

**Synthesis of Some New Annulated Thieno Pyridine, Pyrazolopyridine and Pyrido Pyridine Derivatives**

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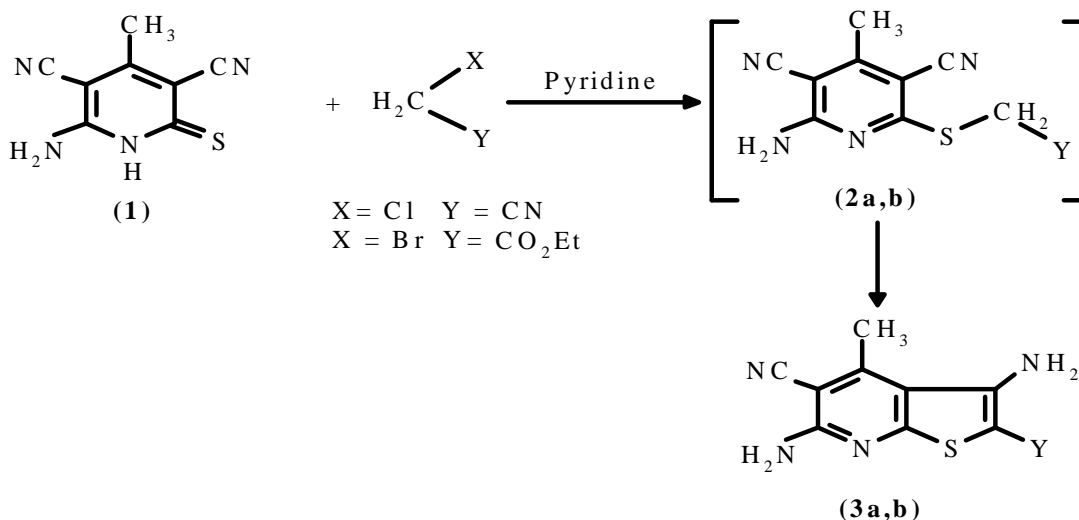
Department of Chemistry, Faculty of Science, Al-Azhar University, Cairo, Egypt.  
[dawounadia@yahoo.com](mailto:dawounadia@yahoo.com)**Abstract:** The reaction of arylidenemalonitrile with cyanothioacetamide afforded pyridine derivatives. This compound 1 reacted further with different nucleophilic and electrophilic reagents yielding different products which were confirmed via spectroscopic analysis.[F.F. Mahmoud, Nadia T.A. Dawood, Nahed F. Abdel-Ghaffar. **Synthesis of Some New Annulated Thieno Pyridine, Pyrazolopyridine and Pyrido Pyridine Derivatives.** Journal of American Science 2011;7(5):210-218]. (ISSN: 1545-1003). <http://www.americanscience.org>.**Keywords:** Arylidene malonitriles, Dihydropyridines, Antimicrobial activity.**1. Introduction**

No doubt that thienopyridines are an interesting class of heterocycles and their chemistry has recently received considerable attention especially because of their potential utility as antibacterial<sup>(1-4)</sup> antihypertensive<sup>(5)</sup>, diabetes mellitus<sup>(6-8)</sup>, as well as analgesics and antiinflammatory, sedatives, anticouglants<sup>(9-11)</sup>, antiatherosclerotics<sup>(12)</sup> and as gonadotropin releasing hormone antagonists<sup>(13)</sup>. The derivatives of thiopyridines are also useful intermediates for the synthesis of some medicines and related compounds. It was discovered that the pyridyl thiolate moiety enhances antifungal and antiinflammatory activities of several important drugs<sup>(14, 15)</sup>. Herein we report some new pyridinethione derivatives and their related product.

**2. Results and Discussion**

Thus pyridinethione derivative 1, which is prepared according to the literature<sup>(16, 17)</sup> was reacted with active methylene compounds namely, chloromalonitrile, and /or ethylbromoacetate in refluxing pyridine to afford the thienopyridine derivatives (3a,b) respectively. The structure of compounds 3a,b was established based on the elemental analysis and spectral data. The mass spectrum of compound 3a is compatible with the molecular ion peak at  $m/z=229$  ( $M^+$ ). Compound 3a is assumed to proceed via reaction of compound 1 with -halo compound to afford the S-alkylated derivative 2a followed by cyclization to 3a.

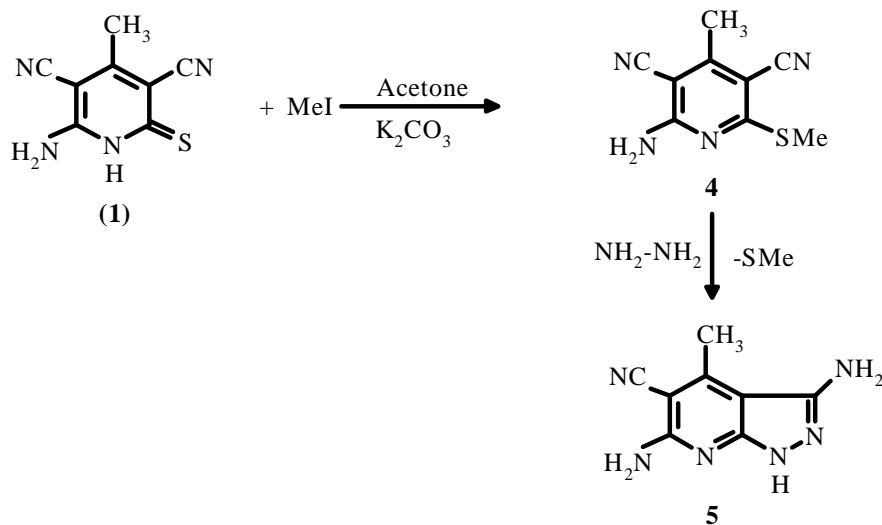
The mass spectrum of compound 3b is compatible with the molecular ion peak at  $m/z = 276$  ( $M^+$ ) (Scheme 1).



Scheme (1)

Alkylation of pyridinethione 1 with methyl iodide gave the S-methyl derivative 4 which was reacted with hydrazine hydrate to give the product 5 in a good yield<sup>(18,19)</sup>. The IR spectrum of 5 showed the presence of absorption peak at  $3412\text{-}3323\text{cm}^{-1}$  for two  $\text{NH}_2$  and  $3280\text{-}3200\text{cm}^{-1}$  for NH group

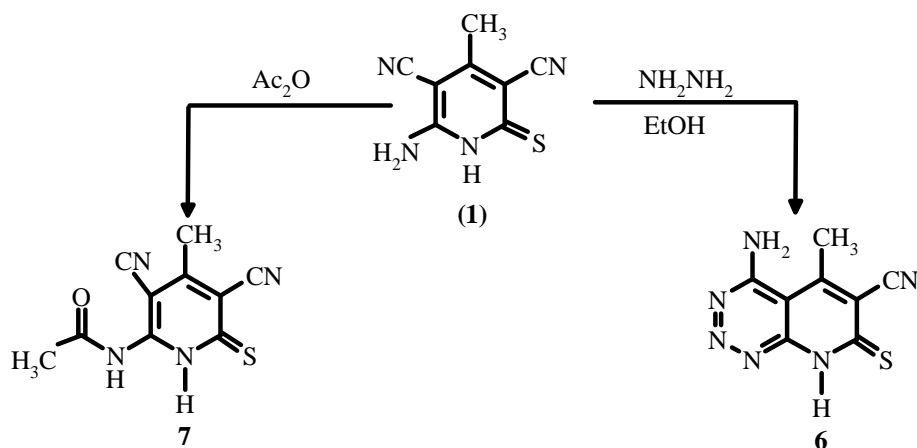
respectively. The  $^1\text{H-NMR}$  spectrum of compound 5 exhibited a singlet at 11.64 ppm for NH group in addition to the signals of  $\text{NH}_2$  and  $\text{CH}_3$  in their proper positions. Accordingly this reaction product could be formulated as [3,6-d] amino pyrazolo[2,3-c]pyridine derivative (Scheme 2).



Scheme 2

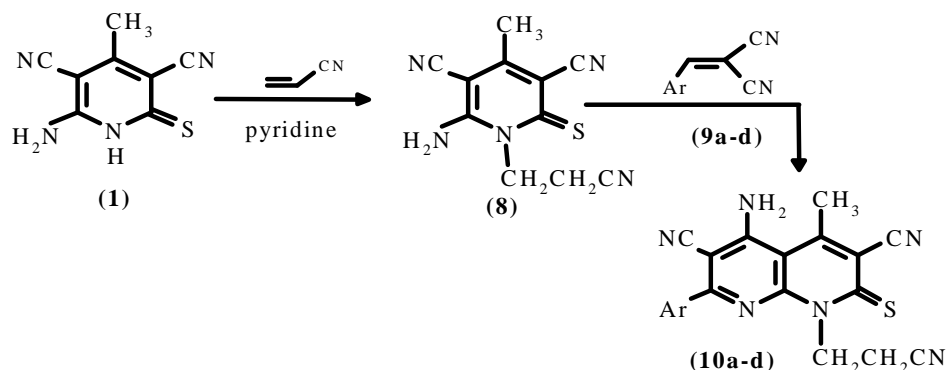
On the other hand, compound 1 was reacted with hydrazine hydrate in ethanolic solution to afford the pyridotriazine derivative 6. The structure of compound 6 was established based on its elemental analysis and spectral data. The mass spectrum of compound 6 showed the molecular ion peak at  $m/z = 216$  ( $\text{M}^+$ ). The IR spectrum agreed well with the proposed structure. Also acetylation of the pyridine thione 1 with acetic anhydride afforded the acetyl derivative 7. The structure of compound 7 was

confirmed by its correct elemental analysis and spectral data. The IR spectrum of compound 7 exhibited the disappearance of the absorption band due to the  $\text{NH}_2$  functional group at  $3450\text{-}3300\text{cm}^{-1}$  and appearance of NH group at  $3346\text{-}3181\text{cm}^{-1}$  and CO acetyl at  $1717\text{cm}^{-1}$ . The  $^1\text{H-NMR}$  of 7 revealed 2.50ppm (s, 3H,  $\text{CH}_3$ ), 3.73ppm (s, 3H,  $\text{COCH}_3$ ), 12.78ppm (br, 1H). Also, the mass spectrum of compound 7 was compatible with the molecular formula  $\text{C}_{10}\text{H}_8\text{N}_4\text{OS}$  at  $m/z = 232$  ( $\text{M}^+$ ) (Scheme 3).



Scheme 3

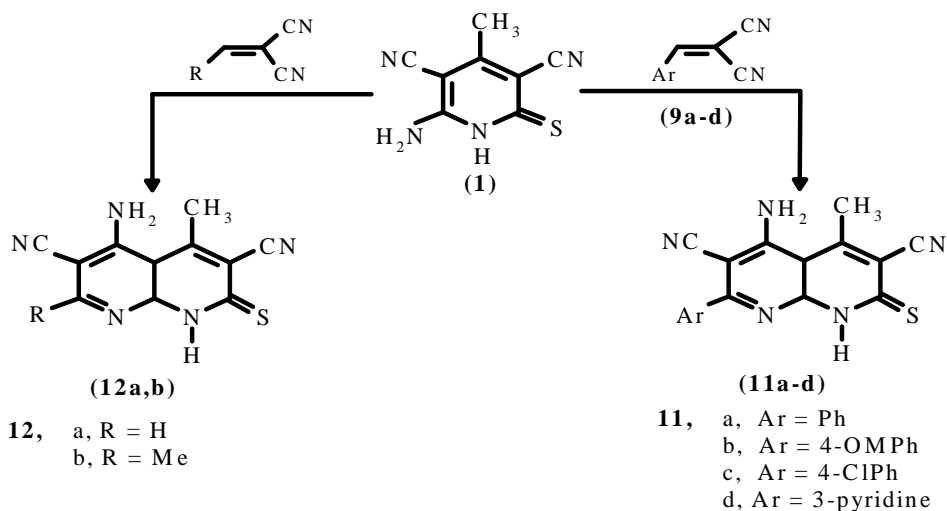
Also, the reaction of compound 1 with acrylonitrile afforded the N-ethylcyano derivative 8. The  $^1\text{H-NMR}$  spectrum of compound 8 revealed the structure of this compound. The mass spectrum of compound 8 is compatible with the molecular ion peak at  $m/z = 274$  ( $M^+$ ) corresponding to the molecular formula  $\text{C}_{11}\text{H}_9\text{N}_5\text{S}$ .



Scheme (4)

Similarly the pyridinethione (1) reacted with arylidene malononitrile 9a-d in boiling pyridine to afford the pyridopyridine derivatives 11a-d. The structures of compounds (11a-d) were confirmed by elemental analysis and spectroscopic data. The IR spectrum of compound 11a showed the presence of absorption peaks at  $3319\text{cm}^{-1}$  for  $\nu\text{NH}_2$ ,  $1630\text{cm}^{-1}$  for  $\nu\text{C}=\text{N}$  and  $1210\text{cm}^{-1}$  for  $\nu\text{C}=\text{S}$  functional groups. The  $^1\text{H-NMR}$  spectrum of 11a exhibited signals at 3.44 ppm for  $\text{NH}_2$  group in addition to the aromatic

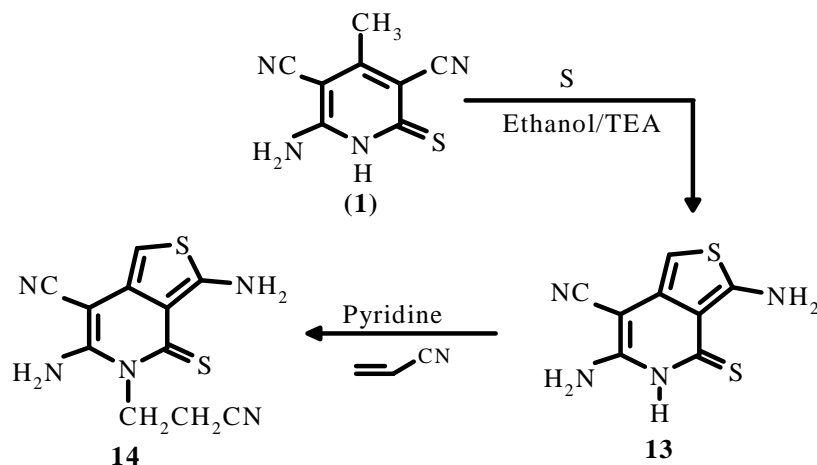
protons. Also the mass spectrum of compound 11b showed a molecular ion peak at  $m/z = 347$  ( $M^+$ ) corresponding to the molecular formula  $\text{C}_{18}\text{H}_{13}\text{N}_5\text{OS}$ . In a similar manner, the reaction of 1 with malononitrile and formaldehyde, and/or acetaldehyde yielded the corresponding 2-thioxopyridopyridine derivatives 12a,b respectively. The structure of compounds 11 and 12 were confirmed by elemental analysis and spectroscopic data (Scheme 5).



Scheme 5

The thienopyridine derivative 13 was readily obtained via the reaction of compound 1 with elemental sulphur. Subsequent treatment of compound 13 with acrylonitrile resulted only in

cyanothethylation product 14. Compounds 13 and 14 were confirmed by elemental analysis and spectroscopic data. (Scheme 6).



### 3. Experimental

Melting points were taken with the help of stuart apparatus and were uncorrected. The IR spectra were produced with a Jasco FT/IR 5300 spectrophotometer using the KBr technique. <sup>1</sup>H-NMR spectra were measured using a Jeol FX-100 spectrometer 60 MHz and a Varian Gemini 200 instrument 200 MHz and 250 & 300 MHz with TMS as an internal reference. Mass spectra were obtained by using of a Shimadzu-GC MS-QP 1000 EX instrument using the direct inlet system. Microanalyses were performed by the microanalytical unit at Cairo University. All compounds gave satisfactory elemental analyses.

#### Synthesis of 6-Amino-4-methyl-6-thioxo - 1,2 - dihydropyridine -3,5-dicarbonitrile (1).

It was prepared according to the literature. The mass spectrum of (1) exhibited a molecular ion peak at m/z (160, 100%). <sup>1</sup>H-NMR spectrum of (1) exhibited signals at 1.21 (3H, s, 3H, CH<sub>3</sub>), 3.34 (2H, s, 2H, NH<sub>2</sub>), 12.76 (br, 1H, cyclic NH).

#### Synthesis of 3,6-Diamino-4-methylthieno [2,3-b] pyridine-2,5-dicarbonitrile (3a).

A mixture of (1) (0.01 mol) and chloroacetonitrile (0.01 mol) in 15ml of pyridine was refluxed for 5h, after cooling the obtained product it was recrystallized from DMF to give (3a). MS of (3a). C<sub>10</sub>H<sub>7</sub>N<sub>5</sub>S, exhibited a molecular ion peak at m/z 229 (M<sup>+</sup>, 100%). <sup>1</sup>H-NMR spectrum of (3a) exhibited signals at 2.50 (3H, s, 3H, CH<sub>3</sub>), 3.33 (2H, s, 2H, NH<sub>2</sub>), 4.29 (2H, s, 2H, NH<sub>2</sub>).

#### Synthesis of 3,6-Diamino-5-cyano-2-ethoxy carbonyl-4-methyl thieno[2,3-b] pyridine(3b).

A mixture of (1) (0.01 mol), ethylbromoacetate (0.01 mol) in 15 ml of pyridine was refluxed for 5h. The reaction mixture was then cooled and the obtained product was recrystallized from ethanol to give (3b). <sup>1</sup>H-NMR spectrum of (3b) exhibited signals at 1.21 (t, CH<sub>2</sub>CH<sub>3</sub>), 4.15 (q, 2H, CH<sub>2</sub>, CH<sub>3</sub>), 3.32 (s, 3H, CH<sub>3</sub>).

#### Synthesis of 2-Amino-4-methyl-6-thioxomethyl pyridine-3, 5-dicarbonitrile (4).

A mixture of 1 (0.01 mol) and methyl iodide (0.01 mol) in 20 ml of dry acetone in the presence of anhydrous potassium carbonate (0.5g) was refluxed for 4h. The reaction mixture was then cooled poured into a beaker containing crushed ice (50 gm). The obtained product was recrystallized from ethanol to give (4). MS of (4) C<sub>9</sub>H<sub>8</sub>N<sub>4</sub>S exhibited a molecular ion peak at m/z (204, 100%). <sup>1</sup>H-NMR spectrum of (4) exhibited signals at 2.56 (s, 3H, CH<sub>3</sub>), 3.61 (s, 3H, S-CH<sub>3</sub>), 3.74 (s, 2H, NH<sub>2</sub>).

#### Synthesis of 3,6-Diamino-4-methyl-1H-pyrazol [3,4-b] pyridine-5-carbonitrile (5).

A mixture of (4) (0.01 mol) with hydrazine hydrate (0.01 mol) was refluxed for 4h. The obtained product was recrystallized from ethanol to give (5). MS of (5) C<sub>8</sub>H<sub>8</sub>N<sub>6</sub> exhibited a molecular ion peak at m/z (188, 100%). <sup>1</sup>H-NMR spectrum of (5) exhibited signals at 2.73 (s, 3H, CH<sub>3</sub>), 5.19 (s, 2H, NH<sub>2</sub>), 6.54 (s, 2H, NH<sub>2</sub>), 11.64 (s, 1H, NH).

cyclic).

**Synthesis of 4-Amino-5-methyl-7-thioxo-7,8-dihydropyrido [2,3-d] [1,2,4] triazine-6-carbonitrile (6).**

A mixture of (1) (0.01 mol) and hydrazine hydrate (0.01 mol), in ethanol (20 ml) was refluxed for 4h. The reaction mixture was then cooled and the obtained product was recrystallized from ethanol to give (6). MS of (6)  $C_8H_6N_6S$  exhibited a molecular ion peak at  $m/z$  218 ( $M^+$ , 25, 9%).  $^1H$ -NMR spectrum of (6) exhibited signals at 2.74 (s, 3H, CH<sub>3</sub>), 3.33 (s, 2H, NH<sub>2</sub>), 12.80 (s, 1H, NH cyclic).

**Synthesis of N-(3, 5-Dicyano-4-methyl-6-thioxo-1, 6-dihydro- Pyridine -2-yl) acetamide (7).**

A mixture of 1 (0.01 mol) and acetic anhydride (0.01 mol) was heated on a steam bath for 4hr. the reaction mixture was then cooled and the obtained product was recrystallized from DMF to give(7).MS of (7) $C_{10}H_8N_4OS$  exhibited a molecular ion peak at  $m/z$  232 ( $M^+$ , 26%).  $^1H$ -NMR spectrum of(7)exhibited signals at 2.50 (s,3H,CH<sub>3</sub>), 3.73 (s,3H,COCH<sub>3</sub>), 12.78 (br,1 H,cyclic NH).

**Synthesis of 6-Amino-1-(2-cyanoethyl)-4-methyl-2-thioxo-1,2-dihydropyridine-3,5-dicarbonitrile (8).**

A mixture of (1) (0.01 mol), and acrylonitrile (0.01 mol) in pyridine (15 ml) was refluxed for 4h. The reaction mixture was then cooled,poured into ice-HCl mixture and the obtained product was recrystallized from ethanol to give (8). MS of (8)  $C_{11}H_9N_5S$  exhibited a molecular ion peak at  $m/z$  (243, 24.7%).  $^1H$ -NMR spectrum exhibited signals at  $\delta$ 2.52 (s,3H,CH<sub>3</sub>) 2.99 (q,2H-NCH<sub>2</sub>), 3.48 (q,2H,CH<sub>2</sub>CN), 3.41 (s,2H,NH<sub>2</sub>).

**Synthesis of 5-Amino-7-aryl-1-(2-cyanoethyl)-4-methyl-2-thioxo-1,2-dihydro[1,8] nphthydrine-3,6-dicarbonitrile (10a-d).**

A mixture of (8), (0.01 mol) and derivatives of malonitrile namely benzylidene malono nitrile,4-methoxy benzylidene and 4-chloro benzylidene (9a-d) (0.01 mol) in pyridine (20 ml) was refluxed for 8h. The reaction mixture was then cooled poured into container of crushed ice (50 gm), neutralized with dil. HCl (5 ml) and the obtained products were recrystallized from ethanol to give (10a-d). MS of (10a)  $C_{20}H_{14}N_6S$  exhibited a molecular ion peak at  $m/z$  370 ( $M^+$ , 19.5%). $^1H$ -NMR spectrum of (10b) exhibited signals at 2.43 (s,3H,CH<sub>3</sub>), 2.99 (t,2H,CH<sub>2</sub>-N), 3.44 (t,2H,CH<sub>2</sub>CN), 3.34 (s,2H,NH<sub>2</sub>). $^1H$ -NMR spectrum of (10d) exhibited signals at 2.51 (s,3H,CH<sub>3</sub>), 3.01 (t,2H,N-CH<sub>2</sub>), 3.47 (t,2H,CH<sub>2</sub>CN), 3.28 (s,2H,NH<sub>2</sub>).

**Synthesis of 5-Amino-7-aryl - 4 -methyl-2- thioxo-1, 2-dihydro - [1,8] naphthylridine -3 , 6-dicarbonitriles (11a-d).**

A mixture of 1 (0.01 mol), substituted arylidene derivatives of malonitrile (0.01 mol) in pyridine (20 ml) was refluxed 10h. The reaction mixture was then cooled poured into container of crushed ice, neutralized with dil. HCl (5 ml) and the obtained product was recrystallized from ethanol to give 11a-d. MS of 11a  $C_{17}H_{11}N_5S$  exhibited as molecular ion peak at  $m/z$  (317, 100%).  $^1HNMR$  spectrum of 11b exhibited signals at 1.07 (3H, s), 2.11 (3H, s), 3.44(2H, s), 7.19-8.03 (4H, m) 12.41 (1H, s),  $^1H$ -NMR spectrum of 11c exhibited signals at 1.21 (3H, t), 2.90 (2H, q), 3.36 (2H, s), 7.37- 7.67 (4H, m), 11.05 (1H, s).

**Synthesis of 5-Amino -4- methyl -2- thioxo-1,2-dihydro - 1,8 , naphthopyridine 3,6 - dicarbonitriles (12a,b) .**

A mixture of 1 (0.01 mol), aliphatic aldehydes namely acetaldehyde and formaldehyde (0.01 mol) in 20 ml of alcohol in the presence of TEA was refluxed for 10h. The reaction mixture was then cooled and the obtained product was recrystallized from ethanol to give 12a,b. MS of 12b  $C_{12}H_9N_5S$  exhibited a molecular ion peak at  $m/z$  = 253 ( $M^+$ , 7%),  $^1H$ -NMR spectrum of 12a exhibited signals at 2.74 (3H,s), 4.69 (2H, s), 7.96 (1H, s), 8.68 (5H, s), 12.31 (1H, s).  $^1H$ -NMR spectrum of 12b exhibited 2.74 (3H, s), 2.90 (3H,s), 3.34(2H,s), 7.94(SH, s), 12.05 (1H, br).

**Synthesis of 3,6 -Diamino -4- thioxo -4,5-dihydrothieno [3,4-c] pyridine-7-carbonitrile (13)**

A mixture of 1 (0.01 mol), and sulphur (0.01 mol) in 20 ml of alcohol/TEA was refluxed for 4h. The reaction mixture was then cooled and the obtained product was recrystallized from ethanol to give 13. MS of 13  $C_8H_6N_4S_2$  exhibited a molecular ion peak at  $m/z$  220 ( $M^+$ , 2.9%).

**Synthesis of 3,6 -Diamino -5- (2-cyanoethyl) -4-thioxo -4,5- dihydro - thieno [3,4-c] pyridine-7 carbonitrile (14)**

A mixture of 13 (0.01 mol) and acrylonitrile (0.01mol), in 15 ml of pyridine was refluxed for 5h. The reaction mixture was then cooled and the obtained product was recrystallized from DMF to give 14. MS of 14  $C_{11}H_9N_5S_2$  exhibited a molecular ion peak at  $m/z$  275 ( $M^+$ , 11%).  $^1H$ -NMR spectrum exhibited signals at  $\delta$  2.98 (2H, q), 3.48 (2H, q), 3.01 (4H, br), 7.86 (1H, s), 7.97 (5H, br).

**Table (1) IR spectra of synthesized compounds**

Compd. No.	$\nu_{\max}$ (cm <sup>-1</sup> )
<b>1</b>	3485(NH <sub>2</sub> ), 3283(NH), 2989 (CH-arom.), 2924(CH aliph.), 2214(C≡N), 1639 (C=C), 1269 (C=S).
<b>3a</b>	3326, 2225 (NH <sub>2</sub> ), 2978 (CH-arom.), 2926 (CH-aliph.), 2217(C≡N), 1629 (C=N), 1561 (C=C).
<b>3b</b>	3329, 3331 (NH <sub>2</sub> ), 3013 (CH-arom.), 2979 (CH-aliph), 2210 (C≡N), 1731 (C=O), 1634 (C=N), 1558(C=C).
<b>4</b>	3409-3345(NH <sub>2</sub> ), 2924(CH-arom.), 2920(CH aliph.), 2216(C≡N), 1673 (C=N), 1649 (C=C).
<b>5</b>	3412, 3323(2NH <sub>2</sub> ), 3229(NH), 2207 (C≡N).
<b>6</b>	3362 (NH <sub>2</sub> ), 3196(NH), 2974 (CH-arom.), 2936 (CH-aliph.), 2212(C≡N), 1643(C=N), 1599 (C=C), 1242 (C=S).
<b>7</b>	3317, 3220(NH), 3100(CH-arom.), 2980 (CH-aliph.), 2222(C≡N), 1736 (C=O), 1636 (C=C), 1272 (C=S).
<b>8</b>	3321, 3223 (NH <sub>2</sub> ), 2979 (CH-arom.), 2947 (CH-aliph.), 2217 (C≡N), 1646 (C=C), 1267 (C=S).
<b>10a</b>	3388, 3322(NH <sub>2</sub> ), 2980(CH-arom.), 2943 (CH-aliph.) 2223 (C≡N), 1698(C=N), 1652 (C=C), 1269 (C=S).
<b>10b</b>	3399, 3330(NH <sub>2</sub> ), 2983(CH-arom., 2931 (CH-aliph.), 2224 (C≡N), 1648 (C=N), 1563 (C=C), 1270 (C=S).
<b>10c</b>	3385, 3325(NH <sub>2</sub> ), 2980(CH-arom.), 2946(CH-aliph.), 2220 (C≡N), 1647 (C=N), 1563 (C=C), 1238(C=S).
<b>10d</b>	3323, 3226(NH <sub>2</sub> ), 2980(CH-arom.), 2947 (CH-aliph.), 2219 (C≡N), 1648 (C=N), 1564 (C=C), 1269(C=S).
<b>11a</b>	3316(NH <sub>2</sub> ), 3215(NH), 2917 (CH-arom.), 2849 (CH-aliph.), 2215(C≡N), 1626(C=N), 1561(C=C), 1242(C=S).
<b>11b</b>	3339(NH <sub>2</sub> ), 3210(NH), 2919 (CH-arom.), 2844(CH-aliph.), 2214(C≡N), 1556(C=C), 1256 (C=S).
<b>11c</b>	3464(NH <sub>2</sub> ), 3195(NH), 2973(CH-arom.), 3933(CH-aliph.), 2212 (C≡N), 1638 (C=N), 1598 (C=C), 1240(C=S).
<b>11d</b>	3317(NH <sub>2</sub> ), 3191(NH), 2921(CH, arom.), 2900 (CH, Aliph.), 2213(C≡), 1635(C=N), 1566(C=C), 1271(C=S)
<b>12a</b>	3326(NH <sub>2</sub> ), 3120(NH), 2927 (CH-arom.), 3050(CH-aliph), 2211 (C≡N), 1671 (C=N), 1629 (C=C), 1267 (C=S).
<b>12b</b>	3345(NH <sub>2</sub> ), 3224(NH), 2974 (CH-arom.), 2923(CH-aliph.), 2214 (C≡N), 1626(C=N) 1563 (C=C), 1248 (C=S).
<b>13</b>	3375, 3310 (NH <sub>2</sub> ), 3194(NH), 3020(CH-arom.) 2974(CH-aliph.), 2214(C≡N), 1636 (C=C), 1250 (C=S).
<b>14</b>	3426, 3324(NH <sub>2</sub> ), 2979(CH-arom.), 2946(CH-aliph.), 2212(C-N), 1647(C=C), 1269 (C=S).

**Table (2) Physical and analytical data of the synthesized compounds**

Compd. No	Yield (%)	M.P.	Cryst. Solvent	Mol. Formula (Mol. Wt)	Elemental analyses Calcd/Found (%)			
					C	H	N	S
1	72	210	ethanol	C <sub>8</sub> H <sub>6</sub> N <sub>4</sub> S	50.51	3.18	29.45	16.86
				(190.23)	50.33	3.15	29.33	16.99
3a	69	256	Ethanol	C <sub>10</sub> H <sub>7</sub> N <sub>5</sub> S	52.39	3.08	30.53	13.99
				(229.26)	54.21	3.12	30.61	13.69
3b	68	178	Ethanol	C <sub>12</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S	52.16	4.38	20.28	11.60
				(276.32)	52.96	4.74	20.34	11.41
4	82	249	ethanol	C <sub>9</sub> H <sub>8</sub> N <sub>4</sub> S	52.92	3.95	27.43	15.70
				(204.25)	52.90	3.64	27.34	15.62
5	89	190	ethanol	C <sub>8</sub> H <sub>8</sub> N <sub>6</sub>	51.06	4.3	44.67	--
				(188.15)	51.29	5.1	45.19	--
6	91	>300	DMF	C <sub>8</sub> H <sub>6</sub> N <sub>6</sub> S	44.03	2.77	38.51	14.69
				(218.24)	44.43	2.13	38.42	14.93
7	85	260	DMF	C <sub>10</sub> H <sub>8</sub> N <sub>4</sub> OS	51.71	3.47	24.12	13.81
				(232.26)	51.67	3.21	24.00	13.91
8	82	262	ethanol	C <sub>11</sub> H <sub>9</sub> N <sub>5</sub> S	54.30	3.73	28.79	13.18
				(243.29)	54.33	3.81	28.86	13.21
10a	69	275	ethanol	C <sub>20</sub> H <sub>14</sub> N <sub>6</sub> S	64.85	3.81	22.69	8.66
				(370.43)	64.59	4.40	22.32	8.93
10b	64	277	ethanol	C <sub>21</sub> H <sub>18</sub> N <sub>6</sub> OS	62.98	4.03	20.99	8.01
				(400.46)	62.19	4.93	20.80	8.09
10c	61	278	ethanol	C <sub>20</sub> H <sub>13</sub> N <sub>6</sub> S	59.33	3.24	20.76	7.92
				(404.88)	59.10	3.79	20.77	7.43
10d	58	274	ethanol	C <sub>19</sub> H <sub>13</sub> N <sub>7</sub> S	61.44	3.53	26.40	8.63
				(371.42)	61.22	3.39	26.00	8.34
11a	75	250	ethanol	C <sub>17</sub> H <sub>11</sub> N <sub>5</sub> S	64.34	3.49	22.07	10.10
				(317.37)	64.01	3.21	22.87	10.32
11b	74	286	ethanol	C <sub>18</sub> H <sub>13</sub> N <sub>5</sub> S	62.23	3.77	20.16	9.23
				(347.39)	62.54	3.05	20.76	9.44
11c	74	>300	ethanol	C <sub>17</sub> H <sub>10</sub> ClN <sub>5</sub> S	58.04	2.86	19.91	9.11
				(351.81)	58.19	2.44	19.53	9.43
11d	75	>300	DMF	C <sub>16</sub> H <sub>10</sub> N <sub>6</sub> S	60.36	3.17	26.40	10.07
				(318.36)	60.57	3.33	26.95	10.05
12a	87	>300	DMF	C <sub>11</sub> H <sub>7</sub> N <sub>5</sub> S	54.76	2.92	29.03	13.29
				(241.27)	54.38	2.99	29.54	13.48
12b	86	>300	ethanol	C <sub>12</sub> H <sub>9</sub> N <sub>5</sub> S	56.45	3.55	27.43	12.56
				(255.30)	56.38	3.91	27.16	12.47
13	78	294	Ethanol	C <sub>8</sub> H <sub>6</sub> N <sub>4</sub> S <sub>2</sub>	43.22	2.72	25.20	28.85
				(222.29)	43.01	2.81	25.98	28.09
14	72	>300	DMF	C <sub>11</sub> H <sub>9</sub> N <sub>5</sub> S <sub>2</sub>	74.98	3.29	25.43	23.29
				(275.36)	74.32	3.09	25.59	23.64

### Antimicrobial Activity

The newly synthesized compounds were screened for their antibacterial activity against two species of Gram positive bacteria, namely *Bacillus subtilis* and *Staphylococcus aureus* and two species of Gram-negative bacteria *Escherichia coli* and *Pseudomonas aeruginos* (Table 3). (In nutrient agar broth) and antifungal activity (in Dox's medium and saboured's agar) by the agar diffusion method<sup>(20,21)</sup> at a concentration 20 mg/ml using DMSO as solvent and blank. The compounds were tested also for their

activities against antifungal such as *Candida alicans* and *Candida parapsilosis* (Table 4).

The antimicrobial screening results were measured by the average diameter of the inhibition zones, expressed in mm.

As shown in the results, all tested compounds displayed significant activities against bacteria, while compounds 1 and 13 were very active against all the tested organisms among all the tested compounds.



**Table (3): Antibacterial activity of synthesized compounds**

Compd. No	<i>Bacillus subtilis</i>	<i>Staphylococcus aureus</i>	<i>Escherichia coli</i>	<i>Pseudomonas aeruginos</i>
1	++	+++	++	+++
3a	++	++	++	++
5	+	+	+++	+
6	++	++	++	++
7	++	++	++	++
8	+	+	-	++
10a	++	++	++	++
10b	++	++	++	++
10c	++	+	++	++
11	++	++	++	++
12	++	++	++	++
13	++	+++	++	++

**Table (4): Antifungal activity of synthesized compounds**

Compd. No	<i>Candida albicans</i>	<i>Candida parapsilosis</i>
3a	+	+
6	+	+
7	++	++
8	+	+
10a	++	++
10b	++	++
10c	+	+
11a	+	+
12	++	++
13	++	++

The present investigation deals with the preparation of thienopyridine derivatives, these compounds are at least as effective as aspirin in preventing vascular events in patients at high risk, and possibly somewhat more<sup>(22,23)</sup>.

One of the major classes of adenosine diphosphate (ADP) receptor antagonists are thienopyridines. Thienopyridines composes a

subcategory of antiplatelet medication, known as receptor inhibitors, used commonly for the treatment of atherosclerotic cardiovascular disease<sup>(24)</sup>.

The thienopyridines derivatives play an important role in antibacterial and anticancer chemotherapy. As shown in the results (Table 5) most of compounds displayed activity as antitumors<sup>(25)</sup>.

**Table (5): Antitumor activity of some prepared compounds**

Compd. No.	% inhibition of cell viability ( $\mu\text{g}/\text{m}$ )		
	100	500	25
1	35	5	0
3a	20	0	0
3b	30	10	0
10a	10	0	0
10b	50	20	0
11a	30	10	0
11b	70	35	0
11c	60	30	5
12	60	30	10



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