <sub>3</sub> O <sub>4</sub> S <sub>2</sub> (467.56)	59.08	4.53	8.99	13.69	13.72
				59.05	4.51	8.96	13.65	13.70
7	198-201 (Et.)	Yellow (70)	C <sub>24</sub> H <sub>21</sub> ClN <sub>6</sub> O <sub>4</sub> S (524.98)	54.91	4.03	16.01	12.19	6.11
				54.89	4.00	15.96	12.15	6.05
8a	140-144 (Et./B.)	Red (75)	C <sub>24</sub> H <sub>20</sub> FN <sub>5</sub> O <sub>4</sub> S (493.51)	58.41	4.08	14.19	12.97	6.50
				58.39	4.05	14.15	12.95	6.47
10	172-175 (Et./B.)	Brown (60)	C <sub>23</sub> H <sub>20</sub> N <sub>6</sub> O <sub>4</sub> S <sub>2</sub> (536.59)	51.48	3.76	20.88	11.93	11.95
				51.45	3.72	20.85	11.90	11.93
11	262-265 (Et./B.)	Brown (70)	C <sub>25</sub> H <sub>22</sub> N <sub>4</sub> O <sub>4</sub> S <sub>3</sub> (538.66)	55.74	4.12	10.40	11.88	17.86
				55.70	4.10	10.35	11.86	17.82
12	190-193 (D.)	Brown (65)	C <sub>23</sub> H <sub>23</sub> N <sub>3</sub> O <sub>4</sub> S <sub>2</sub> (469.58)	58.83	4.94	8.95	13.63	13.66
				58.80	4.92	8.91	13.60	13.62
14a	245-248 (D.)	Yellow (60)	C <sub>28</sub> H <sub>24</sub> N <sub>4</sub> O <sub>4</sub> S <sub>2</sub> (544.64)	61.75	4.44	10.29	11.75	11.77
				61.71	4.41	10.27	11.71	11.75
14b	180-182 (Et./B.)	Brown (60)	C <sub>33</sub> H <sub>26</sub> N <sub>4</sub> O <sub>4</sub> S <sub>2</sub> (606.71)	65.33	4.32	9.23	10.55	10.57
				65.30	4.29	9.21	10.50	10.54
15	300-303 (D.)	Brown (60)	C <sub>39</sub> H <sub>30</sub> N <sub>6</sub> O <sub>4</sub> S <sub>2</sub> (710.82)	65.90	4.25	11.82	9.00	9.02
				65.85	4.21	11.80	8.97	8.98
16	340-345 (DMF)	Black (50)	C <sub>27</sub> H <sub>23</sub> N <sub>5</sub> O <sub>4</sub> S <sub>2</sub> (545.63)	59.43	4.25	12.84	11.73	11.75
				59.40	4.21	12.81	11.70	11.70
20	180-184 (Et./B.)	Brown (75)	C <sub>27</sub> H <sub>22</sub> N <sub>4</sub> O <sub>5</sub> S <sub>2</sub> (546.62)	59.33	4.06	10.25	14.63	11.73
				59.31	4.01	10.23	14.60	11.69
21	290-294 (D.)	Yellow (75)	C <sub>35</sub> H <sub>28</sub> N <sub>4</sub> O <sub>6</sub> S <sub>2</sub> (664.75)	63.24	4.25	8.43	14.44	9.65
				63.21	4.21	8.40	14.40	9.63
23	140-145 (Et./B.)	Yellow (65)	C <sub>27</sub> H <sub>22</sub> N <sub>4</sub> O <sub>5</sub> S <sub>2</sub> (546.62)	59.33	4.06	10.25	14.63	11.73
				59.30	4.00	10.21	14.61	11.70

(B.; benzene, D.; dioxane, DMF; dimethylformamide, Et.; ethanol)

**References**

1. Masquelin T. and Obrecht d. , *Tetrahedron*,57, 153 (2001).
2. Sah. M. M. and Joshi P. C. , *Asian J. Chem.*1, 141 (1989) .
3. El-khawass S. M., Khalil, M. A and Chaaban, I. , *Farmaco* 44, 415 (1989).
4. Misra N. C.and Patnaik k. k. , *Indian J. Appl. Chem.* 34, 148 (1971).
5. Rao R. P. and Singh S. R. , *J. Indian Chem. Soc.* 50, 492 (1973).
6. Parmar S. S., Chamdhari D. A. and Gupta T. K., *J. Med. Chem.* 15, 99 (1972).
7. Pavlenko A.F. and Moshchitskii S. D. , *Khim .Getrosikl Soedin* 3,159 (1967). C.A.68, 114479 (1968).
8. Andoldek A., Stanovanik B. and Tisler M., *J. Med. Chem.* 14, 53 (1971).
9. Singh S. R. , *J. Indian Chem. Soc.* 52, 734 (1975).
10. Chaudhary H. S. and Pujari H. K. , *Indian J. Chem.* 10, 766 (1972).
11. Mallick S. K., Martin A. R. and lingard R. G., *J. Med. Chem.* 14, 528 (1971).
12. Szoko E. and Tabi T., *J. Pharm. Biomed. Anal.* 53(5), 1180 (2010).
13. Zhao H., Shi I., Cao J.Q., Li W., Wen X. .and Zhao Y. Q., *Chin., Chem. Lett.* 21(10), 1216 (2010).
14. Banik B. K. and Becker F. F., *Eur. C. Med. Chem.* 45, 4687, (2010).
15. Rodrigues M. T., Gomes J. C., Smith J. and Coelho F., *Tetrahedron Lett.* 51, (38), 4988, (2010).
16. Malicorne G., Bompert J., Giral L. and Despanx E., *Eur. J. Med. Chem.* 26, 3 (1991).
17. Hargreaves S. I., Pikington B. I., Russell S. E. and Worthington P. A., *Tetrahedron Lett.* 41, (10), 1653(2000).
18. Abdelall M. M., *Phosphorus, Sulphur and Silicon*, 184, 2208-2226 (2009).
19. Hafiz, I. S., *Z. Naturforsch*, 55b, 321 (2000).
20. Tormos J. V., Khodorkovsky Y. U., Neilands O. Y. and Belyakov S. V.,*Tetrahedron* 48, 2863(1992).
21. Sommen G., Comel A. and Kirsch G., *Tetrahedron lett.*, 43, 257 (2002).
22. European Committee for Antimicrobial Susceptibility Testing (EUCAST) of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID). Determination of minimum inhibitory concentrations (MICs) of antibacterial agents by agar dilution, *Clinical Microbiology and Infection*, Vol. 6 Number 9, September 2000, pp: 509-515.

23. National Committee for Clinical Laboratory Standards. Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically, 5th edn. Approved Standard M7-A5. Wayne, PA : NCCLS, 2000.